ウゴービ皮下注 0.25mg SD、同 0.5mg SD、同 1.0mg SD、同 1.7mg SD、同 2.4mg SD に関する資料

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ウゴービ皮下注 0.25mg SD
ウゴービ皮下注 0.5mg SD
ウゴービ皮下注 1.0mg SD
ウゴービ皮下注 1.7mg SD
ウゴービ皮下注 2.4mg SD

1.5 起原又は発見の経緯及び開発の経緯

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略語一覧

AUC	:	area under the curve（曲線下面積）
BMI	:	body mass index（体容量指数）
CI	:	confidence interval（信頼区間）
C_{max}	:	maximum concentration（最高血中濃度）
CT	:	computerised tomography（コンピュータ断層撮影）
DPP-4	:	dipeptidyl peptidase 4（ジペプチジルペプチターゼ-4）
EU	:	European Union（欧州連合）
GLP-1	:	glucagon-like peptide-1（グルカゴン様ペプチド-1）
JASSO	:	Japan Society for the Study of Obesity（日本肥満学会）
JP	:	the Japanese Pharmacopoeia（日本薬局方）
NASH	:	non-alcoholic steatohepatitis（非アルコール性脂肪肝炎）
PMDA	:	Pharmaceuticals and Medical Devices Agency（独立行政法人 医薬品医療機器総合機構）
PK	:	pharmacokinetic（薬物動態）
Ph. Eur	:	European Pharmacopoeia（欧州薬局方）
SD	:	single dose（単回使用）
US	:	United States of America（アメリカ合衆国）
USP	:	United States Pharmacopoeia（米国薬局方）
VFA	:	visceral fat area（内臓脂肪面積）

臨床試験の表記：

肥満症のための皮下投与用セマグルチドの開発プログラムに含まれる臨床試験は、プロジェクト番号 NN9536 と 4 桁の固有の番号（例：NN9536-4373）にて特定する。本書では、臨床試験は 4 桁の固有の番号を用いて「XXXX 試験」と表記する。他の皮下投与用セマグルチドの開発プログラムの臨床試験は、プロジェクト番号と 4 桁の固有の番号（例：NN9535-3744）で表記する。

特記する場合を除き、「セマグルチド 2.4 mg 週 1 回皮下投与」は「セマグルチド 2.4 mg」と表記する。

1.5.1　起原又は発見の経緯

1.5.1.1　メディカルニーズ及び開発の経緯

肥満者の数は世界的に膨大なレベルに達しており、さらに増加を続けている[1,2,3,4,5,6,7]。現在、肥満は、その多大な医学的、社会的及び経済的な影響により、世界的に最も重要な公衆衛生の課題の一つと考えられている[1,6,7,8,9,10]。肥満は様々な健康障害に関与していることが知られている。最も懸念すべき事項として、肥満が早期の死亡に至る主な要因となる心血管疾患や特定の種類のがんの発生リスクを高めることが挙げられる[11,12]。さらに、肥満は、2 型糖尿病、高血圧、脂質異常症、閉塞性睡眠時無呼吸症、変形性関節症、尿失禁、喘息及び非アルコール性脂肪肝炎等を含む重大な疾患の発症に関わる危険因子としてよく知られている[13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29]。

日本においても、肥満者の割合は年々増加している。厚生労働省より発出された国民健康・栄養調査（2019 年）では、成人男性の 33.0%及び成人女性の 22.3%が肥満（BMI 25 kg/m^{2}以上と定義）と報告されている[30]。肥満による医療費の増加は日本でも認められており、合併症（血糖コントロール不良、高血圧及び脂質異常症を含む）の数が増えると医療費はさらに増加するとの報告がある[31,32]。日本肥満学会は、医学的に適切な治療及び管理の重要性を含め、肥満症に対する医学的認識を高めるために、東京宣言（2000 年）[33]、神戸宣言（2006 年）[34]、淡路宣言（2011 年）[35]、名古屋宣言（2015 年）[36]及び神戸宣言（2018 年）[37]と、肥満・肥満症に関する宣言を発表している。最新の神戸宣言では、肥満に関連する 23 学会が「領域横断的肥満症ワーキンググループ」を結成し、肥満症の撲滅を目指して領域を超えて協働することを合意した。さらに、第 41 回日本肥満学会（2021 年 3 月 21～22 日開催）の理事長提言において、肥満症治療の選択肢の 1 つとして、生活習慣改善と薬物療法の併用の展望について言及され、新たな薬物治療に対するメディカルニーズが示された。当該学会では、日本人の肥満 2 型糖尿病患者に対する減量・代謝改善手術に関する日本肥満学会・日本肥満症治療学会・日本糖尿病学会の合同コンセンサスステートメントが発表され、肥満症治療へのニーズが高いことが理解された。

日本肥満学会は最新の治療ガイドライン（以下、JASSO ガイドライン）[33]で「肥満」と「肥満症」を区別し、「肥満症」を治療すべき疾患と定義している。日本人は、欧米人と比較して BMI の高い（>30 kg/m^2）肥満者は少ないものの、軽度の肥満であっても肥満に起因する疾患の有病率は欧米と大きな差がない疾患も多い。BMI 25～30 kg/m^{2}の日本人がここ数十年で 2～4 倍に増加し、この集団では動脈硬化危険因子が集積していたことも報告されている[33]。また、軽度の肥満であっても、内臓脂肪の蓄積があると肥満に関連した合併症を有する傾向があることも報告されており、内臓脂肪面積（VFA）100 cm^{2}以上の蓄積は、肥満に関連する合併症（高血圧、脂質異常症及び血糖コントロール不良を含む）を 1 つ以上有することに相当すると言われている[38]。これらの点を踏まえ、JASSO ガイドラインでは、肥満症の診断基準は「BMI が 25 kg/m^{2}以上で、以下のいずれかの条件を満たす場合：1）肥満に起因ないし関連する健康障害を有するか、健康障害の合併が予測される場合で減量を要するもの、2）腹部コンピュータ断層撮影（CT）検査によって VFA 100 cm^{2}以上と確認された内臓脂肪型肥満（健康障害の合併の有無は問わない）」とされている。

肥満治療は、食事及び運動療法を基本とした生活習慣への介入から開始される。しかしながら、肥満を有する人の多くでは、これは主に反作用的生物反応に関わるホメオスタシス機構による可能性が考えられる[39,40,41,42,43,44,45,46,47,48,49]。

国際的なガイドラインと同様にJASSOガイドラインでは、肥満症と診断されたのち、健康障害の改善のための食事・運動・行動療法からなる生活習慣の改善を試みることが推奨されている。生活習慣改善療法により改善効果がみられない場合に、薬物療法が考慮される。JASSOガイドラインにおける薬物療法の適応基準は、「BMIが25 kg/m^{2}以上で内臓脂肪面積100 cm^{2}以上かつ11の特定された健康障害を2つ以上有する場合」又は「BMIが35 kg/m^{2}以上で11の特定された健康障害を1つ以上有する場合」とされている。一方、BMIの増加と関連する合併症の数及び死亡率の増加との関連がみられており、肥満に関連する合併症の数及び死亡率はBMIが27 kg/m^{2}を超えると増加すると報告されていることから[24,38,50,51,52,53,54,55]、このような患者集団においては医学的介入（薬物治療）の重要性がより高いと考えられる。上述のように、JASSOガイドラインでは、生活習慣改善療法で改善効果がみられない場合に薬物療法を考慮することを推奨しているにもかかわらず、現在日本で利用可能な肥満症治療薬はマジンドール[56]のみである。マジンドールはBMI 35 kg/m^{2}以上に該当するような高度肥満症の患者のみが投与対象となり、かつ3ヵ月を限度とする短期的な使用に限定されている。外科療法は一部の高度肥満症患者に有効な治療法を提供するものであり、日本では高度肥満症患者に適用されてきた。Bariatric Surgery及びMetabolic Surgeryの実施施設に対する施設基準や、外科治療にあたる医師の要件等の条件がBariatric Surgery及びMetabolic Surgery導入の障壁になることもある。高度肥満症を有する患者においても、外科療法による体重減少に近い効果が得られ、かつその体重減少を維持することが可能となるような安全かつ有効な治療選択肢が不足している。

肥満症は生涯にわたる問題に発展することも多いことから、日本におけるアンメットメディカルニーズを満たす新しい治療選択肢が求められている。

このように、肥満に関連する合併症に対するベネフィットを有し、有効かつ安全な肥満症治療薬に対して、明確なアンメットメディカルニーズが存在している。GLP-1受容体作動薬に関しては、安全性プロファイルが十分に確認されており、かつ体重減少効果、血圧、脂質、他の心血管リスク及び糖代謝を改善するなどの複数のベネフィットが示されている。

1.5.1.2 セマグルチド

セマグルチド（遺伝子組換え）（以下、セマグルチド）はGLP-1受容体作動薬に分類されるGLP-1アナログであり、その構造はヒトGLP-1と94%の相同性を有している[57]。

セマグルチドはリラグルチド（販売名：ビクトーザ、Saxenda）と同様にアシル化技術に基づいているが、より長い半減期を得るために構造を改変した。分子内の特異的修飾は次のとおりである：1）ジペプチジルペプチターゼ-4（DPP-4）に対する安定性を向上させるため、ペプチド骨格内第8位をアラニンから2-アミノイソ酪酸に改変、及び34位のリジンをアルギニンへ置換（この位置におけるアシル化防止のため）、2）26位のリジンと脂肪酸が結合しているγグルタミン酸との間に親水性スペーサーを附加、3）末端酸基を有するオクタデカン二酸を附加。スペーサーと脂肪酸はともに、アルブミン結合の増加に寄与し、血漿中セマグルチドの分解を遅延させ、結果的に腎クリアランスを低下させる。DPP-4酵素に対する安定性の向上と合わせて、セマグルチドの半減期は約1週間まで延長され、セマグルチドを週1回皮下投与に適したものにしている[57]。

セマグルチドを有効成分とする注射剤として、本邦では 2018 年 3 月 23 日に「オゼンピック皮下注 2mg」が 2 型糖尿病を効能又は効果として承認され、その後 2020 年 3 月 12 日に「オゼンピック皮下注 0.25mg SD、0.5mg SD、1.0mg SD」が剤形追加品目として承認された。

セマグルチドは、体重に対する効果に加え、糖代謝及び肥満に関連する他の合併症に対する効果も持つことから、体重管理（体重減少及び体重維持を含む）における新たな治療の可能性を有する。また、1 日 1 回投与の GLP-1 アナログであるリラグルチドは、日本以外の世界各国で体重管理を適応として承認を取得している（販売名：Saxenda）。

セマグルチド 2.4 mg の週 1 回皮下投与（以下、セマグルチド 2.4 mg）は、体重管理を適応として 2021 年 6 月 4 日に米国で、2022 年 1 月 6 日に欧州連合（EU）でそれぞれ承認された（販売名：Wegovy）。

1.5.2 開発の経緯

肥満症の適応取得を目的としたセマグルチド皮下投与製剤の開発の経緯図を図 1.5.2-1 に示す。

図 1.5.2-1　　開発の経緯図

	年／	20[redacted]				20[redacted]				20[redacted]				20[redacted]				20[redacted]		
	四半期	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3
品質[注]		[redacted]																		
非臨床: 効力を裏付ける試験																				
臨床																				
4382 試験																				
4373 試験 (主要パート)																				
4374 試験																				
4590 試験																				
NN9535-4588 試験																				

注：[redacted]

1.5.2.1 品質

1.5.2.1.1 原薬

肥満症の適応取得を目的としたセマグルチド皮下投与製剤の製造に用いるセマグルチド原薬は、以下の既承認製剤（販売名：オゼンピック）に用いるものと同一である。

- オゼンピック皮下注 2mg（承認番号：23000AMX00443000）
- オゼンピック皮下注 0.25mg SD（承認番号：30200AMX00415000）
- オゼンピック皮下注 0.5mg SD（承認番号：30200AMX00416000）
- オゼンピック皮下注 1.0mg SD（承認番号：30200AMX00417000）

セマグルチド（遺伝子組換え）は酵母（*Saccharomyces cerevisiae*）を利用した遺伝子組換え DNA 技術を用いて製造される。

1.5.2.1.2　製剤

肥満症の適応取得を目的として、2.4 mg までの用量のセマグルチドを用いた検討を行い、目標とする維持用量はセマグルチド 2.4 mg である。投与は 0.25 mg より開始し、4 週間の間隔で、0.5 mg、1.0 mg、1.7 mg 及び維持用量である 2.4 mg にそれぞれ増量する。

肥満症のためのセマグルチド開発プログラムに含まれる第 3 相試験では、PDS290 ペン型注入器のセマグルチド製剤（処方 B）を用いた。セマグルチド濃度を除き、この製剤の組成は、オゼンピック皮下注 2 mg として承認されたものと同一である。その後、使いやすさ向上のため、患者が取り扱いやすいセマグルチド投与用の単回使用ペン型注入器（注射針が組み込まれた、プレフィルドシリンジを装着した単回使用ペン型注入器）を用いた製剤（処方 D）が開発された。単回使用ペン型注入器を用いた製剤の注入容量は、低用量の 3 用量（0.25、0.5 及び 1.0 mg）では 0.5 mL、高用量の 2 用量（1.7 及び 2.4 mg）では 0.75 mL である。これら 5 つの用量に対応するため、0.5、1.0、2.0、2.27 及び 3.2 mg/mL の 5 つの濃度の単回使用ペン型注入器のセマグルチド製剤（すなわち 5 つの用量規格の製剤）を上市する予定である。

第 3 相試験で用いたセマグルチド製剤と市販予定製剤の組成及び添加剤の配合目的を表 1.5.2-1 に示す。上市予定の製剤の処方（処方 D）は、第 3 相試験で用いたセマグルチド濃度が 1.0 mg/mL 及び 3.0 mg/mL の製剤（処方 B）に基づいて検討されたものであるが、単回使用ペン型注入器で使用する目的から防腐剤であるフェノールは含まれない（表 1.5.2-1）。また、等張化剤としてプロピレングリコールに替えて塩化ナトリウムを含めた。セマグルチド濃度を除き、単回使用ペン型注入器を用いた製剤の組成は、すべての用量規格で同じである。

表 1.5.2-1　　セマグルチド製剤の組成

成分名	第 3 相試験で用いた製剤（PDS290 ペン型注入器を使用）：処方 B	市販予定製剤（単回使用ペン型注入器を使用）：処方 D	配合目的	規格
原薬 セマグルチド	1.0 mg/mL 3.0 mg/mL	0.5 mg/mL 1.0 mg/mL 2.0 mg/mL 2.27 mg/mL 3.2 mg/mL	有効成分	[redacted]
添加剤 リン酸水素二ナトリウム二水和物 プロピレングリコール 塩化ナトリウム フェノール 塩酸 水酸化ナトリウム 注射用水	 1.42 mg/mL 14.0 mg/mL - 5.50 mg/mL 適量 適量 1.00 mL とする	 1.42 mg/mL - 8.25 mg/mL - 適量 適量 1.00 mL とする	 緩衝剤 等張化剤 等張化剤 防腐剤 pH 調節剤 pH 調節剤 溶剤	

略語：[redacted]

セマグルチド製剤（処方 D）の長期保存試験及び加速試験の成績は、臨床試験で用いたセマグルチド 1.0 mg/mL 及び 3.0 mg/mL 製剤（処方 B）及び既承認のオゼンピックと同等／同質の安定性プロファイルを示したことから、セマグルチド製剤の 24 ヵ月の有効期間の妥当性が示された。

申請資料には、長期保存試験より得られる[redacted]ヵ月の安定性試験データを含め、審査期間中に[redacted]ヵ月のデータを追加提出する予定である。安定性試験は有効期間を延長するために[redacted]ヵ月まで継続する。得られる結果を基に、[redacted]により有効期間を[redacted]ヵ月まで延長する予定である。

1.5.2.2 非臨床

2 型糖尿病を適応とするオゼンピック皮下注 2mg の承認取得時に実施したセマグルチドの非臨床試験の包括的なデータパッケージは、オゼンピック皮下注 2mg の承認申請時に提出し、審査されている。非臨床安全性試験及び薬物動態試験に関して、これらの非臨床試験成績は肥満症の適応及び新たに設定する臨床用量においても使用可能であると考え、追加の非臨床安全性試験及び薬物動態試験は実施しなかった。

一方、2 型糖尿病の適応取得時に実施した非臨床試験に加え、肥満症の適応取得に向けて、脳を介したセマグルチドの体重減少メカニズムを詳細に検討した、動物を用いた効力を裏付ける試験を 2 試験実施した。

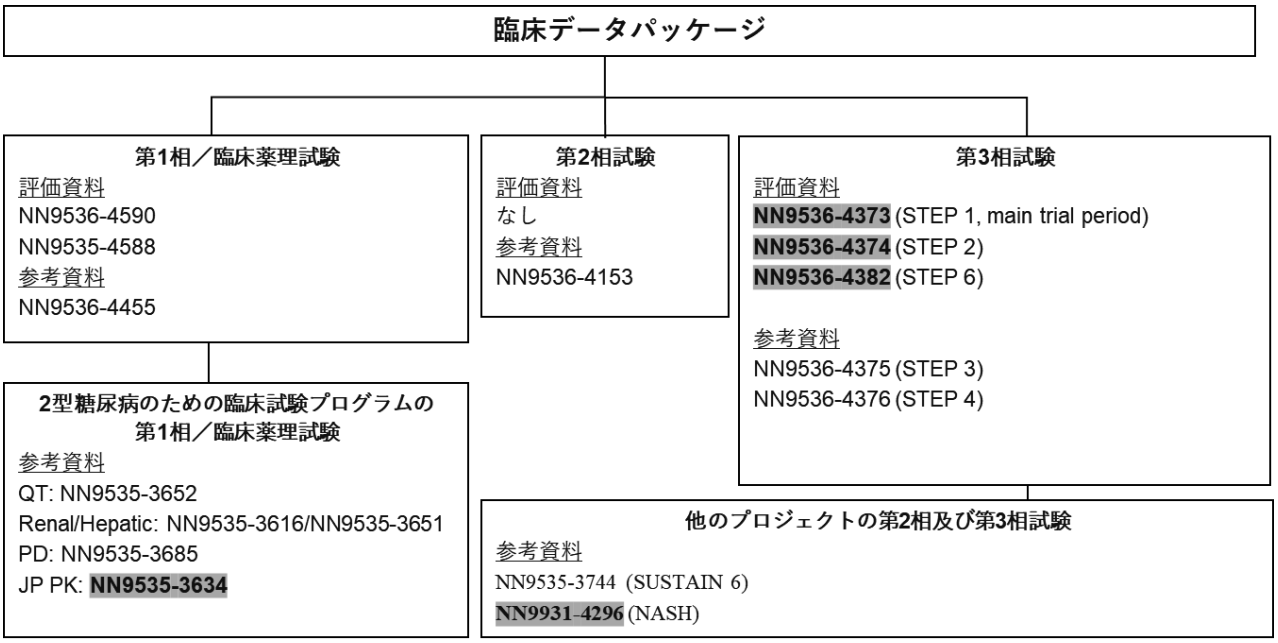
新たに実施した効力を裏付ける試験から、セマグルチドは視床下部及び脳幹において食事摂取の恒常的調節に関与する脳領域に直接作用することが示唆される。また、セマグルチドは中隔、視床及び扁桃体を含む脳領域における直接的・間接的作用を介して、報酬系にも作用する。これらの部位の活性化を通して、セマグルチドは脳の実行機能を伴う恒常的調節機構及び快楽的調節機構に作用し、エネルギー摂取、食欲、報酬及び食物選択を調整すると考えられる。

1.5.2.3 臨床

1.5.2.3.1 臨床データパッケージ

日本の承認申請における臨床データパッケージ（図 1.5.2-2）では、過体重又は肥満患者を対象とした、日本人被験者が参加した 2 つの国際共同第 3 相試験（4373 及び 4374 試験）及び 1 つの東アジア第 3 相試験（4382 試験）ならびに 2 つの生物学的同等性試験（4590 及び NN9535-4588 試験）を評価資料とし、他の 11 試験を参考資料とした。

図 1.5.2-2　　日本の承認申請における臨床データパッケージ：評価資料及び参考資料



注：日本人被験者が参加した試験は太字及びグレーの網掛けで示す。
NN9931-4296：non-alcoholic steatohepatitis（非アルコール性脂肪肝炎；NASH）の開発プログラムにおける第 2 相試験
NN9535-3744 (SUSTAIN 6)：2 型糖尿病を対象とした開発プログラムにおける心血管アウトカム試験
JP: Japan, PK: pharmacokinetic, PD: pharmacodynamic

1.5.2.3.2　規制当局との協議

肥満症を対象としたセマグルチドの開発プログラムを進めるにあたり、独立行政法人医薬品医療機器総合機構（以下、機構）から助言を得た。

[redacted]相談ならびに[redacted]相談及び医薬品対面助言事後相談

国内での[redacted]に先立ち、[redacted]相談（[redacted]番：20[redacted]年[redacted]月[redacted]日）、[redacted]相談（[redacted]番：20[redacted]年[redacted]月[redacted]日）及び医薬品対面助言事後相談（[redacted]番、20[redacted]年[redacted]月[redacted]日）を実施し、主に以下の点について助言を得た。

- [redacted]
- [redacted]（[redacted]）
- [redacted]の妥当性
- [redacted]
- 日本における[redacted]

これらの協議で得た機構の意見及び助言に基づき、[redacted]を再考し、[redacted]試験（[redacted]試験）を実施することとした。また、当該試験においては、機構の助言に従い、日本人の肥満症患者における[redacted]を検討する目的で[redacted]を設定した。

その他の[redacted]相談及び[redacted]相談

先の相談に加え、20[redacted]年[redacted]月[redacted]日に[redacted]相談（[redacted]番）を実施し、[redacted]の適切性につき確認した。また、[redacted]、[redacted]及び[redacted]の[redacted]について機構の助言を得た。

さらに、2回の[redacted]相談（[redacted]番：20[redacted]年[redacted]月[redacted]日、[redacted]番：20[redacted]年[redacted]月[redacted]日）を実施した。

[redacted]相談

20[redacted]年[redacted]月[redacted]日に[redacted]相談（[redacted]番）を実施し、得られたデータに基づく[redacted]ならびに[redacted]の[redacted]の適切性について相談し、[redacted]について助言を得た。さらに、[redacted]と[redacted]の[redacted]について相談し、[redacted]との見解を得た。

これらの相談記録を Module 1.13 に含める。

1.5.2.3.3　評価資料とした臨床試験の概略

第 3 相臨床試験

日本人におけるセマグルチドの肥満症に対する有効性及び安全性は、主に東アジア試験（4382 試験）により評価した。4382 試験は日本及び韓国で実施され、試験対象集団は JASSO ガイドライン[33]に基づき設定した目標とする効能又は効果に合致している。さらに、2 つの国際共同試験（4373 及び 4374 試験）にも日本人被験者が含まれた。これらの試験の試験対象集団は米国／欧州のガイドライン[58,59]に従って設定されており、目標とする効能又は効果に合致している 4382 試験の対象より広範な被験者集団となっている。このため、これらの 2 試験では、JASSO ガイドライン[33]に準じた目標とする効能又は効果に合致した集団におけるサブグループ解析を実施した（表 1.5.2-2）。

表 1.5.2-2　試験対象集団及び JASSO ガイドラインに基づく部分集団（4373 及び 4374 試験）

	試験対象集団	JASSO ガイドラインに基づく部分集団
4373 試験	BMI が 30 kg/m^2 以上、又は 27 kg/m^2 以上かつ 1 つ以上の肥満に関連する合併症（治療の有無を問わない）を有する被験者 合併症は「高血圧」、「脂質異常症」、「閉塞性睡眠時無呼吸」又は「心血管系疾患」	• BMI が 27 kg/m^2 以上であり、2 つ以上の肥満に関連する合併症*（このうち 1 つは「高血圧」又は「脂質異常症」のいずれか）を有する被験者 • BMI が 35 kg/m^2 以上であり、「高血圧」又は「脂質異常症」を有する被験者
4374 試験	BMI が 27 kg/m^2 以上かつ 2 型糖尿病を有する被験者	• BMI が 27 kg/m^2 以上であり、2 つ以上の肥満に関連する合併症*（このうち 1 つは「2 型糖尿病」）を有する被験者 • BMI が 35 kg/m^2 以上であり、「2 型糖尿病」を有する被験者

*JASSO ガイドラインに記載されている肥満症の診断基準に必須な健康障害は以下のとおり：（1）耐糖能障害（2）脂質異常症（3）高血圧（4）高尿酸血症・痛風（5）冠動脈疾患（6）脳梗塞（7）非アルコール性脂肪性肝疾患（8）月経異常・不妊（9）閉塞性睡眠時無呼吸症候群・肥満低換気症候群（10）運動器疾患（11）肥満関連腎臓病

有効性

1 つの東アジア試験（4382 試験）及び 2 つの国際共同試験（4373 及び 4374 試験）では、様々な肥満に関連する合併症を有する過体重又は肥満被験者において、68 週間のセマグルチド 2.4 mg の投与により、臨床的に意味のある体重減少（体重減少率の平均の推定値はそれぞれ 13.19%、14.85%及び 9.64%）が達成された（治療方針 estimand）。いずれの試験でも、体重減少に関してセマグルチド 2.4 mg のプラセボに対する優越性が検証され、仮想 estimand 及び感度分析からもこれを支持する結果が得られた。また、セマグルチド 2.4 mg に割り付けられた被験者の大部分（～90%）は臨床的に意味があるとされている 5%以上の体重減少を達成した。4373 及び 4374 試験では、JASSO ガイドラインに基づく部分集団における有効性の結果は、全集団の結果と同様にセマグルチド 2.4 mg を支持するものであった。

また、これらの第 3 相試験のデータから、セマグルチド 2.4 mg の投与により、肥満に関連する合併症である 2 型糖尿病（糖代謝）、高血圧（血圧）及び脂質異常症（脂質プロファイル）の臨床的に意味のある改善が認められ、JASSO ガイドラインで提唱されているように、体重減少が複数の肥満に関連する合併症の改善につながることが示された。

安全性

セマグルチド 2.4 mg の安全性及び忍容性プロファイルは、2 型糖尿病に対するセマグルチド皮下投与（オゼンピック皮下注）を含む既承認の GLP-1 受容体作動薬と概ね同様であり、予測されない所見は認められなかった。

最も高頻度でみられた有害事象は、予測されたように、胃腸障害の有害事象（悪心、下痢、便秘及び嘔吐）であり、プラセボ群と比較してセマグルチド群で有害事象により治験薬の投与を中止した被験者が多かった主な理由は、これらの事象の発現によるものであった。4382 及び 4374 試験において、有害事象の発現状況及び重篤性及び重症度の分布について、セマグルチドの用量の増加に伴う特定の傾向は認められなかった。

サブグループ別の評価では新たな安全性の懸念は認められず、セマグルチド 2.4 mg の安全性プロファイルに明らかな違いも認められなかったことから、安全性の全般的な結果を申請する効能又は効果内の患者集団に広くあてはめることは可能であると考える。

生物学的同等性試験

市販予定製剤（単回使用ペン型注入器；処方 D）と第 3 相試験で使用した製剤（PDS290 ペン型注入器；処方 B）（表 1.5.2-1）の生物学的同等性を検討するため、2 つの生物学的同等性試験（4590 及び NN9535-4588 試験）を実施した。

これらの試験では、単回使用ペン型注入器で 0.25 mg、1.0 mg 及び 2.4 mg を投与するための製剤濃度〔低濃度（0.5 mg/mL）、中間濃度（2.0 mg/mL）、高濃度（3.2 mg/mL）〕に関する生物学的同等性を評価した。Module 2.7.1 に記載したように、これらの評価は、漸増用量である 0.5 mg 及び 1.7 mg を投与するための製剤についての製剤変更の適切性も支持していると考える。

4590 試験において、セマグルチド 2.4 mg（3.2 mg/mL）及び 1.0 mg（2.0 mg/mL）を投与するための単回使用ペン型注入器の製剤（処方 D）と第 3 相試験で用いた PDS290 ペン型注入器の製剤（処方 B）間の生物学的同等性が確認された。

NN9535-4588 試験は、2 型糖尿病のための皮下投与用セマグルチド（オゼンピック）の開発プログラムにおいて実施された。0.25 mg（0.5 mg/mL）の用量における単回使用ペン型注入器の製剤（処方 D）と PDS290 ペン型注入器の製剤（処方 B）間の比較では、AUC 及び C_{max} の製剤間の比の 90%信頼区間はいずれも（0.80; 1.25）の範囲内であった。

以上より、4590 及び NN9535-4588 試験の結果に基づき、第 3 相試験で得られた有効性及び安全性の成績は、市販予定の単回使用ペン型注入器のセマグルチド製剤にも適用可能であると考えられる。

1.5.3　セマグルチド 2.4 mg の臨床的位置付け

国内において、JASSO ガイドラインの最新版では、「肥満症」は「肥満に起因ないし関連する健康障害を合併するか、その合併が予測される場合で、医学的に減量を必要とする病態」と定義されている。薬物療法を行う条件としては、まず肥満症であることが必須である。1.5.1.1 項に示したように、肥満症と診断された患者は、健康障害の改善のための食事・運動・行動療法からなる生活習慣の改善を試みる。生活習慣改善療法では改善効果がみられない場合に、薬物療法を考慮する対象となるが、JASSO ガイドラインにおける薬物療法の適応基準は、以下のいずれかを満たす場合とされている。

- BMI が 25 kg/m^2 以上で内臓脂肪面積 100 cm^2 以上かつ 11 の特定された健康障害を 2 つ以上有する場合
- BMI が 35 kg/m^2 以上で 11 の特定された健康障害を 1 つ以上有する場合

一方、BMI の増加と関連する合併症の数及び死亡率の増加との関連がみられており、肥満に関連する合併症の数及び死亡率は BMI が 27 kg/m^2 を超えると増加すると報告されていることから[24,38,50,51,52,53,54,55]、このような患者集団においては医学的介入（薬物治療）の重要性がより高いと考えられる。

このように、JASSO ガイドラインでは、生活習慣改善療法で改善効果がみられない場合に薬物療法を考慮することを推奨しているにもかかわらず、現在日本で利用可能な肥満症治療薬はマジンドール[56]のみである。また、マジンドールは BMI 35 kg/m^2 以上に該当するような高度肥満症の患者のみが投与対象となり、かつ 3 ヵ月を限度とする短期的な使用に限定されている。

肥満症は生涯にわたる問題に発展することも多いことから、日本におけるアンメットメディカルニーズを満たす新しい治療の選択肢が求められている。セマグルチド 2.4 mg は、薬物療法が必要な日本人肥満症患者において、週 1 回投与で合併症の改善も含めた有効性が示され、かつ安全性プロファイルが受け入れ可能な効果的な治療となることが期待される。

4382 試験では、JASSO ガイドラインを参照し、上述の薬物治療が必要な肥満症患者の適応基準を考慮して試験対象集団を選択した。2 つの国際共同の第 3 相試験（4373 試験及び 4374 試験）については、試験対象集団は米国／欧州のガイドラインに従って設定されており、4382 試験の対象集団（目標とする効能又は効果に合致した集団）より広範な患者集団となっている。このため、これらの試験では目標とする効能又は効果に合致した集団におけるサブグループ解析を実施した（表 1.5.2-2 参照）。4373 試験の無作為割り付け被験者の約 50%及び 4374 試験の無作為割り付け被験者の約 90%が JASSO ガイドラインに基づく目標とする「効能又は効果」に合致した集団となり、当該集団における主要な有効性の結果は、全集団の結果と同様であり、セマグルチド 2.4 mg を支持するものであった。

上述の試験で得られた主要な結果から、日本における治療対象となる患者集団において、セマグルチド 2.4 mg の有意かつ臨床的に意味のある体重減少、ならびに目標とする「効能又は効果」に含めた肥満に関連する合併症（健康障害）である 2 型糖尿病（糖代謝）、高血圧（血圧）及び脂質異常症（脂質プロファイル）の改善が示された。また、安全性及び忍容性プロファイルは、国内で 2 型糖尿病の治療に広く用いられている既承認の GLP-1 受容体作動薬と同様であった。

以上のことから、セマグルチド 2.4 mg は、治療の選択肢が非常に限定されている国内の肥満症治療におけるアンメットメディカルニーズを満たし、薬物療法の初期から外科療法が必要される前の段階にある肥満症患者まで対象となり得る良好な治療の選択肢となると考える。

1.5.4　申請する製剤、効能又は効果（案）ならびに用法及び用量（案）

1.5.4.1　申請する製剤

- ウゴーヴ皮下注 0.25mg SD
- ウゴーヴ皮下注 0.5mg SD
- ウゴーヴ皮下注 1.0mg SD
- ウゴーヴ皮下注 1.7mg SD
- ウゴーヴ皮下注 2.4mg SD

1.5.4.2　販売名について

ノボ ノルディスク社は、国内市場において、肥満症を適応とするセマグルチド製剤を、「オゼンピック」とは異なる新規の販売名（「ウゴーヴ」：1.5.4.1 項に記載の通り）で発売する予定である。

オゼンピック皮下注の効能又は効果は 2 型糖尿病であり、その最高承認用量は 1.0 mg であるが、肥満症を適応とする本剤の最高用量は 2.4 mg と設定している。仮に同一販売名とした場合には、異なる効能又は効果（用量及び製剤濃度も異なる）に同一販売名を用いることで医療現場での混乱が生じ、肥満症のみに用いられる 1.7 mg 及び 2.4 mg 製剤が肥満症の効能又は効果に該当しない 2 型糖尿病患者に処方される、あるいは現行のオゼンピック皮下注の 2 型糖尿病に対する承認用量である 0.5 mg 及び 1.0 mg が体重コントロールのために肥満症ではない患者に使用される等の投与過誤や適応外使用のリスクが高まる可能性が考えられる。特に最近では、2 型糖尿病治療薬である GLP-1 受容体作動薬の美容・痩身･ダイエット等を目的とした適応外使用が問題となっている。この状況の是正のため、日本糖尿病学会、日本医師会、規制当局及び GLP-1 受容体作動薬（2 型糖尿病治療薬）を販売している製薬会社 4 社において、適応外使用の抑止と適正使用の推進のための情報提供及び注意喚起を行っている。

販売名を現行のオゼンピック皮下注と肥満症用の製剤で明確に区別することにより、肥満症用の製剤が肥満症の治療薬として承認された唯一の GLP-1 受容体作動薬であることが明確化され、医療現場での投与過誤及び GLP-1 受容体作動薬の適応外使用の可能性を低下させ、より明確に適正使用を推進することが可能になると考える。

一方で申請者は、肥満症と 2 型糖尿病の両方を有する患者に対して、オゼンピック皮下注との重複処方が発生する可能性については否定できないことも認識している。しかしながら、販売名に関わらずその他の GLP-1 受容体作動薬との重複処方のリスクも同様に考えられる。ノボ ノルディスク社としては、オゼンピック及び肥満症用の本剤を処方する医師は、いずれの製剤もセマグルチド（遺伝子組換え）を有効成分として含有する GLP-1 受容体作動薬であることについて十分に理解していると想定している。しかしながら、このような重複処方が生じないよう、添付文書あるいは製品情報概要等の各資材を用いて、医療従事者に適切な情報提供を行っていく予定である。

海外において、肥満症（体重管理）を適応とするセマグルチド製剤は、「Wegovy」の販売名で 2021 年 6 月 4 日に米国で、2022 年 1 月 6 日に EU でそれぞれ承認された。

以上の理由から、肥満症については、2 型糖尿病を適応として販売されているオゼンピック皮下注とは異なる、新規かつ世界的にも共通の販売名である「ウゴーヴ」とすることが適切であり、この販売

名の方針により起こり得る重複投与等の安全性のリスクに関しては、慎重かつ適切な情報提供により最小化することが可能と考えている。

1.5.4.3 効能又は効果（案）

肥満症

ただし、高血圧、脂質異常症又は 2 型糖尿病のいずれかを有し、食事療法・運動療法を行っても十分な効果が得られず、以下に該当する場合に限る。

・BMI が 27kg/m^2 以上であり、2 つ以上の肥満に関連する健康障害を有する

・BMI が 35kg/m^2 以上

1.5.4.4 用法及び用量（案）

通常、成人には、セマグルチド（遺伝子組換え）として 0.25mg から投与を開始し、週 1 回皮下注射する。その後は 4 週間の間隔で、週 1 回 0.5mg、1.0mg、1.7mg 及び 2.4mg の順に増量し、以降は 2.4mg を週 1 回皮下注射する。なお、患者の状態に応じて適宜減量する。

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ウゴーヒ皮下注 0.25mg SD
ウゴーヒ皮下注 0.5mg SD
ウゴーヒ皮下注 1.0mg SD
ウゴーヒ皮下注 1.7mg SD
ウゴーヒ皮下注 2.4mg SD

1.6 外国における使用状況等に関する資料

ノボ ノルディスク ファーマ株式会社

目次

表目次

付録

- 米国における本剤の添付文書
- EU における本剤の添付文書
- 企業中核データシート（CCDS）

1.6.1　外国における使用状況

体重管理を目的としたセマグルチド 2.4 mg（週 1 回皮下投与）（以下、本剤とする）の外国における承認申請及び承認状況を表 1.6.1-1 に示す。

表 1.6.1-1　本剤の外国における承認申請及び承認状況

国／地域	承認申請日	承認日
米国	2020 年 12 月 4 日	2021 年 6 月 4 日
カナダ	2020 年 12 月 8 日	2021 年 11 月 24 日
EU	2021 年 1 月 4 日	2022 年 1 月 6 日
英国	2021 年 1 月 5 日	2021 年 9 月 24 日
スイス	2021 年 3 月 29 日	2022 年 2 月 15 日
インド	2021 年 6 月 17 日	2022 年 4 月 25 日
オーストラリア	2021 年 2 月 28 日	2022 年 9 月 1 日
ブラジル	2021 年 3 月 8 日	（未承認）
チリ	2021 年 7 月 14 日	（未承認）
韓国	2021 年 12 月 18 日	（未承認）
台湾	2022 年 1 月 19 日	（未承認）
トルコ	2022 年 2 月 23 日	（未承認）
サウジアラビア	2022 年 2 月 27 日	（未承認）
アルゼンチン	2022 年 3 月 28 日	（未承認）
タイ	2022 年 4 月 7 日	（未承認）
シンガポール	2022 年 4 月 26 日	（未承認）
インドネシア	2022 年 4 月 22 日	（未承認）
マレーシア	2022 年 5 月 23 日	（未承認）
イスラエル	2022 年 7 月 4 日	（未承認）
コロンビア	2022 年 8 月 29 日	（未承認）
パキスタン	2022 年 6 月 14 日	（未承認）
フィリピン	2022 年 5 月 4 日	（未承認）
メキシコ	2022 年 9 月 1 日	（未承認）
UAE	2022 年 10 月 18 日	（未承認）

（2022 年 11 月 15 日現在）

米国及び EU における本剤の承認内容（剤形・含量、効能・効果及び用法・用量）をそれぞれ表 1.6.1-2 及び表 1.6.1-3 に示す（米国の添付文書及び EU の添付文書参照）。

表 1.6.1-2　米国における本剤の承認内容

	米国の添付文書（販売名：WEGOVY）
剤形・含量	注射剤 ・0.25mg 製剤　：0.5 mL 中にセマグルチド（遺伝子組換え）を 0.25 mg 含有する ・0.5mg 製剤　：0.5 mL 中にセマグルチド（遺伝子組換え）を 0.5 mg 含有する ・1mg 製剤　：0.5 mL 中にセマグルチド（遺伝子組換え）を 1 mg 含有する ・1.7mg 製剤　：0.75 mL 中にセマグルチド（遺伝子組換え）を 1.7 mg 含有する ・2.4mg 製剤　：0.75 mL 中にセマグルチド（遺伝子組換え）を 2.4 mg 含有する
効能・効果	以下に該当する BMI［用法・用量（添付文書 2.1 項）参照］を示す成人における、継続的な体重管理のためのカロリーを制限した食事及び身体活動量の増加に対する補助療法： ・BMI が 30 kg/m^2 以上の肥満、もしくは ・BMI が 27 kg/m^2 以上の過体重であり、1 つ以上の肥満に関連する合併症（例：高血圧、2 型糖尿病、脂質異常症）を有する 使用制限 ・本剤はセマグルチドを含有しているため、他のセマグルチド含有製剤あるいはその他の GLP-1 受容体作動薬と併用しないこと。 ・処方薬、市販薬、漢方製剤等、減量を目的とした他の薬剤と併用したときの本剤の安全性及び有効性は確立されていない。 ・膵炎の既往歴のある患者における検討は行われていない。［警告及び注意（添付文書 5.2 項）参照］
用法・用量	・胃腸障害の副作用を最小限に抑えるため、本剤 0.25 mg 週 1 回皮下注射から投与を開始し、添付文書表 2 の用量漸増スケジュールに従うこと。［副作用（添付文書 6.1 項）参照］ 表 2　用量漸増スケジュール 週 / 1 週間あたりの用量 / （空欄） 1～4 週 / 0.25 mg / 用量漸増 5～8 週 / 0.5 mg 9～12 週 / 1 mg 13～16 週 / 1.7 mg 17 週以降 / 2.4 mg / 維持用量 ・用量漸増中に良好な忍容性が得られない患者では、4 週間の用量漸増の延期を検討すること。 ・本剤の維持用量は、2.4 mg の週 1 回皮下注射である。 ・維持用量である週 1 回 2.4 mg で良好な忍容性が得られない患者では、最長 4 週間、週 1 回 1.7 mg に用量を一時的に減量し、4 週間後、維持用量である週 1 回 2.4 mg に増量すること。2.4 mg で良好な忍容性が得られない患者では、本剤の投与を中止すること。 ・2 型糖尿病患者の場合、本剤の投与を開始する前及び投与期間中は血糖値をモニタリングすること。

表 1.6.1-3　EU における本剤の承認内容

<table>
<tr><td></td><td>EU の添付文書（販売名：WEGOVY）</td></tr>
<tr><td>剤形・含量</td><td>注射剤
（単回使用製剤）
・0.25mg 製剤　：0.5 mL 中にセマグルチド（遺伝子組換え）を 0.25 mg 含有する
・0.5mg 製剤　：0.5 mL 中にセマグルチド（遺伝子組換え）を 0.5 mg 含有する
・1mg 製剤　：0.5 mL 中にセマグルチド（遺伝子組換え）を 1 mg 含有する
・1.7mg 製剤　：0.75 mL 中にセマグルチド（遺伝子組換え）を 1.7 mg 含有する
・2.4mg 製剤　：0.75 mL 中にセマグルチド（遺伝子組換え）を 2.4 mg 含有する
（複数回使用製剤）
・0.25mg 製剤　：1.5 mL 中にセマグルチド（遺伝子組換え）を 1 mg 含有する
・0.5mg 製剤　：1.5 mL 中にセマグルチド（遺伝子組換え）を 2 mg 含有する
・1mg 製剤　：3 mL 中にセマグルチド（遺伝子組換え）を 4 mg 含有する
・1.7mg 製剤　：3 mL 中にセマグルチド（遺伝子組換え）を 6.8 mg 含有する
・2.4mg 製剤　：3 mL 中にセマグルチド（遺伝子組換え）を 9.6 mg 含有する</td></tr>
<tr><td>効能・効果</td><td>以下に該当する BMI を示す成人における、体重管理（体重減少及び体重維持）のためのカロリーを制限した食事及び身体活動量の増加に対する補助療法：
・BMI が 30 kg/m^2 以上の肥満、もしくは
・BMI が 27 kg/m^2 以上 30 kg/m^2 未満の過体重であり、1 つ以上の肥満に関連する合併症〔例：血糖異常（pre-diabetes 又は 2 型糖尿病）、高血圧、脂質異常症、閉塞性睡眠時無呼吸症候群又は心血管疾患〕を有する</td></tr>
<tr><td>用法・用量</td><td>本剤 0.25 mg 週 1 回投与から開始し、本剤の維持用量である 2.4 mg 週 1 回投与まで用量を漸増する。胃腸症状の発現を軽減するために、16 週間以上かけて週 1 回 2.4 mg の維持用量へと増量すること（添付文書表 1 参照）。
重大な胃腸症状がみられた場合には、用量漸増スケジュールの延期を検討するか、もしくはその症状が改善するまで漸増する前の用量での投与を検討すること。

表 1　用量漸増スケジュール
<table>
<tr><td>週</td><td>1 週間あたりの用量</td></tr>
<tr><td>1～4 週</td><td>0.25 mg</td></tr>
<tr><td>5～8 週</td><td>0.5 mg</td></tr>
<tr><td>9～12 週</td><td>1 mg</td></tr>
<tr><td>13～16 週</td><td>1.7 mg</td></tr>
<tr><td>維持用量</td><td>2.4 mg</td></tr>
</table>
1 週間あたり 2.4 mg 以上の用量は推奨しない。</td></tr>
</table>

1.6.2　企業中核データシート（CCDS）

本剤の CCDS を添付する。

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use WEGOVY safely and effectively. See full prescribing information for WEGOVY.

WEGOVY (semaglutide) injection, for subcutaneous use
Initial U.S. Approval: 2017

WARNING: RISK OF THYROID C-CELL TUMORS
See full prescribing information for complete boxed warning.

- **In rodents, semaglutide causes thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined (5.1, 13.1).**
- **WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors (4, 5.1).**

INDICATIONS AND USAGE

WEGOVY is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of

- 30 kg/m^2 or greater (obesity) or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia). (1)

Limitations of Use:

- WEGOVY should not be used in combination with other semaglutide-containing products or any other GLP-1 receptor agonist (1).
- The safety and efficacy of coadministration with other products for weight loss have not been established (1).
- WEGOVY has not been studied in patients with a history of pancreatitis (1).

DOSAGE AND ADMINISTRATION

- Administer WEGOVY once weekly, on the same day each week, at any time of day, with or without meals (2.2).
- Inject subcutaneously in the abdomen, thigh or upper arm (2.2).
- Initiate at 0.25 mg once weekly for 4 weeks. In 4 week intervals, increase the dose until a dose of 2.4 mg is reached (2.3).
- The maintenance dose of WEGOVY is 2.4 mg once weekly (2.3).
- In patients with type 2 diabetes, monitor blood glucose prior to starting and during WEGOVY treatment.

DOSAGE FORMS AND STRENGTHS

- Injection: pre-filled, single-dose pen that delivers doses of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg or 2.4 mg (3).

CONTRAINDICATIONS

- Personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (4, 5.1).
- Known hypersensitivity to semaglutide or any of the excipients in WEGOVY (4).

WARNINGS AND PRECAUTIONS

- *Thyroid C-cell Tumors*: See Boxed Warning (5.1).
- *Acute Pancreatitis:* Has occurred in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed (5.2).
- *Acute Gallbladder Disease:* Has occurred in clinical trials. If cholelithiasis is suspected, gallbladder studies and clinical follow-up are indicated (5.3).
- *Hypoglycemia:* Concomitant use with an insulin secretagogue or insulin may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing the dose of insulin secretagogue or insulin may be necessary. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia (5.4, 7.1).
- *Acute Kidney Injury:* Has occurred. Monitor renal function when initiating or escalating doses of WEGOVY in patients reporting severe adverse gastrointestinal reactions or in those with renal impairment reporting severe adverse gastrointestinal reactions (5.5).
- *Hypersensitivity:* Anaphylactic reactions and angioedema have been reported postmarketing. Discontinue WEGOVY if suspected and promptly seek medical advice (5.6).
- *Diabetic Retinopathy Complications in Patients with Type 2 Diabetes:* Has been reported in trials with semaglutide. Patients with a history of diabetic retinopathy should be monitored (5.7).
- *Heart Rate Increase:* Monitor heart rate at regular intervals (5.8).
- *Suicidal Behavior and Ideation:* Monitor for depression or suicidal thoughts. Discontinue WEGOVY if symptoms develop (5.9).

ADVERSE REACTIONS

The most common adverse reactions, reported in greater than or equal to 5% of patients treated with WEGOVY are: nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with type 2 diabetes, flatulence, gastroenteritis, and gastroesophageal reflux disease (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc., at 1-833-934-6891 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

WEGOVY delays gastric emptying. May impact absorption of concomitantly administered oral medications. Use with caution (7.2).

USE IN SPECIFIC POPULATIONS

- *Pregnancy:* May cause fetal harm. When pregnancy is recognized, discontinue WEGOVY (8.1).
- *Females and Males of Reproductive Potential:* Discontinue WEGOVY at least 2 months before a planned pregnancy because of the long half-life of semaglutide (8.3).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 06/2021

FULL PRESCRIBING INFORMATION: CONTENTS*
WARNING: RISK OF THYROID C-CELL TUMORS

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: RISK OF THYROID C-CELL TUMORS

- **In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined *[see Warnings and Precautions (5.1) and Nonclinical Toxicology (13.1)]*.**
- **WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Contraindications (4)]*. Counsel patients regarding the potential risk for MTC with the use of WEGOVY and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY *[see Contraindications (4) and Warnings and Precautions (5.1)]*.**

1 INDICATIONS AND USAGE

WEGOVY is indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of *[see Dosage and Administration (2.1)]*:

- 30 kg/m^2 or greater (obesity) or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia)

Limitation of Use

- WEGOVY contains semaglutide and should not be coadministered with other semaglutide-containing products or with any other GLP-1 receptor agonist.
- The safety and effectiveness of WEGOVY in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.
- WEGOVY has not been studied in patients with a history of pancreatitis *[see Warnings and Precautions (5.2)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for WEGOVY treatment as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management based on their BMI. BMI is calculated by dividing weight (in kilograms) by height (in meters) squared. A chart for determining BMI based on height and weight is provided in Table 1.

Table 1. BMI Conversion Chart

Weight	(lb)	125	130	135	140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	215	220	225
	(kg)	56. 8	59. 1	61. 4	63. 6	65. 9	68. 2	70. 5	72. 7	75. 0	77. 3	79. 5	81. 8	84. 1	86. 4	88. 6	90. 9	93. 2	95. 5	97. 7	100. 0	102. 3
Height																						
(in)	(cm)																					
58	147. 3	26	27	28	29	30	31	32	34	35	36	37	38	39	40	41	42	43	44	45	46	47
59	149. 9	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	43	44	45	46
60	152. 4	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44
61	154. 9	24	25	26	27	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43
62	157. 5	23	24	25	26	27	27	28	29	30	31	32	33	34	35	36	37	38	38	39	40	41
63	160. 0	22	23	24	25	26	27	28	28	29	30	31	32	33	34	35	36	36	37	38	39	40
64	162. 6	22	22	23	24	25	26	27	28	28	29	30	31	32	33	34	34	35	36	37	38	39
65	165. 1	21	22	23	23	24	25	26	27	28	28	29	30	31	32	33	33	34	35	36	37	38
66	167. 6	20	21	22	23	23	24	25	26	27	27	28	29	30	31	32	32	33	34	35	36	36
67	170. 2	20	20	21	22	23	24	24	25	26	27	27	28	29	30	31	31	32	33	34	35	35
68	172. 7	19	20	21	21	22	23	24	24	25	26	27	27	28	29	30	30	31	32	33	34	34
69	175. 3	18	19	20	21	21	22	23	24	24	25	26	27	27	28	29	30	30	31	32	33	33
70	177. 8	18	19	19	20	21	22	22	23	24	24	25	26	27	27	28	29	29	30	31	32	32
71	180. 3	17	18	19	20	20	21	22	22	23	24	24	25	26	27	27	28	29	29	30	31	31
72	182. 9	17	18	18	19	20	20	21	22	22	23	24	24	25	26	27	27	28	29	29	30	31
73	185. 4	17	17	18	19	19	20	20	21	22	22	23	24	24	25	26	26	27	28	28	29	30
74	188. 0	16	17	17	18	19	19	20	21	21	22	23	23	24	24	25	26	26	27	28	28	29
75	190. 5	16	16	17	18	18	19	19	20	21	21	22	23	23	24	24	25	26	26	27	28	28
76	193. 0	15	16	16	17	18	18	19	20	20	21	21	22	23	23	24	24	25	26	26	27	27

2.2 Important Administration Instructions

- Prior to initiation of WEGOVY, train patients on proper injection technique. Refer to the accompanying Instructions for Use for complete administration instructions with illustrations.
- Inspect WEGOVY visually prior to each injection. Only use if solution is clear, colorless, and contains no particles.
- Administer WEGOVY once weekly, on the same day each week, at any time of day, with or without meals.
- Administer WEGOVY subcutaneously in the abdomen, thigh, or upper arm. The time of day and the injection site can be changed without dose adjustment.
- If one dose is missed and the next scheduled dose is more than 2 days away (48 hours), administer WEGOVY as soon as possible. If one dose is missed and the next scheduled dose is less than 2 days away (48 hours), do not administer the dose. Resume dosing on the regularly scheduled day of the week.
- If more than 2 consecutive doses are missed, resume dosing as scheduled or, if needed, reinitiate WEGOVY and follow the dose escalation schedule, which may reduce the occurrence of gastrointestinal symptoms associated with reinitiation of treatment.

2.3 Recommended Dosage

- Initiate WEGOVY with a dose of 0.25 mg injected subcutaneously once-weekly and follow the dose escalation schedule in Table 2 to minimize gastrointestinal adverse reactions *[see Adverse Reactions (6.1)]*.

Table 2. Dose Escalation Schedule

Weeks	Weekly Dose	
1 through 4	0.25 mg	Dose escalation
5 through 8	0.5 mg	
9 through 12	1 mg	
13 through 16	1.7 mg	
Week 17 and onward	2.4 mg	Maintenance dose

- If patients do not tolerate a dose during dose escalation, consider delaying dose escalation for 4 weeks.
- The maintenance dose of WEGOVY is 2.4 mg injected subcutaneously once-weekly.
- If patients do not tolerate the maintenance 2.4 mg once-weekly dose, the dose can be temporarily decreased to 1.7 mg once-weekly, for a maximum of 4 weeks. After 4 weeks, increase WEGOVY to the maintenance 2.4 mg once-weekly. Discontinue WEGOVY if the patient cannot tolerate the 2.4 mg dose.
- In patients with type 2 diabetes, monitor blood glucose prior to starting WEGOVY and during WEGOVY treatment.

3 DOSAGE FORMS AND STRENGTHS

Injection: clear, colorless solution available in 5 pre-filled, disposable, single-dose pens:

Dose per Injection	Total Strength per Total Volume
0.25 mg	0.25 mg / 0.5 mL
0.5 mg	0.5 mg / 0.5 mL
1 mg	1 mg / 0.5 mL
1.7 mg	1.7 mg / 0.75 mL
2.4 mg	2.4 mg / 0.75 mL

4 CONTRAINDICATIONS

WEGOVY is contraindicated in the following conditions:

- A personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Warnings and Precautions (5.1)]*.
- A prior serious hypersensitivity reaction to semaglutide or to any of the excipients in WEGOVY. Serious hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with semaglutide *[see Warnings and Precautions (5.6)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Thyroid C-Cell Tumors

In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures *[see Nonclinical Toxicology (13.1)]*. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.

Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.

WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of WEGOVY and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values greater than 50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

5.2 Acute Pancreatitis

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists, including semaglutide. Acute pancreatitis was observed in patients treated with WEGOVY in clinical trials *[see Adverse Reactions (6)]*. After initiation of WEGOVY, observe patients carefully for signs and symptoms of acute pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back, and which may or may not be accompanied by vomiting). If acute pancreatitis is suspected, WEGOVY should promptly be discontinued and appropriate management should be initiated. If acute pancreatitis is confirmed, WEGOVY should not be restarted.

WEGOVY has not been studied in patients with a history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on WEGOVY.

5.3 Acute Gallbladder Disease

In WEGOVY randomized clinical trials, cholelithiasis was reported by 1.6% of WEGOVY-treated patients and 0.7% of placebo-treated patients. Cholecystitis was reported by 0.6% of WEGOVY-treated patients and 0.2% of placebo-treated patients. Substantial or rapid weight loss can increase the risk of cholelithiasis; however, the incidence of acute gallbladder disease was greater in WEGOVY-treated patients than in placebo-treated patients, even after accounting for the degree of weight loss. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

5.4 Hypoglycemia

WEGOVY lowers blood glucose and can cause hypoglycemia.

In a trial of patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2, hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in 6.2% of WEGOVY-treated patients versus 2.5% of placebo-treated patients. One episode of severe hypoglycemia (requiring the assistance of another person) was reported in one WEGOVY-treated patient versus no placebo-treated patients.

Patients with type 2 diabetes mellitus taking WEGOVY in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia *[see Adverse Reactions (6.1)]*. Hypoglycemia has been observed in patients treated with semaglutide at doses of 0.5 and 1 mg in combination with insulin. The addition of WEGOVY in patients treated with insulin has not been evaluated.

Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In patients with type 2 diabetes, monitor blood glucose prior to starting WEGOVY and during WEGOVY treatment. When initiating WEGOVY, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia *[see Drug Interactions (7)]*.

5.5 Acute Kidney Injury

There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which have in some cases required hemodialysis, in patients treated with semaglutide. Patients with renal impairment may be at greater risk of acute kidney injury, but some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, or diarrhea, leading to volume depletion *[see Adverse Reactions (6)]*.

Monitor renal function when initiating or escalating doses of WEGOVY in patients reporting severe adverse gastrointestinal reactions. Monitor renal function in patients with renal impairment reporting any adverse reactions that could lead to volume depletion.

5.6 Hypersensitivity

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with semaglutide. If hypersensitivity reactions occur, discontinue use of WEGOVY, treat promptly per standard of care, and monitor

until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity to semaglutide or any of the excipients in WEGOVY *[see Contraindications (4)]*.

Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of anaphylaxis or angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to these reactions with WEGOVY.

5.7 Diabetic Retinopathy Complications in Patients with Type 2 Diabetes

In a trial of patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2, diabetic retinopathy was reported by 4.0% of WEGOVY-treated patients and 2.7% placebo-treated patients.

In a 2-year trial with semaglutide 0.5 mg and 1 mg once-weekly injection in patients with type 2 diabetes and high cardiovascular risk, diabetic retinopathy complications (which was a 4-component adjudicated endpoint) occurred in patients treated with semaglutide injection (3.0%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline (semaglutide injection 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (semaglutide injection 0.7%, placebo 0.4%).

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

5.8 Heart Rate Increase

Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed in WEGOVY-treated patients compared to placebo in clinical trials. More patients treated with WEGOVY compared with placebo had maximum changes from baseline at any visit of 10 to 19 bpm (41% versus 34%, respectively) and 20 bpm or more (26% versus 16%, respectively).

Monitor heart rate at regular intervals consistent with usual clinical practice. Instruct patients to inform their healthcare providers of palpitations or feelings of a racing heartbeat while at rest during WEGOVY treatment. If patients experience a sustained increase in resting heart rate, discontinue WEGOVY.

5.9 Suicidal Behavior and Ideation

Suicidal behavior and ideation have been reported in clinical trials with other weight management products. Monitor patients treated with WEGOVY for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue WEGOVY in patients who experience suicidal thoughts or behaviors. Avoid WEGOVY in patients with a history of suicidal attempts or active suicidal ideation.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:

- Risk of Thyroid C-Cell Tumors *[see Warnings and Precautions (5.1)]*
- Acute Pancreatitis *[see Warnings and Precautions (5.2)]*
- Acute Gallbladder Disease *[see Warnings and Precautions (5.3)]*
- Hypoglycemia *[see Warnings and Precautions (5.4)]*
- Acute Kidney Injury *[see Warnings and Precautions (5.5)]*
- Hypersensitivity *[see Warnings and Precautions (5.6)]*
- Diabetic Retinopathy Complications in Patients with Type 2 Diabetes *[see Warnings and Precautions (5.7)]*
- Heart Rate Increase *[see Warnings and Precautions (5.8)]*

- Suicidal Behavior and Ideation *[see Warnings and Precautions (5.9)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

WEGOVY was evaluated for safety in 3 randomized, double-blind, placebo-controlled trials that included 2116 patients with overweight or obesity treated with WEGOVY for up to 68 weeks and a 7 week off drug follow-up period. Baseline characteristics included a mean age of 48 years, 71% women, 72% White, 42% with hypertension, 19% with type 2 diabetes, 43% with dyslipidemia, 28% with a BMI greater than 40 kg/m^2, and 4% with cardiovascular disease.

In clinical trials, 6.8% of patients treated with WEGOVY and 3.2% of patients treated with placebo permanently discontinued treatment as a result of adverse reactions. The most common adverse reactions leading to discontinuation were nausea (1.8% versus 0.2%), vomiting (1.2% versus 0%), and diarrhea (0.7% versus 0.1%) for WEGOVY and placebo, respectively.

Adverse reactions reported in greater than or equal to 2% of WEGOVY-treated patients and more frequently than in placebo-treated patients are shown in Table 3.

Table 3. Adverse Reactions Occurring in ≥ 2% of WEGOVY-treated Patients and More Frequently than with Placebo

	Placebo N = 1261 %	**WEGOVY N = 2116 %**
Nausea	16	44
Diarrhea	16	30
Vomiting	6	24
Constipation	11	24
Abdominal Pain[a]	10	20
Headache	10	14
Fatigue[b]	5	11
Dyspepsia	3	9
Dizziness	4	8
Abdominal Distension	5	7
Eructation	<1	7
Hypoglycemia in T2DM[c]	2	6
Flatulence	4	6
Gastroenteritis	4	6
Gastroesophageal Reflux Disease	3	5
Gastritis[d]	1	4
Gastroenteritis Viral	3	4
Hair Loss	1	3

[a]Includes abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal pain, abdominal tenderness, abdominal discomfort and epigastric discomfort

[b]Includes fatigue and asthenia

[c]Defined as blood glucose <54 mg/dL with or without symptoms of hypoglycemia or severe hypoglycemia (requiring the assistance of another person) in patients with type 2 diabetes not on concomitant insulin (Study 2, WEGOVY N=403, Placebo N=402). See text below for further information regarding hypoglycemia in patients with and without type 2 diabetes. T2DM = type 2 diabetes mellitus

[d]Includes chronic gastritis, gastritis, gastritis erosive, and reflux gastritis

Acute Pancreatitis

In WEGOVY clinical trials, acute pancreatitis was confirmed by adjudication in 4 WEGOVY-treated patients (0.2 cases per 100 patient years) versus 1 in placebo-treated patients (less than 0.1 cases per 100 patient years). One additional case of acute pancreatitis was confirmed in a patient treated with WEGOVY in another clinical trial.

Acute Gallbladder Disease

In WEGOVY clinical trials, cholelithiasis was reported by 1.6% of WEGOVY-treated patients and 0.7% of placebo-treated patients. Cholecystitis was reported by 0.6% of WEGOVY-treated patients and 0.2% of placebo-treated patients.

Hypoglycemia

Patients with Type 2 Diabetes

In a trial of patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2, clinically significant hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in 6.2% of WEGOVY-treated patients versus 2.5% of placebo-treated patients. A higher rate of clinically significant hypoglycemic episodes was reported with WEGOVY (semaglutide 2.4 mg) versus semaglutide 1 mg (10.7 vs. 7.2 episodes per 100 patient years of exposure, respectively); the rate in the placebo-treated group was 3.2 episodes per 100 patient years of exposure. In addition, one episode of severe hypoglycemia requiring intravenous glucose was reported in a WEGOVY-treated patient versus none in placebo-treated patients. The risk of hypoglycemia was increased when WEGOVY was used with a sulfonylurea.

Patients without Type 2 Diabetes

Episodes of hypoglycemia have been reported with GLP-1 receptor agonists in patients without type 2 diabetes mellitus. In WEGOVY clinical trials in patients without type 2 diabetes mellitus, there was no systematic capturing or reporting of hypoglycemia.

Acute Kidney Injury

Acute kidney injury occurred in clinical trials in 7 patients (0.4 cases per 100 patient years) receiving WEGOVY versus 4 patients (0.2 cases per 100 patient years of exposure) receiving placebo. Some of these adverse reactions occurred in association with gastrointestinal adverse reactions or dehydration. In addition, 2 patients treated with WEGOVY had acute kidney injury with dehydration in other clinical trials. The risk of renal adverse reactions with WEGOVY was increased in patients with a history of renal impairment (trials included 65 patients with a history of moderate or severe renal impairment at baseline), and occurred more frequently during dose titration.

Retinal Disorders in Patients with Type 2 Diabetes

In a trial of patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2, retinal disorders were reported by 6.9% of patients treated with WEGOVY (semaglutide 2.4 mg), 6.2% of patients treated with semaglutide 1 mg, and 4.2% of patients treated with placebo. The majority of events were reported as diabetic retinopathy (4.0%, 2.7%, and 2.7%, respectively) and non-proliferative retinopathy (0.7%, 0%, and 0%, respectively).

Increase in Heart Rate

Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed with routine clinical monitoring in WEGOVY-treated patients compared to placebo in clinical trials. In trials in which patients were randomized prior to dose-escalation, more patients treated with WEGOVY, compared with placebo, had maximum changes from baseline at any visit of 10 to 19 bpm (41% versus 34%, respectively) and 20 bpm or more (26% versus 16%, respectively).

Hypotension and Syncope
Adverse reactions related to hypotension (hypotension, orthostatic hypotension, and decreased blood pressure) were reported in 1.3% of WEGOVY-treated patients versus 0.4% of placebo-treated patients and syncope was reported in 0.8% of WEGOVY-treated patients versus 0.2% of placebo-treated patients. Some reactions were related to gastrointestinal adverse reactions and volume loss associated with WEGOVY. Hypotension and orthostatic hypotension were more frequently seen in patients on concomitant antihypertensive therapy.

Appendicitis
Appendicitis (including perforated appendicitis) occurred in 10 (0.5%) WEGOVY-treated patients and 2 (0.2%) patients receiving placebo.

Gastrointestinal Adverse Reactions
In clinical trials, 73% of WEGOVY-treated patients and 47% of patients receiving placebo reported gastrointestinal disorders. The most frequently reported reactions were nausea (44% vs. 16%), vomiting (25% vs. 6%), and diarrhea (30% vs. 16%). Other common reactions that occurred at a higher incidence among WEGOVY-treated patients included dyspepsia, abdominal pain, abdominal distension, eructation, flatulence, gastroesophageal reflux disease, gastritis, and hemorrhoids. These reactions increased during dose escalation.

Permanent discontinuation of treatment as a result of a gastrointestinal adverse reaction occurred in 4.3% of WEGOVY-treated patients versus 0.7% of placebo-treated patients.

Injection Site Reactions
In clinical trials, 1.4% of WEGOVY-treated patients and 1.0% of patients receiving placebo experienced injection site reactions (including injection site pruritus, erythema, inflammation, induration, and irritation).

Laboratory Abnormalities
Patients treated with WEGOVY had a mean increase from baseline in amylase of 16% and lipase of 39%. These changes were not observed in the placebo group. The clinical significance of elevations in lipase or amylase with WEGOVY is unknown in the absence of other signs and symptoms of pancreatitis.

6.2 Immunogenicity
Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with WEGOVY may develop anti-semaglutide antibodies. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, the incidence of antibodies to semaglutide in the studies described below cannot be directly compared with the incidence of antibodies in other studies or to other products.

Across the clinical trials with antibody assessments, 50 (2.9%) WEGOVY-treated patients developed anti-drug antibodies (ADAs) to the active ingredient in WEGOVY (i.e., semaglutide). Of the 50 semaglutide-treated patients that developed semaglutide ADAs, 28 patients (1.6% of the total WEGOVY-treated study population) developed antibodies cross-reacting with native GLP-1. The in vitro neutralizing activity of the antibodies is uncertain at this time.

6.3 Postmarketing Experience
The following adverse reactions have been reported during post-approval use of semaglutide, the active ingredient of WEGOVY. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal Disorders: acute pancreatitis and necrotizing pancreatitis, sometimes resulting in death
Hypersensitivity: anaphylaxis, angioedema, rash, urticaria

Renal and Urinary Disorders: acute kidney injury

7 DRUG INTERACTIONS

7.1 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or Insulin

WEGOVY lowers blood glucose and can cause hypoglycemia. The risk of hypoglycemia is increased when WEGOVY is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. The addition of WEGOVY in patients treated with insulin has not been evaluated.

When initiating WEGOVY, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia *[see Warnings and Precautions (5.4) and Adverse Reactions (6.1)]*.

7.2 Oral Medications

WEGOVY causes a delay of gastric emptying and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials with semaglutide 1 mg, semaglutide did not affect the absorption of orally administered medications *[see Clinical Pharmacology (12.3)]*. Nonetheless, monitor the effects of oral medications concomitantly administered with WEGOVY.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to semaglutide during pregnancy. Pregnant women exposed to WEGOVY and healthcare providers are encouraged to contact Novo Nordisk at 1-800-727-6500.

Risk Summary

Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. Additionally, weight loss offers no benefit to a pregnant patient and may cause fetal harm. When a pregnancy is recognized, advise the pregnant patient of the risk to a fetus, and discontinue WEGOVY *(see Clinical Considerations)*. Available pharmacovigilance data and data from clinical trials with WEGOVY use in pregnant patients are insufficient to establish a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

In pregnant rats administered semaglutide during organogenesis, embryofetal mortality, structural abnormalities and alterations to growth occurred at maternal exposures below the maximum recommended human dose (MRHD) based on AUC. In rabbits and cynomolgus monkeys administered semaglutide during organogenesis, early pregnancy losses and structural abnormalities were observed at below the MRHD (rabbit) and greater than or equal to 2-fold the MRHD (monkey). These findings coincided with a marked maternal body weight loss in both animal species (see Data).

The estimated background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

Appropriate weight gain based on pre-pregnancy weight is currently recommended for all pregnant patients, including those who already have overweight or obesity, because of the obligatory weight gain that occurs in maternal tissues during pregnancy.

Data

Animal Data

In a combined fertility and embryofetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.04-, 0.1-, and 0.4-fold the MRHD) were administered to males for 4 weeks prior to and throughout mating and to females for 2 weeks prior to mating, and throughout organogenesis to Gestation Day 17. In parental animals, pharmacologically mediated reductions in body weight gain and food consumption were observed at all dose levels. In the offspring, reduced growth and fetuses with visceral (heart blood vessels) and skeletal (cranial bones, vertebra, ribs) abnormalities were observed at the human exposure.

In an embryofetal development study in pregnant rabbits, subcutaneous doses of 0.0010, 0.0025 or 0.0075 mg/kg/day (0.01-, 0.1-, and 0.9-fold the MRHD) were administered throughout organogenesis from Gestation Day 6 to 19. Pharmacologically mediated reductions in maternal body weight gain and food consumption were observed at all dose levels. Early pregnancy losses and increased incidences of minor visceral (kidney, liver) and skeletal (sternebra) fetal abnormalities were observed at greater than or equal to 0.0025 mg/kg/day, at clinically relevant exposures.

In an embryofetal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.4-, 2-, and 6-fold the MRHD) were administered throughout organogenesis, from Gestation Day 16 to 50. Pharmacologically mediated, marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with the occurrence of sporadic abnormalities (vertebra, sternebra, ribs) at greater than or equal to 0.075 mg/kg twice weekly (greater than or equal to 2 times human exposure).

In a pre- and postnatal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.2-, 1-, and 3-fold the MRHD) were administered from Gestation Day 16 to 140. Pharmacologically mediated marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with an increase in early pregnancy losses and led to delivery of slightly smaller offspring at greater than or equal to 0.075 mg/kg twice weekly (greater than or equal to 1 time human exposure).

8.2 Lactation

Risk Summary

There are no data on the presence of semaglutide or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Semaglutide was present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk *(see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for WEGOVY and any potential adverse effects on the breastfed infant from WEGOVY or from the underlying maternal condition.

Data

In lactating rats, semaglutide was detected in milk at levels 3-12 fold lower than in maternal plasma.

8.3 Females and Males of Reproductive Potential

Because of the potential for fetal harm, discontinue WEGOVY in patients at least 2 months before they plan to become pregnant to account for the long half-life of semaglutide *[see Use in Specific Populations (8.1)]*.

8.4 Pediatric Use

Safety and efficacy of WEGOVY have not been established in pediatric patients.

8.5 Geriatric Use

In the WEGOVY clinical trials, 233 (8.8%) WEGOVY-treated patients were between 65 and 75 years of age and 23 (0.9%) WEGOVY-treated patients were 75 years of age and over. No overall differences in safety or efficacy were detected between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

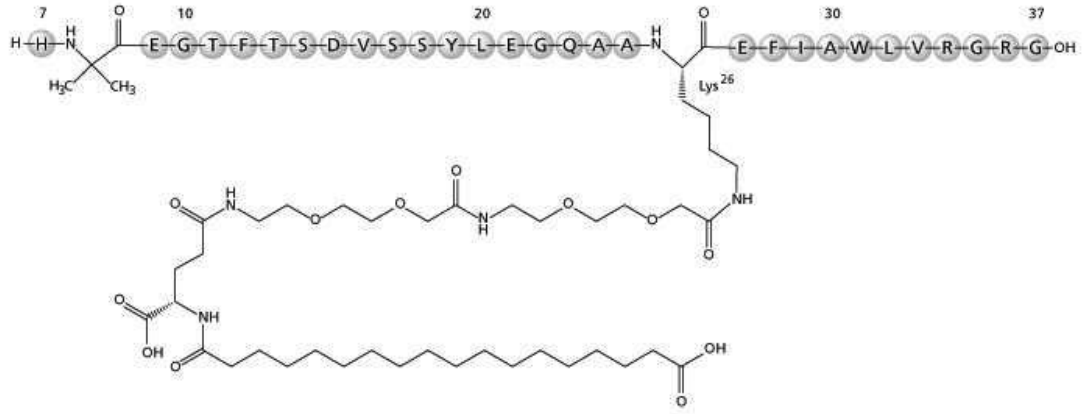
8.6 Renal Impairment
No dose adjustment of WEGOVY is recommended for patients with renal impairment. In a study in subjects with renal impairment, including end-stage renal disease, no clinically relevant change in semaglutide pharmacokinetics was observed *[see Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment
No dose adjustment of WEGOVY is recommended for patients with hepatic impairment. In a study in subjects with different degrees of hepatic impairment, no clinically relevant change in semaglutide pharmacokinetics was observed *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE
Overdoses have been reported with other GLP-1 receptor agonists. Effects have included severe nausea, severe vomiting, and severe hypoglycemia. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the long half-life of WEGOVY of approximately 1 week.

11 DESCRIPTION
WEGOVY (semaglutide) injection, for subcutaneous use, contains semaglutide, a human GLP-1 receptor agonist (or GLP-1 analog). The peptide backbone is produced by yeast fermentation. The main protraction mechanism of semaglutide is albumin binding, facilitated by modification of position 26 lysine with a hydrophilic spacer and a C18 fatty di-acid. Furthermore, semaglutide is modified in position 8 to provide stabilization against degradation by the enzyme dipeptidyl-peptidase 4 (DPP-4). A minor modification was made in position 34 to ensure the attachment of only one fatty di-acid. The molecular formula is $C_{187}H_{291}N_{45}O_{59}$ and the molecular weight is 4113.58 g/mol.

Figure 1. Structural Formula of semaglutide



WEGOVY is a sterile, aqueous, clear, colorless solution. Each 0.5 mL single-dose pen contains a solution of WEGOVY containing 0.25 mg, 0.5 mg or 1 mg of semaglutide; and each 0.75 mL single-dose pen contains a solution of WEGOVY containing 1.7 or 2.4 mg of semaglutide. Each 1 mL of WEGOVY contains the following inactive ingredients: disodium phosphate dihydrate, 1.42 mg; sodium chloride, 8.25 mg; and water for injection. WEGOVY has a pH of approximately 7.4. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action

Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1.

GLP-1 is a physiological regulator of appetite and caloric intake, and the GLP-1 receptor is present in several areas of the brain involved in appetite regulation. Animal studies show that semaglutide distributed to and activated neurons in brain regions involved in regulation of food intake.

12.2 Pharmacodynamics

Semaglutide lowers body weight through decreased calorie intake. The effects are likely mediated by affecting appetite.

As with other GLP-1 receptor agonists, semaglutide stimulates insulin secretion and reduces glucagon secretion in a glucose-dependent manner. These effects can lead to a reduction of blood glucose.

Cardiac electrophysiology (QTc)

The effect of semaglutide on cardiac repolarization was tested in a thorough QTc trial. Semaglutide did not prolong QTc intervals at doses up to 1.5 mg at steady state.

12.3 Pharmacokinetics

Absorption

Absolute bioavailability of semaglutide is 89%. Maximum concentration of semaglutide is reached 1 to 3 days post dose.

Similar exposure was achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm.

The average semaglutide steady state concentration following subcutaneous administration of WEGOVY was approximately 75 nmol/L in patients with either obesity (BMI greater than or equal to 30 kg/m^2) or overweight (BMI greater than or equal to 27 kg/m^2). The steady state exposure of WEGOVY increased proportionally with doses up to 2.4 mg once-weekly.

Distribution

The mean volume of distribution of semaglutide following subcutaneous administration in patients with obesity or overweight is approximately 12.5 L. Semaglutide is extensively bound to plasma albumin (greater than 99%) which results in decreased renal clearance and protection from degradation.

Elimination

The apparent clearance of semaglutide in patients with obesity or overweight is approximately 0.05 L/h. With an elimination half-life of approximately 1 week, semaglutide will be present in the circulation for about 5 to 7 weeks after the last dose of 2.4 mg.

Metabolism

The primary route of elimination for semaglutide is metabolism following proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain.

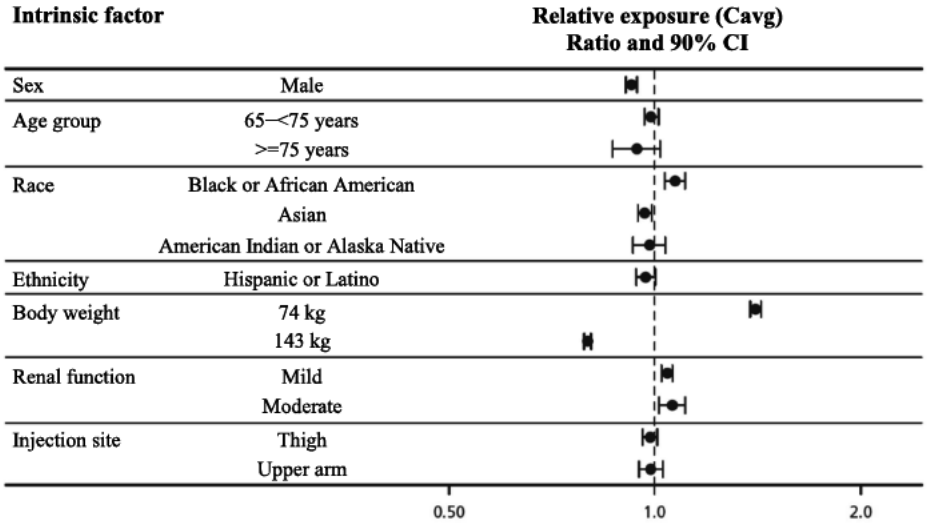
Excretion

The primary excretion routes of semaglutide-related material are via the urine and feces. Approximately 3% of the dose is excreted in the urine as intact semaglutide.

Special Populations

The effects of intrinsic factors on the pharmacokinetics of semaglutide are shown in Figure 2.

Figure 2. Impact of intrinsic factors on semaglutide exposure



Data are steady-state dose-normalized average semaglutide exposures relative to a reference subject profile (non-Hispanic or Latino, white female aged 18 to less than 65 years, with a body weight of 110 kg and normal renal function, who injected in the abdomen). Body weight categories (74 and 143 kg) represent the 5% and 95% percentiles in the dataset.

Renal Impairment

Renal impairment did not impact the exposure of semaglutide in a clinically relevant manner. The pharmacokinetics of semaglutide were evaluated following a single dose of 0.5 mg semaglutide in a study of patients with different degrees of renal impairment (mild, moderate, severe, or ESRD) compared with subjects with normal renal function. The pharmacokinetics were also assessed in subjects with overweight (BMI 27-29.9 kg/m^2) or obesity (BMI greater than or equal to 30 kg/m^2) and mild to moderate renal impairment, based on data from clinical trials.

Hepatic Impairment

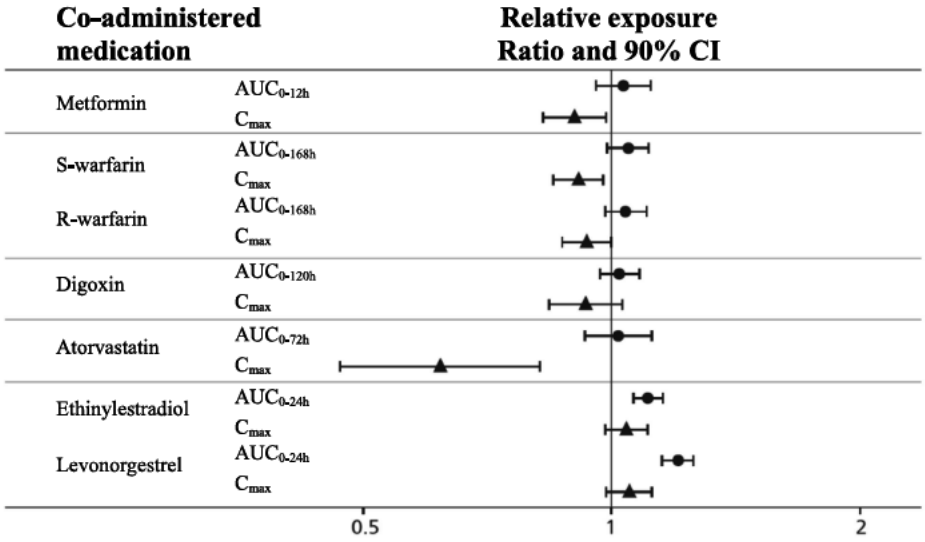
Hepatic impairment did not impact the exposure of semaglutide. The pharmacokinetics of semaglutide were evaluated following a single dose of 0.5 mg semaglutide in a study of patients with different degrees of hepatic impairment (mild, moderate, severe) compared with subjects with normal hepatic function.

Drug Interactions

In vitro studies have shown very low potential for semaglutide to inhibit or induce CYP enzymes, or to inhibit drug transporters.

The delay of gastric emptying with semaglutide may influence the absorption of concomitantly administered oral medications *[see Drug Interactions (7.2)]*. The potential effect of semaglutide on the absorption of co-administered oral medications was studied in trials at semaglutide 1 mg steady-state exposure. No clinically relevant drug-drug interactions with semaglutide (Figure 3) were observed based on the evaluated medications. In a separate study, no apparent effect on the rate of gastric emptying was observed with semaglutide 2.4 mg.

Figure 3. Impact of semaglutide 1 mg on the pharmacokinetics of co-administered medications



Relative exposure in terms of AUC and C_{max} for each medication when given with semaglutide compared to without semaglutide. Metformin and oral contraceptive drug (ethinylestradiol/levonorgestrel) were assessed at steady state. Warfarin (S-warfarin/R-warfarin), digoxin and atorvastatin were assessed after a single dose.
Abbreviations: AUC: area under the curve, C_{max}: maximum concentration, CI: confidence interval.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year carcinogenicity study in CD-1 mice, subcutaneous doses of 0.3, 1 and 3 mg/kg/day (2-, 8-, and 22-fold the maximum recommended human dose [MRHD] of 2.4 mg/week, based on AUC) were administered to the males, and 0.1, 0.3 and 1 mg/kg/day (0.6-, 2-, and 5-fold MRHD) were administered to the females.
A statistically significant increase in thyroid C-cell adenomas and a numerical increase in C-cell carcinomas were observed in males and females at all dose levels (greater than or equal to 0.6 times human exposure).

In a 2-year carcinogenicity study in Sprague Dawley rats, subcutaneous doses of 0.0025, 0.01, 0.025 and 0.1 mg/kg/day were administered (below quantification, 0.2-, 0.4-, and 2-fold the exposure at the MRHD).
A statistically significant increase in thyroid C-cell adenomas was observed in males and females at all dose levels, and a statistically significant increase in thyroid C-cell carcinomas was observed in males at greater than or equal to 0.01 mg/kg/day, at clinically relevant exposures.

Human relevance of thyroid C-cell tumors in rats is unknown and could not be determined by clinical studies or nonclinical studies *[see Boxed Warning and Warnings and Precautions (5.1)]*. Semaglutide was not mutagenic or clastogenic in a standard battery of genotoxicity tests (bacterial mutagenicity [Ames] human lymphocyte chromosome aberration, rat bone marrow micronucleus).

In a combined fertility and embryo-fetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.04-, 0.1-, and 0.4-fold the MRHD) were administered to male and female rats. Males were dosed for 4 weeks prior to mating, and females were dosed for 2 weeks prior to mating and throughout organogenesis until Gestation Day 17. No effects were observed on male fertility. In females, an increase in estrus cycle length was observed at all dose levels, together with a small reduction in numbers of corpora lutea at greater than or equal to 0.03 mg/kg/day. These effects were likely an adaptive response secondary to the pharmacological effect of semaglutide on food consumption and body weight.

14 CLINICAL STUDIES

Overview of Clinical Studies

The safety and efficacy of WEGOVY for chronic weight management (weight loss and maintenance) in conjunction with a reduced calorie diet and increased physical activity were studied in three 68-week,

randomized, double-blind, placebo-controlled trials and one 68-week, randomized, double-blind, placebo withdrawal trial. In Studies 1, 2, and 3, WEGOVY or matching placebo was escalated to 2.4 mg subcutaneous weekly during a 16-week period followed by 52 weeks on maintenance dose. In Study 4, WEGOVY was escalated during a 20-week run-in period, and patients who reached WEGOVY 2.4 mg after the run-in period were randomized to either continued treatment with WEGOVY or placebo for 48 weeks.

In Studies 1, 2 and 4, all patients received instruction for a reduced calorie meal diet (approximately 500 kcal/day deficit) and increased physical activity counseling (recommended to a minimum of 150 min/week) that began with the first dose of study medication or placebo and continued throughout the trial. In Study 3, patients received an initial 8-week low-calorie diet (total energy intake 1000 to 1200 kcal/day) followed by 60 weeks of a reduced calorie diet (1200-1800 kcal/day) and increased physical activity (100 mins/week with gradual increase to 200 mins/week).

Study 1 was a 68-week trial that enrolled 1961 patients with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition, such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. Patients were randomized in a 2:1 ratio to either WEGOVY or placebo. At baseline, mean age was 46 years (range 18-86), 74.1% were women, 75.1% were White, 13.3% were Asian and 5.7% were Black or African American. A total of 12.0% were Hispanic or Latino. Mean baseline body weight was 105.3 kg and mean BMI was 37.9 kg/m^2.

Study 2 was a 68-week trial that enrolled 807 patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2. Patients included in the trial had HbA_{1c} 7-10% and were treated with either: diet and exercise alone or 1 to 3 oral anti-diabetic drugs (metformin, sulfonylurea, glitazone or sodium-glucose co-transporter 2 inhibitor). Patients were randomized in a 1:1 ratio to receive either WEGOVY or placebo. At baseline, the mean age was 55 years (range 19-84), 50.9% were women, 62.1% were White, 26.2% were Asian and 8.3% were Black or African American. A total of 12.8% were Hispanic or Latino. Mean baseline body weight was 99.8 kg and mean BMI was 35.7 kg/m^2.

Study 3 was a 68-week trial that enrolled 611 patients with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. The patients were randomized in a 2:1 ratio to receive either WEGOVY or placebo. At baseline, the mean age was 46 years, 81.0% were women, 76.1% were White, 19.0% were Black or African American and 1.8% were Asian. A total of 19.8% were Hispanic or Latino. Mean baseline body weight was 105.8 kg and mean BMI was 38.0 kg/m^2.

Study 4 was a 68-week trial that enrolled 902 patients with obesity (BMI greater than or equal to 30 kg/m^2) or with overweight (BMI 27-29.9 kg/m^2) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. Mean body weight at baseline for the 902 patients was 106.8 kg and mean BMI was 38.3 kg/m^2. All patients received WEGOVY during the run-in period of 20 weeks that included 16 weeks of dose escalation. Trial product was permanently discontinued before randomization in 99 of 902 patients (11%); the most common reason was adverse reactions (n=48, 5.3%); 803 patients reached WEGOVY 2.4 mg and were then randomized in a 2:1 ratio to either continue on WEGOVY or receive placebo. Among the 803 randomized patients, the mean age was 46 years, 79% were women, 83.7% were White, 13% were Black or African American, and 2.4% Asian. A total of 7.8% were Hispanic or Latino. Mean body weight at randomization (week 20) was 96.1 kg and mean BMI at randomization (week 20) was 34.4 kg/m^2.

The proportions of patients who discontinued study drug in Studies 1, 2, and 3 was 16.0% for the WEGOVY-treated group and 19.1% for the placebo-treated group, and 6.8% of patients treated with WEGOVY and 3.2% of patients treated with placebo discontinued treatment due to an adverse reaction *[see Adverse Reactions (6.1)]*. In Study 4, the proportions of patients who discontinued study drug were 5.8% and 11.6% for WEGOVY and placebo, respectively.

14.1 Weight Management Studies in Adults with Overweight or Obesity

For Studies 1, 2 and 3, the primary efficacy parameters were mean percent change in body weight and the percentages of patients achieving greater than or equal to 5% weight loss from baseline to week 68.

After 68 weeks, treatment with WEGOVY resulted in a statistically significant reduction in body weight compared with placebo. Greater proportions of patients treated with WEGOVY achieved 5%, 10% and 15% weight loss than those treated with placebo as shown in Table 4.

Table 4. Changes in Body Weight at Week 68 in Studies 1, 2 and 3

	Study 1 (Obesity or overweight with comorbidity)		**Study 2 (Type 2 diabetes with obesity or overweight)**		**Study 3 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)**	
Intention-to-Treat[a]	**PLACEBO N = 655**	**WEGOVY N = 1306**	**PLACEBO N = 403**	**WEGOVY N = 404**	**PLACEBO N = 204**	**WEGOVY N = 407**
Body Weight						
Baseline mean (kg)	105.2	105.4	100.5	99.9	103.7	106.9
% change from baseline (LSMean)	-2.4	-14.9	-3.4	-9.6	-5.7	-16.0
% difference from placebo (LSMean) (95% CI)		-12.4 (-13.3; -11.6)*		-6.2 (-7.3; -5.2)*		-10.3 (-11.8; -8.7)*
% of Patients losing greater than or equal to 5% body weight	31.1	83.5	30.2	67.4	47.8	84.8
% difference from placebo (LSMean) (95% CI)		52.4 (48.1; 56.7)*		37.2 (30.7; 43.8)*		37.0 (28.9; 45.2)*
% of Patients losing greater than or equal to 10% body weight	12.0	66.1	10.2	44.5	27.1	73.0
% difference from placebo (LSMean) (95% CI)		54.1 (50.4; 57.9)*		34.3 (28.4; 40.2)*		45.9 (38.0; 53.7)*
% of Patients losing greater than or equal to 15% body weight	4.8	47.9	4.3	25.1	13.2	53.4
% difference from placebo (LSMean) (95% CI)		43.1 (39.8; 46.3)*		20.7 (15.7; 25.8)*		40.2 (33.1; 47.3)*

LSMean = least squares mean; CI = confidence interval

[a]The intent-to-treat population includes all randomized patients. In Study 1, at week 68, the body weight was missing for 7.2% and 11.9% of patients randomized to WEGOVY and placebo, respectively. In Study 2, at week 68, the body weight was missing for 4.0% and 6.7% of patients randomized to WEGOVY and placebo, respectively. In Study 3, at week 68, the body weight was missing for 8.4% and 7.4% of patients randomized to WEGOVY and placebo, respectively. Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

* $p<0.0001$ (unadjusted 2-sided) for superiority.

For Study 4, the primary efficacy parameter was mean percent change in body weight from randomization (week 20) to week 68.

From randomization (week 20) to week 68, treatment with WEGOVY resulted in a statistically significant reduction in body weight compared with placebo (Table 5). Because patients who discontinued WEGOVY during titration and those who did not reach the 2.4 mg weekly dose were not eligible for the randomized treatment period, the results may not reflect the experience of patients in the general population who are first starting WEGOVY.

Table 5. Changes in Body Weight at Week 68 - Study 4 (Obesity or overweight with comorbidity after 20 week run-in)

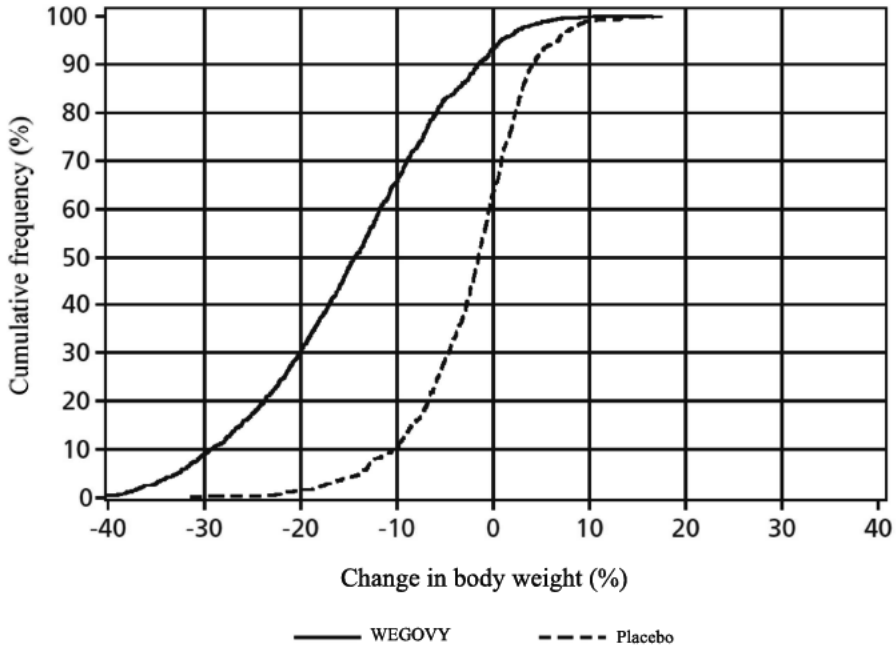
	WEGOVY N = 803[a]	
Body Weight (only randomized patients)		
Mean at week 0 (kg)	107.2	
	PLACEBO N = 268	**WEGOVY N = 535**
Body Weight		
Mean at week 20 (SD) (kg)	95.4 (22.7)	96.5 (22.5)
% change from week 20 at week 68 (LSMean)	6.9	-7.9
% difference from placebo (LSMean) (95% CI)		-14.8 (-16.0; -13.5)[*]

LSMean = least squares mean; CI = confidence interval
[a]902 patients were enrolled at week 0 with a mean baseline body weight of 106.8 kg. The intent-to-treat population includes all randomized patients. At week 68, the body weight was missing for 2.8% and 6.7% of patients randomized to WEGOVY and placebo, respectively. Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).
[*]$p<0.001$ (unadjusted 2-sided) for superiority, controlled for multiplicity.

A reduction in body weight was observed with WEGOVY irrespective of age, sex, race, ethnicity, BMI at baseline, body weight (kg) at baseline, and level of renal function impairment.

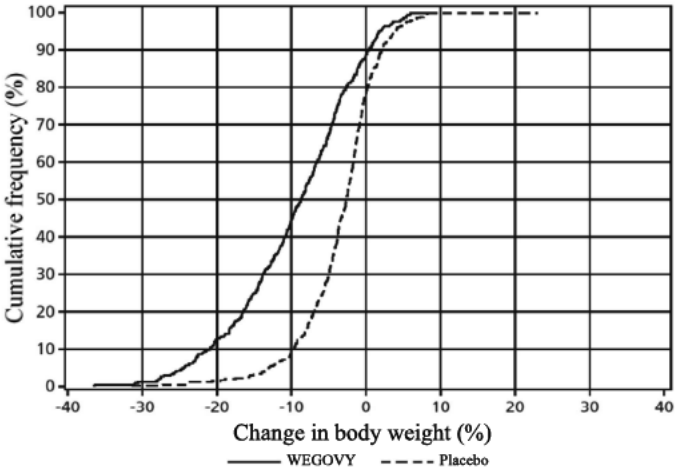
The cumulative frequency distributions of change in body weight are shown in Figure 4 and Figure 5 for Studies 1 and 2. One way to interpret this figure is to select a change in body weight of interest on the horizontal axis and note the corresponding proportions of patients (vertical axis) in each treatment group who achieved at least that degree of weight loss. For example, note that the vertical line arising from -10% in Study 1 intersects the WEGOVY and placebo curves at approximately 66%, and 12%, respectively, which correspond to the values shown in Table 4.

Figure 4. Change in body weight (%) from baseline to week 68 (Study 1)



Observed data from in-trial period including imputed data for missing observations (RD-MI).

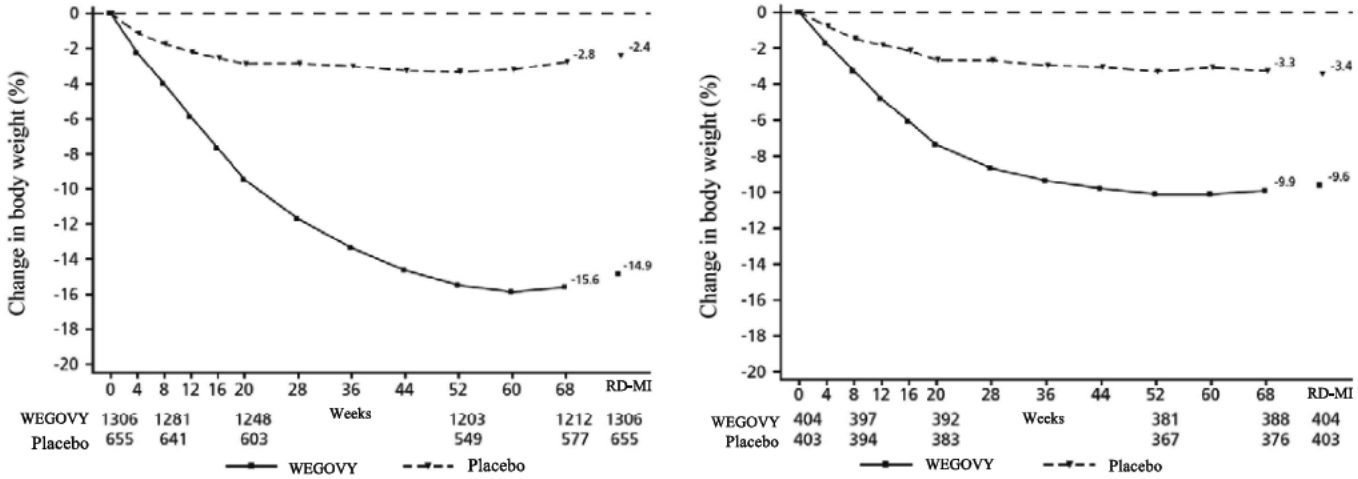
Figure 5. Change in body weight (%) from baseline to week 68 (Study 2)



Observed data from in-trial period including imputed data for missing observations (RD-MI).

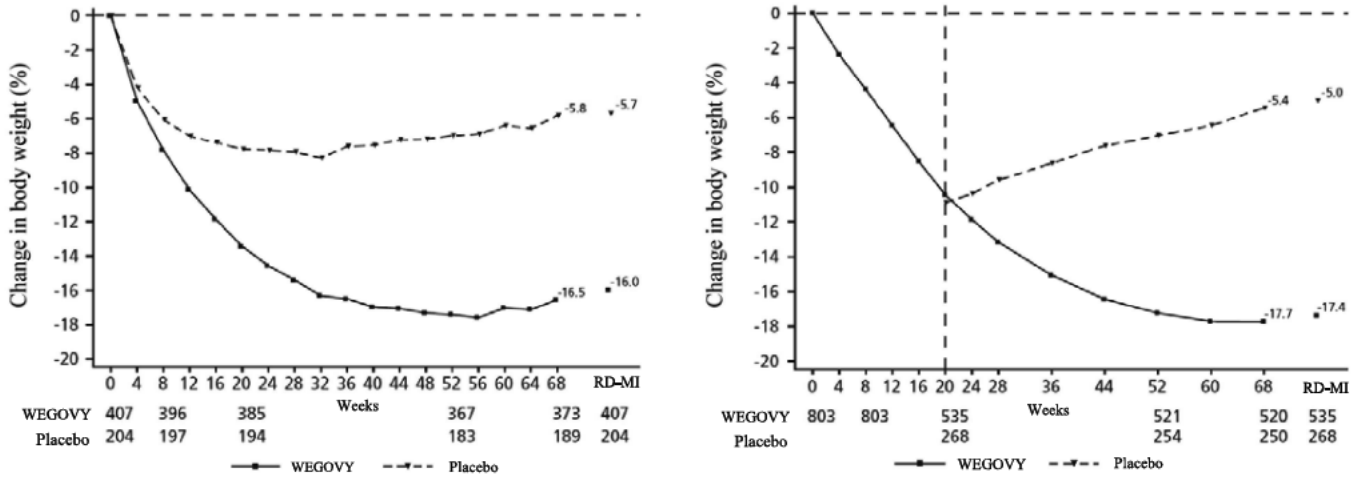
The time courses of weight loss with WEGOVY and placebo from baseline through week 68 are depicted in Figures 6 and Figure 7.

Figure 6. Change from baseline (%) in body weight (Study 1 on left and Study 2 on right)



Observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI)

Figure 7. Change from baseline (%) in body weight (Study 3 on left and Study 4[a] on right)



Observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI)

[a]Change from week 0 was not a primary endpoint in study 4. Dotted line indicates time of randomization. Randomized patients (shown) do not include 99 patients that discontinued during the 20 week run-in period.

14.2 Effect of WEGOVY on Anthropometry and Cardiometabolic Parameters

Changes in waist circumference and cardiometabolic parameters with WEGOVY are shown in Table 6 for Studies 1, 2, and 3 and in Table 7 for Study 4, respectively.

Table 6. Changes in Anthropometry and Cardiometabolic Parameters at Week 68 in Studies 1, 2 and 3

	Study 1 (Obesity or overweight with comorbidity)		Study 2 (Type 2 diabetes with obesity or overweight)		Study 3 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)	
Intention-to-Treat	PLACEBO N = 655	WEGOVY N = 1306	PLACEBO N = 403	WEGOVY N = 404	PLACEBO N = 204	WEGOVY N = 407
Waist Circumference (cm)						
Baseline	114.8	114.6	115.5	114.5	111.8	113.6
Changes from baseline (LSMean[1])	-4.1	-13.5	-4.5	-9.4	-6.3	-14.6
Difference from placebo (LSMean)		-9.4		-4.9		-8.3
Systolic Blood Pressure (mmHg)						
Baseline	127	126	130	130	124	124
Changes from baseline (LSMean[1])	-1.1	-6.2	-0.5	-3.9	-1.6	-5.6
Difference from placebo (LSMean)		-5.1		-3.4		-3.9
Diastolic Blood Pressure (mmHg)[2]						
Baseline	80	80	80	80	81	80
Changes from baseline (LSMean[1])	-0.4	-2.8	-0.9	-1.6	-0.8	-3.0
Difference from placebo (LSMean)		-2.4		-0.7		-2.2
Heart Rate[2,3]						
Baseline	72	72	76	75	71	71
Changes from baseline (LSMean)	-0.7	3.5	-0.2	2.5	2.1	3.1
Difference from placebo (LSMean)		4.3		2.7		1.0

	Study 1 (Obesity or overweight with comorbidity)		Study 2 (Type 2 diabetes with obesity or overweight)		Study 3 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)	
Intention-to-Treat	PLACEBO N = 655	WEGOVY N = 1306	PLACEBO N = 403	WEGOVY N = 404	PLACEBO N = 204	WEGOVY N = 407
HbA1c (%)[2]						
Baseline	5.7	5.7	8.1	8.1	5.8	5.7
Changes from baseline (LSMean[1])	-0.2	-0.4	-0.4	-1.6	-0.3	-0.5
Difference from placebo (LSMean)		-0.3		-1.2		-0.2
Total Cholesterol (mg/dL)[2*]						
Baseline	192.1	189.6	170.8	170.8	188.7	185.4
Percent Change from baseline (LSMean[1])	0.1	-3.3	-0.5	-1.4	2.1	-3.9
Relative difference from placebo (LSMean)		-3.3		-0.9		-5.8
LDL Cholesterol (mg/dL)[2*]						
Baseline	112.5	110.3	90.1	90.1	111.8	107.7
Percent Change from baseline (LSMean[1])	1.3	-2.5	0.1	0.5	2.6	-4.7
Relative difference from placebo (LSMean)		-3.8		0.4		-7.1
HDL (mg/dL)[2*]						
Baseline	49.5	49.4	43.8	44.7	50.9	51.6
Percent Change from baseline (LSMean[1])	1.4	5.2	4.1	6.9	5.0	6.5
Relative difference from placebo (LSMean)		3.8		2.7		1.5
Triglycerides (mg/dL)[2*]						
Baseline	127.9	126.2	159.5	154.9	110.9	107.9
Percent Change from baseline (LSMean[1])	-7.3	-21.9	-9.4	-22.0	-6.5	-22.5
Relative difference from placebo (LSMean)		-15.8		-13.9		-17.0

Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI)

[1]Model based estimates based on an analysis of covariance model including treatment (and stratification factors for Study 2 only) as a factor and baseline value as a covariate

[2]Not included in the pre-specified hierarchical testing (except HbA_{1c} for Study 2)

[3]Model based estimates based on a mixed model for repeated measures including treatment (and stratification factors for Study 2 only) as a factor and baseline values as a covariate

*Baseline value is the geometric mean

Table 7. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 4 (Obesity or overweight with comorbidity after 20 week run-in)

	PLACEBO N = 268		WEGOVY N = 535		
	Randomization (week 20)	**Change from Randomization (week 20) to week 68 (LSMean[1])**	**Randomization (week 20)**	**Change from Randomization (week 20) to week 68 (LSMean[1])**	**Difference from placebo (LSMean)**
Waist Circumference (cm)	104.7	3.3	105.5	-6.4	-9.7
Systolic Blood Pressure (mmHg)	121	4.4	121	0.5	-3.9
Diastolic Blood Pressure (mmHg)[2]	78	0.9	78	0.3	-0.5
Heart Rate[2,3]	76	-5.3	76	-2.0	3.3
HbA1c (%)[2]	5.4	0.1	5.4	-0.1	-0.2
	Randomization (week 20)	**% Change from Randomization (week 20) (LSMean[1])**	**Randomization (week 20)**	**% Change from Randomization (week 20) (LSMean[1])**	**Relative difference from placebo (LSMean)**
Total Cholesterol (mg/dL)[2*]	175.1	11.4	175.9	4.9	-5.8
LDL Cholesterol (mg/dL)[2*]	109.1	7.6	108.7	1.1	-6.1
HDL Cholesterol (mg/dL)[2*]	43.6	17.8	44.5	18.2	0.3
Triglycerides (mg/dL)[2*]	95.3	14.8	98.1	-5.6	-17.8

Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI)
[1]Model based estimates based on an analysis of covariance model including treatment as a factor and baseline value as a covariate
[2]Not included in the pre-specified hierarchical testing
[3]Model based estimates based on a mixed model for repeated measures including treatment as a factor and baseline values as a covariate
*Baseline value is the geometric mean

14.3 Cardiovascular Outcomes Trial of Semaglutide 0.5 mg and 1 mg in Patients with Type 2 Diabetes and Cardiovascular Disease

Semaglutide 0.5 mg and 1 mg (OZEMPIC®) are used in the treatment of type 2 diabetes mellitus in adults. The efficacy of semaglutide at doses of 0.5 mg and 1 mg have not been established for chronic weight management.

SUSTAIN 6 was a 104-week, double-blind trial in which 3297 patients with type 2 diabetes and atherosclerotic cardiovascular disease were randomized to semaglutide 0.5 mg once-weekly, semaglutide 1 mg once-weekly, or placebo in addition to standard-of-care for a median study observation time of 2.1 years. In total, 2,735 (83%) of the patients had a history of cardiovascular disease and 562 (17%) were at high risk but without known cardiovascular disease. The mean age at baseline was 65 years, and 61% were men. Overall, 83% were White, 7% were Black or African American, and 8% were Asian. A total of 16% were identified as Hispanic or Latino.

In total, 98.0% of the patients completed the trial and the vital status was known at the end of the trial for 99.6%. The primary composite endpoint was the time from randomization to first occurrence of a major adverse cardiovascular event (MACE): cardiovascular death, non-fatal myocardial infarction or non-fatal stroke. The total number of primary component MACE endpoints was 254 (108 [6.6%] with semaglutide and 146 [8.9%] with placebo). No increased risk for MACE was observed with semaglutide 0.5 mg and 1 mg.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

WEGOVY injection is a clear, colorless solution in a pre-filled, disposable, single-dose pen-injector with an integrated needle in the following packaging configurations:

Total Strength per Total Volume	Dose per Pen	Carton Contents	NDC
0.25 mg/0.5 mL	1 dose of 0.25 mg	4 pens	0169-4525-14
0.5 mg/0.5 mL	1 dose of 0.5 mg	4 pens	0169-4505-14
1 mg/0.5 mL	1 dose of 1 mg	4 pens	0169-4501-14
1.7 mg/0.75 mL	1 dose of 1.7 mg	4 pens	0169-4517-14
2.4 mg/0.75 mL	1 dose of 2.4 mg	4 pens	0169-4524-14

Recommended Storage

Store the WEGOVY single-dose pen in the refrigerator from 2°C to 8°C (36°F to 46°F). If needed, prior to cap removal, the pen can be kept from 8°C to 30°C (46°F to 86°F) up to 28 days. Do not freeze. Protect WEGOVY from light. WEGOVY must be kept in the original carton until time of administration. Discard the WEGOVY pen after use.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Risk of Thyroid C-cell Tumors

Inform patients that semaglutide causes thyroid C-cell tumors in rodents and that the human relevance of this finding has not been determined. Counsel patients to report symptoms of thyroid tumors (e.g., a lump in the neck, hoarseness, dysphagia, or dyspnea) to their physician *[see Boxed Warning and Warnings and Precautions (5.1)]*.

Acute Pancreatitis

Inform patients of the potential risk for acute pancreatitis. Instruct patients to discontinue WEGOVY promptly and contact their physician if pancreatitis is suspected (severe abdominal pain that may radiate to the back, and which may or may not be accompanied by vomiting) *[see Warnings and Precautions (5.2)]*.

Acute Gallbladder Disease

Inform patients of the risk of acute gallbladder disease. Advise patients that substantial or rapid weight loss can increase the risk of gallbladder disease, but that gallbladder disease may also occur in the absence of substantial or rapid weight loss. Instruct patients to contact their healthcare provider for appropriate clinical follow-up if gallbladder disease is suspected *[see Warnings and Precautions (5.3)]*.

Hypoglycemia

Inform patients of the risk of hypoglycemia and educate patients on the signs and symptoms of hypoglycemia. Advise patients with type 2 diabetes mellitus on glycemic lowering therapy that they may have an increased risk of hypoglycemia when using WEGOVY and to report signs and/or symptoms of hypoglycemia to their healthcare provider *[see Warnings and Precautions (5.4)]*.

Dehydration and Renal Impairment

Advise patients treated with WEGOVY of the potential risk of dehydration due to gastrointestinal adverse reactions and take precautions to avoid fluid depletion. Inform patients of the potential risk for worsening renal function and explain the associated signs and symptoms of renal impairment, as well as the possibility of dialysis as a medical intervention if renal failure occurs *[see Warnings and Precautions (5.5)]*.

Hypersensitivity

Inform patients that serious hypersensitivity reactions have been reported during postmarketing use of semaglutide, the active ingredient in WEGOVY. Advise patients on the symptoms of hypersensitivity reactions and instruct them to stop taking WEGOVY and seek medical advice promptly if such symptoms occur *[see Warnings and Precautions (5.6)]*.

Diabetic Retinopathy Complications in Patients with Type 2 Diabetes
Inform patients with type 2 diabetes to contact their physician if changes in vision are experienced during treatment with WEGOVY *[see Warnings and Precautions (5.7)]*.

Heart Rate Increase
Instruct patients to inform their healthcare providers of palpitations or feelings of a racing heartbeat while at rest during WEGOVY treatment *[see Warnings and Precautions (5.8)]*.

Suicidal Behavior and Ideation
Advise patients to report emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Inform patients that if they experience suicidal thoughts or behaviors, they should stop taking WEGOVY *[see Warnings and Precautions (5.9)]*.

Pregnancy
WEGOVY may cause fetal harm. Advise patients to inform their healthcare provider of a known or suspected pregnancy. Advise patients who are exposed to WEGOVY during pregnancy to contact Novo Nordisk at 1-800-727-6500 *[see Use in Specific Populations (8.1)]*.

Manufactured by:
Novo Nordisk A/S
DK-2880 Bagsvaerd
Denmark

For information about WEGOVY contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536
1-833-934-6891

Date of Issue: June 2021
Version: 1

PATENT INFORMATION: http://www.novonordisk-us.com/products/product-patents.html

Medication Guide

WEGOVY™ (wee-GOH-vee)

(semaglutide) injection, for subcutaneous use

Read this Medication Guide and Instructions for Use before you start using WEGOVY and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about WEGOVY?

WEGOVY may cause serious side effects, including:

- **Possible thyroid tumors, including cancer.** Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rodents, WEGOVY and medicines that work like WEGOVY caused thyroid tumors, including thyroid cancer. It is not known if WEGOVY will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.
- Do not use WEGOVY if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC), or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

What is WEGOVY?

WEGOVY is an injectable prescription medicine used for adults with obesity or overweight (excess weight) who also have weight-related medical problems to help them lose weight and keep the weight off.

- WEGOVY should be used with a reduced calorie meal plan and increased physical activity.
- WEGOVY contains semaglutide and should not be used with other semaglutide-containing products or other GLP-1 receptor agonist medicines.
- It is not known if WEGOVY is safe and effective when taken with other prescription, over-the-counter, or herbal weight loss products.
- It is not known if WEGOVY can be used safely in people with a history of pancreatitis.
- It is not known if WEGOVY is safe and effective for use in children under 18 years of age.

Do not use WEGOVY if:

- you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC) or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- you have had a serious allergic reaction to semaglutide or any of the ingredients in WEGOVY. See the end of this Medication Guide for a complete list of ingredients in WEGOVY. Symptoms of a serious allergic reaction include:
    - swelling of your face, lips, tongue or throat
    - problems breathing or swallowing
    - severe rash or itching
    - fainting or feeling dizzy
    - very rapid heartbeat

Before using WEGOVY, tell your healthcare provider if you have any other medical conditions, including if you:

- have or have had problems with your pancreas or kidneys.
- have type 2 diabetes and a history of diabetic retinopathy.
- have or have had depression or suicidal thoughts, or mental health issues.
- are pregnant or plan to become pregnant. WEGOVY may harm your unborn baby. You should stop using WEGOVY 2 months before you plan to become pregnant.
    - **Pregnancy Exposure Registry**: There is a pregnancy exposure registry for women who use WEGOVY during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry or you may contact Novo Nordisk at 1-800-727-6500.
- are breastfeeding or plan to breastfeed. It is not known if WEGOVY passes into your breast milk. You should talk with your healthcare provider about the best way to feed your baby while using WEGOVY.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. WEGOVY may affect the way some medicines work and some medicines may affect the way WEGOVY works. Tell your healthcare provider if you are taking other medicines to treat diabetes,

including sulfonylureas or insulin. WEGOVY slows stomach emptying and can affect medicines that need to pass through the stomach quickly.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use WEGOVY?

- Read the **Instructions for Use** that comes with WEGOVY.
- Use WEGOVY exactly as your healthcare provider tells you to.
- **Your healthcare provider should show you how to use WEGOVY before you use it for the first time.**
- WEGOVY is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm. **Do not** inject WEGOVY into a muscle (intramuscularly) or vein (intravenously).
- Change (rotate) your injection site with each injection. **Do not** use the same site for each injection.
- **Use WEGOVY 1 time each week, on the same day each week, at any time of the day.**
- Start WEGOVY with 0.25 mg per week in your first month. In your second month, increase your weekly dose to 0.5 mg. In the third month, increase your weekly dose to 1 mg. In the fourth month, increase your weekly dose to 1.7 mg and in the fifth month onwards, increase your weekly dose to the full dose of 2.4 mg. If you need to change the day of the week, you may do so as long as your last dose of WEGOVY was given **2** or more days before.
- If you miss a dose of WEGOVY and the next scheduled dose is more than 2 days away (48 hours), take the missed dose as soon as possible. If you miss a dose of WEGOVY and the next schedule dose is less than 2 days away (48 hours), do not administer the dose. Take your next dose on the regularly scheduled day.
- If you miss doses of WEGOVY for more than 2 weeks, take your next dose on the regularly scheduled day or call your healthcare provider to talk about how to restart your treatment.
- You can take WEGOVY with or without food.
- If you take too much WEGOVY, you may have severe nausea, severe vomiting and severe low blood sugar. Call your healthcare provider or go to the nearest hospital emergency room right away if you experience any of these symptoms.

What are the possible side effects of WEGOVY?

WEGOVY may cause serious side effects, including:

- **See "What is the most important information I should know about WEGOVY?"**
- **inflammation of your pancreas (pancreatitis).** Stop using WEGOVY and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.
- **gallbladder problems.** WEGOVY may cause gallbladder problems including gallstones. Some gallbladder problems need surgery. Call your healthcare provider if you have any of the following symptoms:
  - pain in your upper stomach (abdomen)
  - fever
  - yellowing of skin or eyes (jaundice)
  - clay-colored stools
- **increased risk of low blood sugar (hypoglycemia) in patients with type 2 diabetes, especially those who also take medicines to treat type 2 diabetes mellitus such as sulfonylureas or insulin.** Low blood sugar in patients with type 2 diabetes who receive WEGOVY can be both a serious and common side effect. Talk to your healthcare provider about how to recognize and treat low blood sugar. You should check your blood sugar before you start taking WEGOVY and while you take WEGOVY. Signs and symptoms of low blood sugar may include:
  - dizziness or light-headedness
  - blurred vision
  - anxiety
  - irritability or mood changes
  - sweating
  - slurred speech
  - hunger
  - confusion or drowsiness
  - shakiness
  - weakness
  - headache
  - fast heartbeat
  - feeling jittery
- **kidney problems (kidney failure).** In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse. It is important for you to drink fluids to help reduce your chance of dehydration.

- **serious allergic reactions.** Stop using WEGOVY and get medical help right away, if you have any symptoms of a serious allergic reaction including:
  - swelling of your face, lips, tongue or throat
  - problems breathing or swallowing
  - severe rash or itching
  - fainting or feeling dizzy
  - very rapid heartbeat
- **change in vision in people with type 2 diabetes.** Tell your healthcare provider if you have changes in vision during treatment with WEGOVY.
- **increased heart rate.** WEGOVY can increase your heart rate while you are at rest. Your healthcare provider should check your heart rate while you take WEGOVY. Tell your healthcare provider if you feel your heart racing or pounding in your chest and it lasts for several minutes.
- **depression or thoughts of suicide.** You should pay attention to any mental changes, especially sudden changes in your mood, behaviors, thoughts, or feelings. Call your healthcare provider right away if you have any mental changes that are new, worse, or worry you.

The most common side effects of WEGOVY may include:

- nausea
- diarrhea
- vomiting
- constipation
- stomach (abdomen) pain
- headache
- tiredness (fatigue)
- upset stomach
- dizziness
- feeling bloated
- belching
- gas
- stomach flu
- heartburn

Talk to your healthcare provider about any side effect that bothers you or does not go away. These are not all the possible side effects of WEGOVY.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of WEGOVY.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use WEGOVY for a condition for which it was not prescribed. Do not give WEGOVY to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about WEGOVY that is written for health professionals.

What are the ingredients in WEGOVY?

Active Ingredient: semaglutide

Inactive Ingredients: disodium phosphate dihydrate, sodium chloride, and water for injection

Manufactured by: Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark

WEGOVY™ is a trademark of Novo Nordisk A/S.

PATENT Information: http://novonordisk-us.com/products/product-patents.html

For more information, go to startWegovy.com or call 1-833-Wegovy-1.

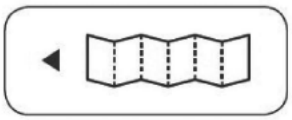
This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: 06/2021

Instructions for Use
WEGOVY™
(semaglutide) injection
WEGOVY comes in five strengths:

0.25 mg / 0.5 mL	0.5 mg / 0.5 mL	1 mg / 0.5 mL	1.7 mg / 0.75 mL	2.4 mg / 0.75 mL

Before you use your WEGOVY pen for the first time, talk to your healthcare provider or your caregiver about how to prepare and inject WEGOVY correctly.

Pull out to get started



Important information

Read this Instructions for Use before you start using WEGOVY. This information does not replace talking to your healthcare provider about your medical condition or treatment.

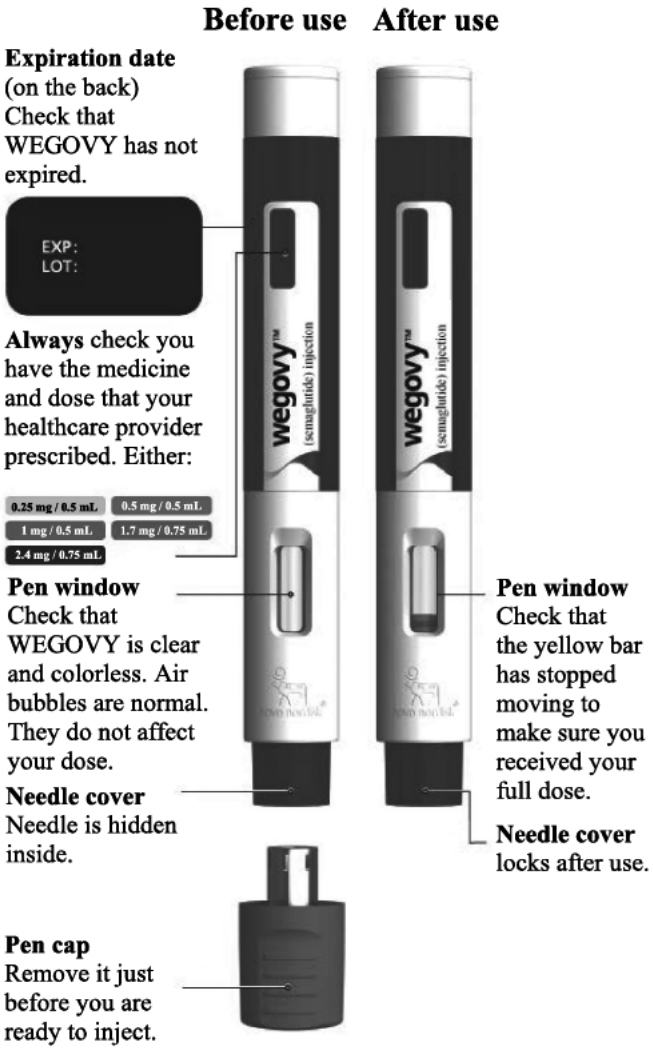
· **Your WEGOVY pen is for 1 time use only.** The WEGOVY pen is for subcutaneous (under the skin) use only.
· **The dose of WEGOVY is already set on your pen.**
· **The needle is covered by the needle cover and the needle will not be seen.**
· Do not remove the pen cap until you are ready to inject.
· Do not touch or push on the needle cover**.** You could get a needle stick injury.
· Your WEGOVY injection will begin when the needle cover is pressed against your skin.
· **Do not** remove the pen from your skin before the yellow bar in the pen window has stopped moving. If the needle is removed earlier, you may not get your full dose of WEGOVY.
· If the yellow bar does not start moving or stops during the injection, contact your healthcare provider or Novo Nordisk at startWegovy.com or call Novo Nordisk Inc. at 1-833-934-6891.
· The needle cover will lock when the pen is removed from your skin**. You cannot stop the injection and restart it later.**
· People who are blind or have vision problems should not use the WEGOVY pen without help from a person trained to use the WEGOVY pen**.**

How do I store WEGOVY?

- Store the WEGOVY pen in the refrigerator between 2°C to 8°C (36°F to 46°F).
- If needed, before removing the pen cap, WEGOVY can be stored from 8°C to 30°C (46°F to 86°F) in the original carton for up to 28 days.
- Keep WEGOVY in the original carton to protect it from light.
- **Do not freeze**.
- Throw away the pen if WEGOVY has been frozen, has been exposed to light or temperatures above 30°C (86°F), or has been out of the refrigerator for 28 days or longer.

Keep WEGOVY and all medicines out of the reach of children.

WEGOVY pen parts



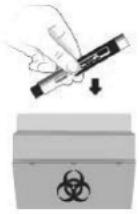
How to use your WEGOVY pen	**Do not use your WEGOVY pen without receiving training from your healthcare provider.** Make sure that you or your caregiver know how to give an injection with the pen before you start your treatment.

Read and follow the instructions so that you use your WEGOVY pen correctly:

Preparation

Step 1. Prepare for your injection.

- **Supplies you will need to give your WEGOVY injection:**
  - WEGOVY pen
  - 1 alcohol swab or soap and water
  - 1 gauze pad or cotton ball
  - 1 sharps disposable container for used WEGOVY pens



- **Wash your hands.**
- **Check your WEGOVY pen.**
  Do not use your WEGOVY pen if:
  - The pen appears to have been used or any part of the pen appears broken, for example if it has been dropped.
  - The WEGOVY medicine is not clear and colorless through the pen window.
  - The expiration date (EXP) has passed.

Contact Novo Nordisk at 1-833-934-6891 if your WEGOVY pen fails any of these checks.

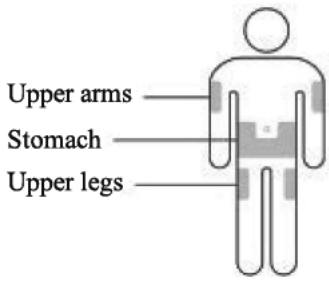
Step 2. Choose your injection site.

• Your healthcare provider can help you choose the injection site that is best for you
  - You may inject into your upper legs (front of the thighs) or lower stomach (keep 2 inches away from your belly button).
  - Another person may give the injection in the upper arm.

• Do not inject into an area where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

• You may inject in the same body area each week, but make sure it is not in the same spot each time.

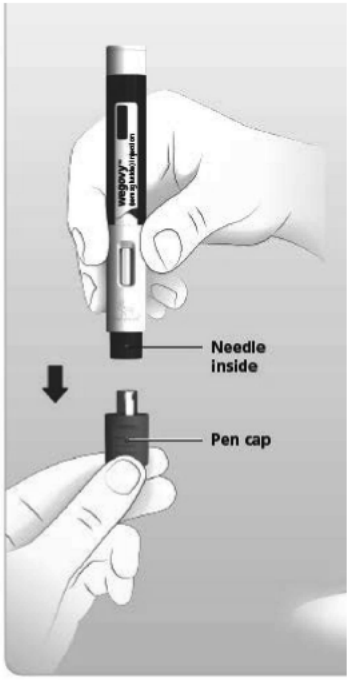
Clean the injection site with an alcohol swab or soap and water. Do not touch the injection site after cleaning.



Injection

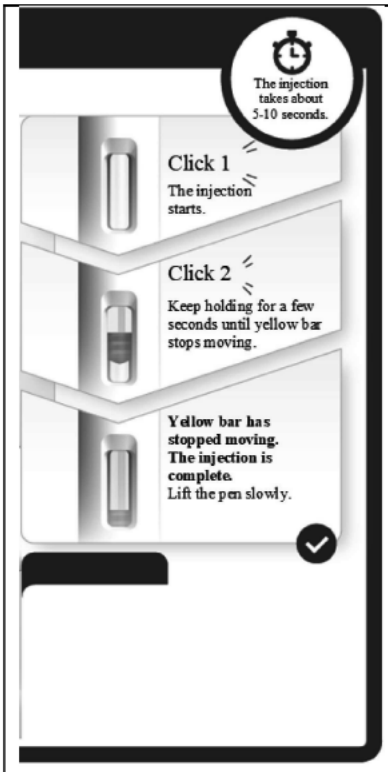
Step 3. Remove pen cap.

• Pull the pen cap straight off your pen.



Step 4. Inject WEGOVY.

- **Push the pen firmly against your skin until the yellow bar has stopped moving.**
  If the yellow bar does not start moving, press the pen more firmly against your skin.
- **You will hear 2 clicks during the injection.**
  - Click 1: the injection has started.
  - Click 2: the injection is ongoing.



Throw away pen

Step 5. Throw away (dispose of) pen.

Safely dispose of the WEGOVY pen right away after each use. See **"How do I throw away (dispose of) WEGOVY pens?"**

• What if blood appears after injection?

If blood appears at the injection site, press the site lightly with a gauze pad or cotton ball.

How do I throw away (dispose of) WEGOVY pens?

Put the used WEGOVY pen in an FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of)** the pen in your household trash.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- able to be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe

How do I care for my pen?

Protect your pen

- Do not drop your pen or knock it against hard surfaces.
- Do not expose your pen to any liquids.
- If you think that your pen may be damaged, do not try to fix it. Use a new one.
- Keep the pen cap on until you are ready to inject. Your pen will no longer be sterile if you store an unused pen without the cap, if you pull the pen cap off and put it on again, or if the pen cap

sharps disposal, and for specific sharps disposal in the state that you live in, go to the FDA's website at http://www.fda.gov/safesharpsdisposal. · Do not reuse the pen. · Do not recycle the pen or sharps disposal container, or throw them into household trash. **Important:** Keep your WEGOVY pen, sharps disposal container and all medicines out of the reach of children.	is missing. This could lead to an infection. If you have any questions about WEGOVY, go to startWegovy.com or call Novo Nordisk Inc. at 1-833-Wegovy-1

Manufactured by:
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsvaerd, Denmark

For information about WEGOVY, go to startWegovy.com or contact:
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Issued: 06/2021
Version: 1

WEGOVY™ is a trademark of Novo Nordisk A/S.

PATENT Information: http://novonordisk-us.com/products/product-patents.html

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 0.25 mg solution for injection in pre-filled pen
Wegovy 0.5 mg solution for injection in pre-filled pen
Wegovy 1 mg solution for injection in pre-filled pen
Wegovy 1.7 mg solution for injection in pre-filled pen
Wegovy 2.4 mg solution for injection in pre-filled pen
Wegovy 0.25 mg FlexTouch solution for injection in pre-filled pen
Wegovy 0.5 mg FlexTouch solution for injection in pre-filled pen
Wegovy 1 mg FlexTouch solution for injection in pre-filled pen
Wegovy 1.7 mg FlexTouch solution for injection in pre-filled pen
Wegovy 2.4 mg FlexTouch solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pre-filled pen, single-dose

Wegovy 0.25 mg solution for injection
Each single-dose pre-filled pen contains 0.25 mg semaglutide* in 0.5 mL solution. One mL of solution contains 0.5 mg of semaglutide*.

Wegovy 0.5 mg solution for injection
Each single-dose pre-filled pen contains 0.5 mg semaglutide* in 0.5 mL solution. One mL of solution contains 1 mg of semaglutide*.

Wegovy 1 mg solution for injection
Each single-dose pre-filled pen contains 1 mg semaglutide* in 0.5 mL solution. One mL of solution contains 2 mg of semaglutide*.

Wegovy 1.7 mg solution for injection
Each single-dose pre-filled pen contains 1.7 mg semaglutide* in 0.75 mL solution. One mL of solution contains 2.27 mg of semaglutide*.

Wegovy 2.4 mg solution for injection
Each single-dose pre-filled pen contains 2.4 mg semaglutide* in 0.75 mL solution. One mL of solution contains 3.2 mg of semaglutide*.

Pre-filled pen, FlexTouch

Wegovy 0.25 mg FlexTouch solution for injection
Each pre-filled pen contains 1 mg semaglutide* in 1.5 mL solution. One mL of solution contains 0.68 mg semaglutide*. One pre-filled pen contains 4 doses of 0.25 mg.

Wegovy 0.5 mg FlexTouch solution for injection
Each pre-filled pen contains 2 mg semaglutide* in 1.5 mL solution. One mL of solution contains 1.34 mg semaglutide*. One pre-filled pen contains 4 doses of 0.5 mg.

Wegovy 1 mg FlexTouch solution for injection
Each pre-filled pen contains 4 mg semaglutide* in 3 mL solution. One mL of solution contains 1.34 mg semaglutide*. One pre-filled pen contains 4 doses of 1 mg.

Wegovy 1.7 mg FlexTouch solution for injection
Each pre-filled pen contains 6.8 mg semaglutide* in 3 mL solution. One mL of solution contains 2.27 mg semaglutide*. One pre-filled pen contains 4 doses of 1.7 mg.

Wegovy 2.4 mg FlexTouch solution for injection
Each pre-filled pen contains 9.6 mg semaglutide* in 3 mL solution. One mL of solution contains 3.2 mg semaglutide*. One pre-filled pen contains 4 doses of 2.4 mg.

*human glucagon-like peptide-1 (GLP-1) analogue produced in *Saccharomyces cerevisiae* cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)
Clear and colourless isotonic solution; pH=7.4.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Wegovy is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management, including weight loss and weight maintenance, in adults with an initial Body Mass Index (BMI) of

- ≥30 kg/m^2 (obesity), or
- ≥27 kg/m^2 to <30 kg/m^2 (overweight) in the presence of at least one weight-related comorbidity e.g. dysglycaemia (prediabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease.

4.2 Posology and method of administration

Posology

The maintenance dose of semaglutide 2.4 mg once-weekly is reached by starting with a dose of 0.25 mg. To reduce the likelihood of gastrointestinal symptoms, the dose should be escalated over a 16-week period to a maintenance dose of 2.4 mg once weekly (see Table 1). In case of significant gastrointestinal symptoms, consider delaying dose escalation or lowering to the previous dose until symptoms have improved.

Table 1 Dose escalation schedule

Dose escalation	**Weekly dose**
Week 1–4	0.25 mg
Week 5–8	0.5 mg
Week 9–12	1 mg
Week 13–16	1.7 mg
Maintenance dose	2.4 mg

Weekly doses higher than 2.4 mg are not recommended.

Patients with type 2 diabetes
When initiating semaglutide in patients with type 2 diabetes, consider reducing the dose of concomitantly administered insulin or insulin secretagogues (such as sulfonylureas) to reduce the risk of hypoglycaemia, see section 4.4.

Missed dose
If a dose is missed, it should be administered as soon as possible and within 5 days after the missed dose. If more than 5 days have passed, the missed dose should be skipped, and the next dose should be administered on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule. If more doses are missed, reducing the starting dose for re-initiation should be considered.

Special populations

Elderly (≥65 years old)
No dose adjustment is required based on age. Therapeutic experience in patients ≥75 years of age is limited, and greater sensitivity of some older individuals cannot be excluded.

Patients with renal impairment
No dose adjustment is required for patients with mild or moderate renal impairment. Experience with the use of semaglutide in patients with severe renal impairment is limited. Semaglutide is not recommended for use in patients with severe renal impairment (eGFR <30 mL/min/1.73m^2) including patients with end-stage renal disease (see sections 4.4, 4.8 and 5.2).

Patients with hepatic impairment
No dose adjustment is required for patients with mild or moderate hepatic impairment. Experience with the use of semaglutide in patients with severe hepatic impairment is limited. Semaglutide is not recommended for use in patients with severe hepatic impairment and should be used cautiously in patients with mild or moderate hepatic impairment (see sections 4.4 and 5.2).

Paediatric population
The safety and efficacy of semaglutide in children and adolescents below 18 years have not yet been established. No data are available.

Method of administration

Subcutaneous use.

Wegovy is administered once weekly at any time of the day, with or without meals.

It is to be injected subcutaneously in the abdomen, in the thigh or in the upper arm. The injection site can be changed. It should not be administered intravenously or intramuscularly.

The day of weekly administration can be changed if necessary, as long as the time between two doses is at least 3 days (>72 hours). After selecting a new dosing day, once-weekly dosing should be continued.

When administering Wegovy pre-filled pen for single use, the pen should be pressed firmly against the skin until the yellow bar has stopped moving. The injection takes about 5–10 seconds.

Patients should be advised to read the instruction for use included in the package leaflet carefully before administering the medicinal product.

For further information before administration see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Dehydration

Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions that can cause dehydration, which in rare cases can lead to a deterioration of renal function.
Patients should be advised of the potential risk of dehydration in relation to gastrointestinal side effects and take precautions to avoid fluid depletion.

Acute pancreatitis

Acute pancreatitis has been observed with the use of GLP-1 receptor agonists (see section 4.8).
Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, semaglutide should be discontinued; if confirmed, semaglutide should not be restarted.
Caution should be exercised in patients with a history of pancreatitis.
In the absence of other signs and symptoms of acute pancreatitis, elevations in pancreatic enzymes alone are not predictive of acute pancreatitis.

Patients with type 2 diabetes

Semaglutide should not be used as a substitute for insulin in patients with type 2 diabetes.

Semaglutide should not be used in combination with other GLP-1 receptor agonist products. It has not been evaluated and an increased risk of adverse reactions related to overdose is considered likely.

Hypoglycaemia in patients with type 2 diabetes

Insulin and sulfonylurea are known to cause hypoglycaemia. Patients treated with semaglutide in combination with a sulfonylurea or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia can be lowered by reducing the dose of sulfonylurea or insulin when initiating treatment with a GLP-1 receptor agonist. The addition of Wegovy in patients treated with insulin has not been evaluated.

Diabetic retinopathy in patients with type 2 diabetes

In patients with diabetic retinopathy treated with semaglutide, an increased risk of developing diabetic retinopathy complications has been observed (see section 4.8). Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy, but other mechanisms cannot be excluded. Patients with diabetic retinopathy using semaglutide should be monitored closely and treated according to clinical guidelines. There is no experience with Wegovy in patients with type 2 diabetes with uncontrolled or potentially unstable diabetic retinopathy. In these patients, treatment with Wegovy is not recommended.

Populations not studied

The safety and efficacy of Wegovy have not been investigated in patients:
– treated with other products for weight management,
– with type 1 diabetes,
– with severe renal impairment (see section 4.2),
– with severe hepatic impairment (see section 4.2),
– with congestive heart failure New York Heart Association (NYHA) class IV.

Use in these patients is not recommended.

There is limited experience with Wegovy in patients:
– aged 75 years or more (see section 4.2),
– with mild or moderate hepatic impairment (see section 4.2),
– with inflammatory bowel disease,
– with diabetic gastroparesis.
Use with caution in these patients.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Semaglutide delays gastric emptying and could potentially influence the absorption of concomitantly administered oral medicinal products. No clinically relevant effect on the rate of gastric emptying was observed with semaglutide 2.4 mg, probably due to a tolerance effect. Semaglutide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption.

Paracetamol

Semaglutide delays the rate of gastric emptying as assessed by paracetamol pharmacokinetics during a standardised meal test. Paracetamol $AUC_{0\text{-}60min}$ and C_{max} were decreased by 27% and 23%, respectively, following concomitant use of semaglutide 1 mg. The total paracetamol exposure ($AUC_{0\text{-}5h}$) was not affected. No clinically relevant effect on paracetamol was observed with semaglutide. No dose adjustment of paracetamol is necessary when administered with semaglutide.

Oral contraceptives

Semaglutide is not anticipated to decrease the effectiveness of oral contraceptives. It did not change the overall exposure of ethinylestradiol and levonorgestrel to a clinically relevant degree, when an oral contraceptive combination medicinal product (0.03 mg ethinylestradiol/0.15 mg levonorgestrel) was co-administered with semaglutide. Exposure of ethinylestradiol was not affected; an increase of 20% was observed for levonorgestrel exposure at steady state. C_{max} was not affected for any of the compounds.

Atorvastatin

Semaglutide did not change the overall exposure of atorvastatin following a single dose administration of atorvastatin (40 mg). Atorvastatin C_{max} was decreased by 38%. This was assessed not to be clinically relevant.

Digoxin

Semaglutide did not change the overall exposure or C_{max} of digoxin following a single dose of digoxin (0.5 mg).

Metformin

Semaglutide did not change the overall exposure or C_{max} of metformin following dosing of 500 mg twice daily over 3.5 days.

Warfarin

Semaglutide did not change overall exposure or C_{max} of R- and S-warfarin following a single dose of warfarin (25 mg), and the pharmacodynamic effects of warfarin as measured by the international normalised ratio were not affected in a clinically relevant manner. However, upon initiation of semaglutide treatment in patients on warfarin or other coumarin derivatives, frequent monitoring of international normalised ratio (INR) is recommended.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential are recommended to use contraception when treated with semaglutide (see section 4.5).

Pregnancy

Studies in animals have shown reproductive toxicity (see section 5.3). There are limited data from the use of semaglutide in pregnant women. Therefore, semaglutide should not be used during pregnancy. If a patient wishes to become pregnant, or pregnancy occurs, semaglutide should be discontinued. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half-life (see section 5.2).

Breast-feeding

In lactating rats, semaglutide was excreted in milk. A risk to a breast-fed child cannot be excluded. Semaglutide should not be used during breast-feeding.

Fertility

The effect of semaglutide on fertility in humans is unknown. Semaglutide did not affect male fertility in rats. In female rats, an increase in oestrous length and a small reduction in number of ovulations were observed at doses associated with maternal body weight loss.

4.7 Effects on ability to drive and use machines

Semaglutide has no or negligible influence on the ability to drive or use machines. However, dizziness can be experienced mainly during the dose escalation period. Driving or use of machines should be done cautiously if dizziness occurs.

Patients with type 2 diabetes

If semaglutide is used in combination with a sulfonylurea or insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines (see section 4.4).

4.8 Undesirable effects

Summary of safety profile

In four phase 3a trials, 2,650 patients were exposed to Wegovy. The duration of the trials were 68 weeks. The most frequently reported adverse reactions were gastrointestinal disorders including nausea, diarrhoea, constipation and vomiting.

Tabulated list of adverse reactions

Table 2 lists adverse reactions identified in phase 3a clinical trials. The frequencies are based on a pool of the phase 3a trials.

Adverse reactions associated with Wegovy are listed by system organ class and frequency. Frequency categories are defined as: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Table 2 Adverse reactions from controlled phase 3 trials

MedDRA system organ class	**Very common**	**Common**	**Uncommon**	**Rare**
Immune system disorders				Anaphylactic reaction
Metabolism and nutrition disorders		Hypoglycaemia in patients with type 2 diabetes[a]		
Nervous system disorders	Headache[b]	Dizziness[b]		
Eye disorders		Diabetic retinopathy in patients with type 2 diabetes[a]		
Cardiac disorders			Hypotension Orthostatic hypotension Increased heart rate[a,c]	
Gastrointestinal disorders	Vomiting[a,b] Diarrhoea[a,b] Constipation[a,b] Nausea[a,b] Abdominal pain[b,c]	Gastritis[b,c] Gastrooesophageal reflux disease[b] Dyspepsia[b] Eructation[b] Flatulence[b] Abdominal distension[b]	Acute pancreatitis[a]	
Hepatobiliary disorders		Cholelithiasis[a]		
Skin and subcutaneous tissue disorders		Hair loss[a]		Angioedema
General disorders and administration site conditions	Fatigue[b,c]	Injection site reactions[c]		
Investigations			Increased amylase[c] Increased lipase[c]	

[a)] see description of selected adverse reactions below
[b)] mainly seen in the dose-escalation period
[c)] Grouped preferred terms

Description of selected adverse reactions

Gastrointestinal adverse reactions

Over the 68 weeks trial period, nausea occurred in 43.9% of patients when treated with semaglutide (16.1% for placebo), diarrhoea in 29.7% (15.9% for placebo) and vomiting in 24.5% (6.3% for placebo). Most events were mild to moderate in severity and of short duration. Constipation occurred in 24.2% of patients treated with semaglutide (11.1% for placebo) and was mild to moderate in severity and of longer duration. In patients treated with semaglutide, median duration of nausea was 8 days, vomiting 2 days, diarrhoea 3 days, and constipation 47 days.

Patients with moderate renal impairment (eGFR ≥30 mL/min/1.73m^2) may experience more gastrointestinal effects when treated with semaglutide.

The gastrointestinal events led to permanent treatment discontinuation in 4.3% of patients.

Acute pancreatitis
The frequency of adjudication-confirmed acute pancreatitis reported in phase 3a clinical trials was 0.2% for semaglutide and <0.1% for placebo, respectively.

Acute gallstone disease/Cholelithiasis
Cholelithiasis was reported in 1.6% and led to cholecystitis in 0.6% of patients treated with semaglutide. Cholelithiasis and cholecystitis was reported in 1.1% and 0.3%, respectively, of patients treated with placebo.

Hair loss
Hair loss was reported in 2.5% of patients treated with semaglutide and in 1.0% of patients treated with placebo. The events were mainly of mild severity and most patients recovered while on continued treatment. Hair loss was reported more frequently in patients with a greater weight loss (≥20%).

Increased heart rate
In the phase 3a trials, a mean increase of 3 beats per minute (bpm) from a baseline mean of 72 bpm was observed in patients treated with semaglutide. The proportions of subjects with an increase in pulse from baseline ≥10 bpm at any timepoint during the on-treatment period were 67.0% in the semaglutide group vs. 50.1% in the placebo group.

Immunogenicity
Consistent with the potentially immunogenic properties of medicinal products containing proteins or peptides, patients may develop antibodies following treatment with semaglutide. The proportion of patients testing positive for anti-semaglutide antibodies at any time post-baseline was low (2.9%) and no patients had anti-semaglutide neutralising antibodies or anti-semaglutide antibodies with endogenous GLP-1 neutralising effect at end-of-trial. During treatment, high semaglutide concentrations might have lowered the sensitivity of the assays, hence the risk of false negatives cannot be excluded. However, in subjects testing positive for antibodies during and after treatment, the presence of antibodies was transient and with no apparent impact on efficacy and safety.

Hypoglycaemia in patients with type 2 diabetes
In STEP 2, clinically significant hypoglycaemia was observed in 6.2% (0.1 events/patient year) of subjects treated with semaglutide compared with 2.5% (0.03 events/patient year) of subjects treated with placebo. Hypoglycaemia with semaglutide was seen both with and without concomitant use of sulfonylurea. One episode (0.2% of subjects, 0.002 events/patient year) was reported as severe in a subject not concomitantly treated with a sulfonylurea. The risk of hypoglycaemia was increased when semaglutide was used with a sulfonylurea.

Diabetic retinopathy in patients with type 2 diabetes
A 2-year clinical trial investigated semaglutide 0.5 mg and 1 mg vs. placebo in 3,297 patients with type 2 diabetes, with high cardiovascular risk, long duration of diabetes and poorly controlled blood glucose. In this trial, adjudicated events of diabetic retinopathy complications occurred in more patients treated with semaglutide (3.0%) compared to placebo (1.8%). This was observed in insulin-treated patients with known diabetic retinopathy. The treatment difference appeared early and persisted throughout the trial. In STEP 2, retinal disorders were reported by 6.9% of patients treated with Wegovy, 6.2% of patients treated with semaglutide 1 mg, and 4.2% of patients treated with placebo. The majority of events were reported as diabetic retinopathy (4.0%, 2.7%, and 2.7%, respectively) and non-proliferative retinopathy (0.7%, 0%, and 0%, respectively).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Overdose with semaglutide may be associated with gastrointestinal disorders which could lead to dehydration. In the event of overdose the patient should be observed for clinical signs and appropriate supportive treatment initiated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, glucagon-like peptide-1 (GLP-1) analogues, ATC code: A10BJ06

Mechanism of action

Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1.

GLP-1 is a physiological regulator of appetite and calorie intake, and the GLP-1 receptor is present in several areas of the brain involved in appetite regulation.

Animal studies show that semaglutide works in the brain through the GLP-1 receptor. Semaglutide has direct effects on areas in the brain involved in homeostatic regulation of food intake in the hypothalamus and the brainstem. Semaglutide may affect the hedonic reward system through direct and indirect effects in brain areas including the septum, thalamus and amygdala.

Clinical studies show that semaglutide reduces energy intake, increases feelings of satiety, fullness and control of eating, reduces feelings of hunger, and frequency and intensity of cravings. In addition, semaglutide reduces the preference for high fat foods.

Semaglutide orchestrates the homeostatic and hedonic contributions with executive function to regulate caloric intake, appetite, reward and food choice.

In addition, in clinical studies semaglutide have shown to reduce blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase. During hypoglycaemia, semaglutide diminishes insulin secretion and does not impair glucagon secretion.

GLP-1 receptors are also expressed in the heart, vasculature, immune system and kidneys. Semaglutide has a beneficial effect on plasma lipids, lowered systolic blood pressure and reduced inflammation in clinical studies. Furthermore, animal studies have shown that semaglutide attenuated the development of atherosclerosis and had an anti-inflammatory action in the cardiovascular system.

Pharmacodynamic effects

Appetite, energy intake and food choice
Semaglutide reduces appetite by increasing feelings of fullness and satiety, while lowering hunger and prospective food consumption. In a phase 1 trial, energy intake during an ad libitum meal was 35% lower with semaglutide compared to placebo after 20 weeks of dosing. This was supported by improved control of eating, less food cravings and a relative lower preference for high fat food. Food cravings were further assessed in STEP 5 by a Control of Eating Questionnaire (CoEQ). At week 104, the estimated treatment difference both for control of cravings and craving of savoury food significantly favoured semaglutide, whereas no clear effect was seen for craving of sweet food.

Fasting and postprandial lipids
Semaglutide 1 mg compared to placebo lowered fasting triglyceride and very low density lipoproteins (VLDL) concentrations by 12% and 21%, respectively. The postprandial triglyceride and VLDL response to a high fat meal was reduced with >40%.

Clinical efficacy and safety

The efficacy and safety of semaglutide for weight management in combination with a reduced calorie intake and increased physical activity were evaluated in four 68 weeks double-blinded randomised placebo-controlled phase 3a trials (STEP 1-4). A total of 4,684 patients (2,652 randomised to treatment with semaglutide) were included in these trials. Furthermore, the two-year efficacy and safety of semaglutide compared to placebo were evaluated in a double-blinded randomised placebo-controlled phase 3b trial (STEP 5) including 304 patients (152 in treatment with semaglutide).

Treatment with semaglutide demonstrated superior, clinically meaningful, and sustained weight loss compared with placebo in patients with obesity (BMI ≥30 kg/m^2), or overweight (BMI ≥27 kg/m^2 to <30 kg/m^2) and at least one weight-related comorbidity. Furthermore, across the trials, a higher proportion of patients achieved ≥5%, ≥10%, ≥15% and ≥20% weight loss with semaglutide compared with placebo. The reduction in body weight occurred irrespective of the presence of gastrointestinal symptoms such as nausea, vomiting or diarrhoea.

Treatment with semaglutide also showed statistically significant improvements in waist circumference, systolic blood pressure and physical functioning compared to placebo.

Efficacy was demonstrated regardless of age, sex, race, ethnicity, baseline body weight, BMI, presence of type 2 diabetes and level of renal function. Variations in efficacy existed within all subgroups. Relatively greater weight loss was observed in women and in patients without type 2 diabetes as well as in patients with a lower versus higher baseline body weight.

STEP 1: Weight management

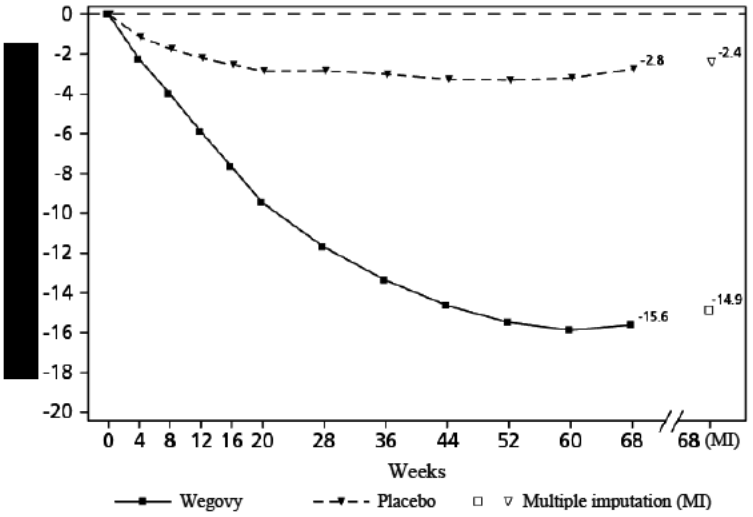
In a 68-week double-blind trial, 1,961 patients with obesity (BMI ≥30 kg/m^2), or with overweight (BMI ≥27 kg/m^2 to <30 kg/m^2) and at least one weight-related comorbidity were randomised to semaglutide or placebo. All patients were on a reduced-calorie diet and increased physical activity throughout the trial.

Weight loss occurred early and continued throughout the trial. At end of treatment (week 68), the weight loss was superior and clinically meaningful compared with placebo (see Table 3 and Figure 1). Furthermore, a higher proportion of patients achieved ≥5%, ≥10%, ≥15% and ≥20% weight loss with semaglutide compared with placebo (see Table 3). Among patients with prediabetes at baseline, a higher proportion of patients had a normo-glycaemic status at end of treatment with semaglutide compared to placebo (84.1% vs. 47.8%).

Table 3 STEP 1: Results at week 68

	Wegovy	Placebo
Full analysis set (N)	1,306	655
Body weight		
Baseline (kg)	105.4	105.2
Change (%) from baseline[1,2]	-14.9	-2.4
Difference (%) from placebo[1] [95% CI]	-12.4 [-13.4; -11.5]*	-
Change (kg) from baseline	-15.3	-2.6
Difference (kg) from placebo[1] [95% CI]	-12.7 [-13.7; -11.7]	-
Patients (%) achieving weight loss ≥5%[3]	83.5*	31.1
Patients (%) achieving weight loss ≥10%[3]	66.1*	12.0
Patients (%) achieving weight loss ≥15%[3]	47.9*	4.8
Waist circumference (cm)		
Baseline	114.6	114.8
Change from baseline[1]	-13.5	-4.1
Difference from placebo[1] [95% CI]	-9.4 [-10.3; -8.5]*	-
Systolic blood pressure (mmHg)		
Baseline	126	127
Change from baseline[1]	-6.2	-1.1
Difference from placebo[1] [95% CI]	-5.1 [-6.3; -3.9]*	-

* p<0.0001 (unadjusted 2-sided) for superiority.
[1] Estimated using an ANCOVA model using multiple imputation based on all data irrespective of discontinuation of randomised treatment or initiation of other anti-obesity medication or bariatric surgery.
[2] During the trial, randomised treatment was permanently discontinued by 17.1% and 22.4% of patients randomised to semaglutide 2.4 mg and placebo, respectively. Assuming that all randomised patients stayed on treatment and did not receive additional anti-obesity therapies, the estimated changes from randomisation to week 68 for body weight based on a Mixed Model for Repeated Measures including all observations until first discontinuation were -16.9% and -2.4% for semaglutide 2.4 mg and placebo respectively.
[3] Estimated from binary regression model based on same imputation procedure as in primary analysis.



Observed values for patients completing each scheduled visit, and estimates with multiple imputations (MI) from retrieved dropouts

Figure 1 STEP 1: Mean change in body weight (%) from baseline to week 68

Following the 68-week trial, a 52-week off-treatment extension was conducted including 327 patients who had completed the main trial period on the maintenance dose of semaglutide or placebo. In the off-treatment period from week 68 to week 120, mean body weight increased in both treatment groups. However, for patients that had been treated with semaglutide for the main trial period the weight remained 5.6% below baseline compared to 0.1% for the placebo group.

STEP 2: Weight management in patients with type 2 diabetes

In a 68-week, double-blind trial, 1,210 patients with overweight or obesity (BMI ≥27 kg/m^2) and type 2 diabetes were randomised to either semaglutide 2.4 mg, semaglutide 1 mg once-weekly or placebo. Patients included in the trial had insufficiently controlled diabetes (HbA_{1c} 7–10%) and were treated with either: diet and exercise alone or 1–3 oral antidiabetic drugs. All patients were on a reduced-calorie diet and increased physical activity throughout the trial.

Treatment with semaglutide for 68 weeks resulted in superior and clinically meaningful reduction in body weight and in HbA_{1c} compared to placebo (see Table 4 and Figure 2).

Table 4 STEP 2: Results at week 68

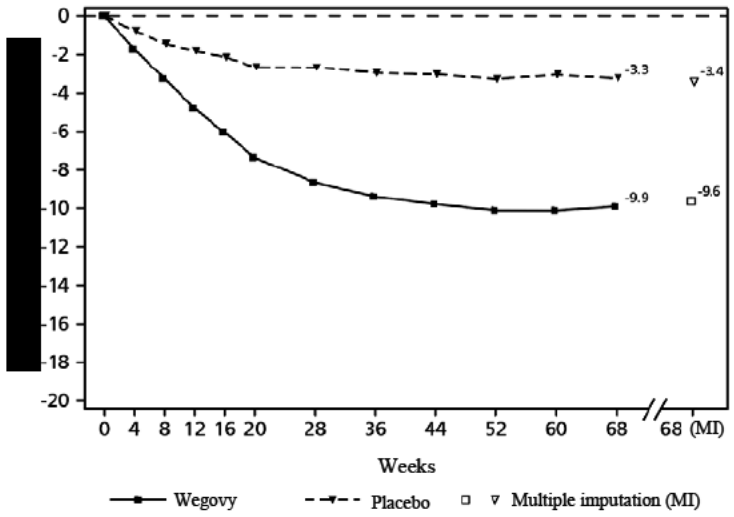
	Wegovy	**Placebo**
Full analysis set (N)	404	403
Body weight		
Baseline (kg)	99.9	100.5
Change (%) from baseline[1,2]	-9.6	-3.4
Difference (%) from placebo[1] [95% CI]	-6.2 [-7.3;-5.2]*	-
Change (kg) from baseline	-9.7	-3.5
Difference (kg) from placebo[1] [95% CI]	-6.1 [-7.2;-5.0]	-
Patients (%) achieving weight loss ≥5%[3]	67.4*	30.2
Patients (%) achieving weight loss ≥10%[3]	44.5*	10.2
Patients (%) achieving weight loss ≥15%[3]	25.0*	4.3
Waist circumference (cm)		
Baseline	114.5	115.5
Change from baseline[1]	-9.4	-4.5
Difference from placebo[1] [95% CI]	-4.9 [-6.0; -3.8]*	-
Systolic blood pressure (mmHg)		
Baseline	130	130
Change from baseline[1]	-3.9	-0.5
Difference from placebo[1] [95% CI]	-3.4 [-5.6; -1.3]**	-
HbA_{1c} (mmol/mol (%))		
Baseline	65.3 (8.1)	65.3 (8.1)
Change from baseline[1]	-17.5 (-1.6)	-4.1 (-0.4)
Difference from placebo[1] [95% CI]	-13.5 [-15.5; -11.4] (-1.2 [-1.4; -1.1])*	- -

* p<0.0001 (unadjusted 2-sided) for superiority; **p<0.05 (unadjusted 2-sided) for superiority

[1] Estimated using an ANCOVA model using multiple imputation based on all data irrespective of discontinuation of randomised treatment or initiation of other anti-obesity medication or bariatric surgery.

[2] During the trial, randomised treatment was permanently discontinued by 11.6% and 13.9% of patients randomised to semaglutide 2.4 mg and placebo, respectively. Assuming that all randomised patients stayed on treatment and did not receive additional anti-obesity therapies, the estimated changes from randomisation to week 68 for body weight based on a Mixed Model for Repeated Measures including all observations until first discontinuation were -10.6% and -3.1% for semaglutide 2.4 mg and placebo respectively

[3] Estimated from binary regression model based on same imputation procedure as in primary analysis.



Observed values for patients completing each scheduled visit, and estimates with multiple imputations (MI) from retrieved dropouts

Figure 2 STEP 2: Mean change in body weight (%) from baseline to week 68

STEP 3: Weight management with intensive behavioural therapy

In a 68-week double-blind trial, 611 patients with obesity (BMI ≥30 kg/m^2), or with overweight (BMI ≥27 kg/m^2 to <30 kg/m^2) and at least one weight-related comorbidity were randomised to semaglutide or placebo. During the trial, all patients received intensive behavioural therapy (IBT) consisting of a very restrictive diet, increased physical activity and behavioural counselling.

Treatment with semaglutide and IBT for 68 weeks resulted in superior and clinically meaningful reduction in body weight compared to placebo (see Table 5).

Table 5 STEP 3: Results at week 68

	Wegovy	**Placebo**
Full analysis set (N)	407	204
Body weight		
Baseline (kg)	106.9	103.7
Change (%) from baseline[1,2]	-16.0	-5.7
Difference (%) from placebo[1] [95% CI]	-10.3 [-12.0;-8.6]*	-
Change (kg) from baseline	-16.8	-6.2
Difference (kg) from placebo[1] [95% CI]	-10.6 [-12.5;-8.8]	-
Patients (%) achieving weight loss ≥5%[3]	84.8*	47.8
Patients (%) achieving weight loss ≥10%[3]	73.0*	27.1
Patients (%) achieving weight loss ≥15%[3]	53.5*	13.2
Waist circumference (cm)		
Baseline	113.6	111.8
Change from baseline[1]	-14.6	-6.3
Difference from placebo[1] [95% CI]	-8.3 [-10.1; -6.6]*	-
Systolic blood pressure (mmHg)		
Baseline	124	124
Change from baseline[1]	-5.6	-1.6
Difference from placebo[1] [95% CI]	-3.9 [-6.4; -1.5]*	-

* p<0.005 (unadjusted 2-sided) for superiority

[1] Estimated using an ANCOVA model using multiple imputation based on all data irrespective of discontinuation of randomised treatment or initiation of other anti-obesity medication or bariatric surgery.

[2] During the trial, randomised treatment was permanently discontinued by 16.7% and 18.6% of patients randomised to semaglutide 2.4 mg and placebo, respectively. Assuming that all randomised patients stayed on treatment and did not receive additional anti-obesity therapies, the estimated changes from randomisation to week 68 for body weight based on a Mixed Model for Repeated Measures including all observations until first discontinuation were -17.6% and -5.0% for semaglutide

2.4 mg and placebo respectively
[3] Estimated from binary regression model based on same imputation procedure as in primary analysis.

STEP 4: Sustained weight management

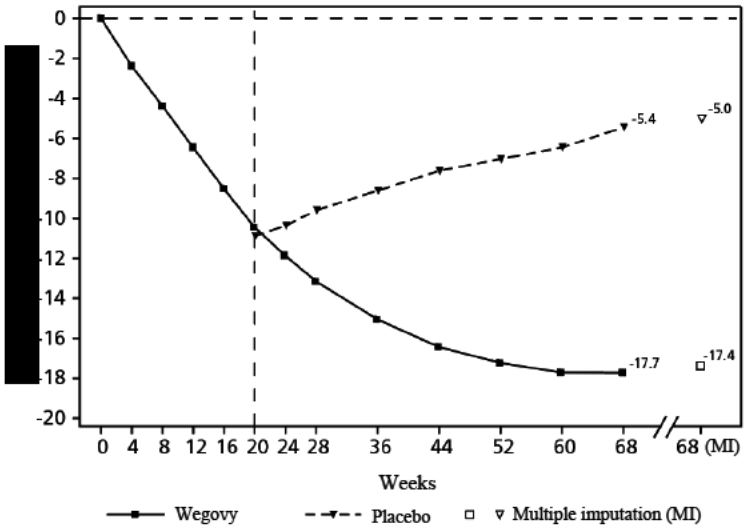
In a 68-week double-blind trial, 902 patients with obesity (BMI ≥30 kg/m^2), or with overweight (BMI ≥27 kg/m^2 to <30 kg/m^2) and at least one weight-related comorbidity were included in the trial. All patients were on a reduced-calorie diet and increased physical activity throughout the trial. From week 0 to week 20 (run-in), all patients received semaglutide. At week 20 (baseline), patients who had reached the maintenance dose of 2.4 mg were randomised to continue treatment or switch to placebo. At week 0 (start of run-in period) patients had a mean body weight of 107.2 kg and a mean BMI of 38.4 kg/m^2.

Patients who had reached the maintenance dose of 2.4 mg at week 20 (baseline) and continued treatment with semaglutide for 48 weeks (week 20–68) continued losing weight and had a superior and clinically meaningful reduction in body weight compared to those switched to placebo (see Table 6 and Figure 3). The body weight increased steadily from week 20 to week 68 in patients switching to placebo at week 20 (baseline). Nevertheless, the observed mean body weight was lower at week 68 than at start of the run-in period (week 0) (see Figure 3). Patients treated with semaglutide from week 0 (run-in) to week 68 (end of treatment) achieved a mean change in body weight of -17.4%, with weight loss ≥5% achieved by 87.8%, ≥10% achieved by 78.0%, ≥15% achieved by 62.2% and ≥20% achieved by 38.6% of these patients.

Table 6 STEP 4: Results from week 20 to week 68

	Wegovy	**Placebo**
Full analysis set (N)	535	268
Body weight		
Baseline[1] (kg)	96.5	95.4
Change (%) from baseline[1,2,3]	-7.9	6.9
Difference (%) from placebo[2] [95% CI]	-14.8 [-16.0; -13.5]*	-
Change (kg) from baseline	-7.1	6.1
Difference (kg) from placebo[2] [95% CI]	-13.2 [-14.3; -12.0]	-
Waist circumference (cm)		
Baseline	105.5	104.7
Change from baseline[1]	-6.4	3.3
Difference from placebo[2] [95% CI]	-9.7 [-10.9; -8.5]*	-
Systolic blood pressure (mmHg)		
Baseline[1]	121	121
Change from baseline[1,2]	0.5	4.4
Difference from placebo[2] [95% CI]	-3.9 [-5.8; -2.0]*	-

* p<0.0001 (unadjusted 2-sided) for superiority,
[1] Baseline = week 20
[2] Estimated using an ANCOVA model using multiple imputation based on all data irrespective of discontinuation of randomised treatment or initiation of other anti-obesity medication or bariatric surgery.
[3] During the trial, randomised treatment was permanently discontinued by 5.8% and 11.6% of patients randomized to semaglutide 2.4 mg and placebo, respectively. Assuming that all randomised patients stayed on treatment and did not receive additional anti-obesity therapies, the estimated changes from randomisation to week 68 for body weight based on a Mixed Model for Repeated Measures including all observations until first discontinuation were -8.1% and 6.5% for semaglutide 2.4 mg and placebo respectively.



Observed values for patients completing each scheduled visit, and estimates with multiple imputations (MI) from retrieved dropouts

Figure 3 STEP 4: Mean change in body weight (%) from week 0 to week 68

STEP 5: 2-year data

In a 104-week double-blind trial, 304 patients with obesity (BMI ≥30 kg/m^2), or with overweight (BMI ≥27 to <30 kg/m^2) and at least one weight-related comorbidity, were randomised to semaglutide or placebo. All patients were on a reduced-calorie diet and increased physical activity throughout the trial. At baseline, patients had a mean BMI of 38.5 kg/m^2, a mean body weight of 106.0 kg.

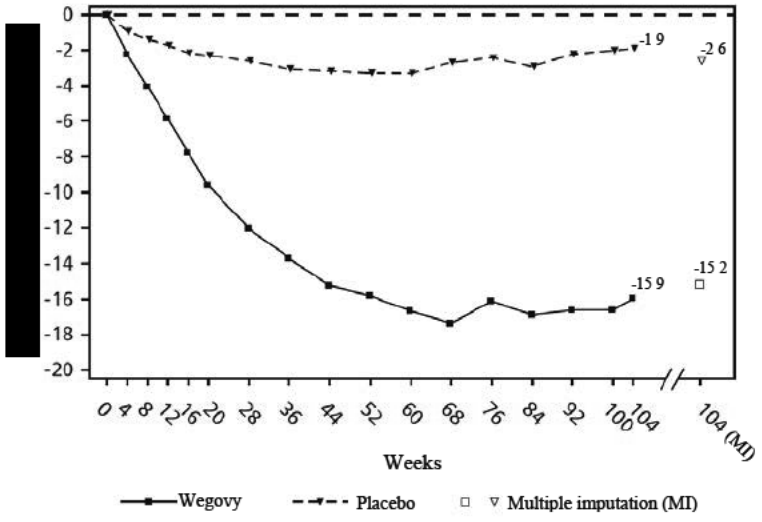
Treatment with semaglutide for 104 weeks resulted in a superior and clinically meaningful reduction in body weight compared to placebo. Mean body weight decreased from baseline through to week 68 with semaglutide after which a plateau was reached. With placebo, mean body weight decreased less, and a plateau was reached after approximately 20 weeks of treatment (see Table 7 and Figure 4). Patients treated with semaglutide achieved a mean change in body weight of -15.2%, with weight loss ≥5% achieved by 74.7%, ≥10% achieved by 59.2% and ≥15% achieved by 49.7% of these patients. Among patients with prediabetes at baseline, 80% and 37% achieved a normo-glycaemic status at end of treatment with semaglutide and placebo, respectively.

Table 7 STEP 5: Results at week 104

	Wegovy	**Placebo**
Full analysis set (N)	152	152
Body weight		
Baseline (kg)	105.6	106.5
Change (%) from baseline[1, 2]	-15.2	-2.6
Difference (%) from placebo[1] [95% CI]	-12.6 [-15.3; -9.8]*	-
Change (kg) from baseline	-16.1	-3.2
Difference (kg) from placebo[1] [95% CI]	-12.9 [-16.1; -9.8]	-
Patients (%) achieving weight loss ≥5%[3]	74.7*	37.3
Patients (%) achieving weight loss ≥10%[3]	59.2*	16.8
Patients (%) achieving weight loss ≥15%[3]	49.7*	9.2
Waist circumference (cm)		
Baseline	115.8	115.7
Change from baseline[1]	-14.4	5.2
Difference from placebo[1] [95% CI]	-9.2 [-12.2; -6.2]*	-
Systolic blood pressure (mmHg)		
Baseline	126	125
Change from baseline[1]	-5.7	-1.6
Difference from placebo[1] [95% CI]	-4.2 [-7.3; -1.0]*	-

* p<0.0001 (unadjusted 2-sided) for superiority.

[1] Estimated using an ANCOVA model using multiple imputation based on all data irrespective of discontinuation of randomised treatment or initiation of other anti-obesity medication or bariatric surgery.
[2] During the trial, randomised treatment was permanently discontinued by 13.2% and 27.0% of patients randomised to semaglutide and placebo, respectively. Assuming that all randomised patients stayed on treatment and did not receive additional anti-obesity therapies, the estimated changes from randomisation to week 68 for body weight based on a Mixed Model for Repeated Measures including all observations until first discontinuation were -16.7% and -0.6% for semaglutide and placebo respectively.
[3] Estimated from binary regression model based on same imputation procedure as in primary analysis.



Observed values for patients completing each scheduled visit, and estimates with multiple imputations (MI) from retrieved dropouts

Figure 4 STEP 5: Mean change in body weight (%) from week 0 to week 104

STEP 8: Semaglutide vs liraglutide

In a 68-week, randomised, open-label, pairwise placebo-controlled trial, 338 patients with obesity (BMI ≥30 kg/m^2), or with overweight (BMI ≥27 to <30 kg/m^2) and at least one weight-related comorbidity, were randomised to semaglutide once weekly, liraglutide 3 mg once daily or placebo. Semaglutide once weekly and liraglutide 3 mg were open-label, but each active treatment group was double-blinded against placebo administered at the same dosing frequency. All patients were on a reduced-calorie diet and increased physical activity throughout the trial. At baseline, patients had a mean BMI of 37.5 kg/m^2, a mean body weight of 104.5 kg.

Treatment with semaglutide once weekly for 68 weeks resulted in superior and clinically meaningful reduction in body weight compared to liraglutide. Mean body weight decreased from baseline through to week 68 with semaglutide. With liraglutide, mean body weight decreased less (see Table 8). 37.4% of the patients treated with semaglutide lost ≥20%, compared to 7.0% treated with liraglutide. Table 8 shows the results of the confirmatory endpoints ≥10%, ≥15% and ≥20% weight loss.

Table 8 STEP 8: Results of a 68-week trial comparing semaglutide with liraglutide

	Wegovy	**Liraglutide 3 mg**
Full analysis set (N)	126	127
Body weight		
Baseline (kg)	102.5	103.7
Change (%) from baseline[1, 2]	-15.8	-6.4
Difference (%) from liraglutide[1] [95% CI]	-9.4 [-12.0;-6.8]*	-
Change (kg) from baseline	-15.3	-6.8
Difference (kg) from liraglutide[1] [95% CI]	-8.5 [-11.2;-5.7]	-
Patients (%) achieving weight loss ≥10%[3]	69.4*	27.2
Patients (%) achieving weight loss ≥15%[3]	54.0*	13.4
Patients (%) achieving weight loss ≥20%[3]	37.4*	7.0

* p<0.005 (unadjusted 2-sided) for superiority
[1] Estimated using an ANCOVA model using multiple imputation based on all data irrespective of discontinuation of randomised treatment or initiation of other anti-obesity medication or bariatric surgery.
[2] During the trial, randomised treatment was permanently discontinued by 13.5% and 27.6% of patients randomised to semaglutide and

liraglutide, respectively. Assuming that all randomised patients stayed on treatment and did not receive additional anti-obesity therapies, the estimated changes from randomisation to week 68 for body weight based on a Mixed Model for Repeated Measures including all observations until first discontinuation were -16.7% and -6.7% for semaglutide and liraglutide respectively.
[3] Estimated from binary regression model based on same imputation procedure as in primary analysis.

Effect on body composition
In a sub-study in STEP 1 (N = 140), body composition was measured using dual energy X-ray absorptiometry (DEXA). The results of the DEXA assessment showed that treatment with semaglutide was accompanied by greater reduction in fat mass than in lean body mass leading to an improvement in body composition compared to placebo after 68 weeks. Furthermore, this reduction in total fat mass was accompanied by a reduction in visceral fat. These results suggest that most of the total weight loss was attributable to a reduction in fat tissue, including visceral fat.

Improvement in physical functioning
Semaglutide showed small improvements in physical functioning scores. Physical functioning was assessed using both the generic health-related quality of life questionnaire Short Form-36v2 Health Survey, Acute Version (SF-36) and the obesity-specific questionnaire Impact of Weight on Quality of Life Lite Clinical Trials Version (IWQOL-Lite-CT).

Cardiovascular evaluation
In the SUSTAIN 6 trial, 3,297 patients with insufficiently controlled type 2 diabetes and at high risk of cardiovascular events were randomised to semaglutide s.c. 0.5 mg or 1 mg once-weekly or placebo in addition to standard-of-care. The treatment duration was 104 weeks. The mean age was 65 years and the mean BMI was 33 kg/m^2.

The primary endpoint was the time from randomisation to first occurrence of a major adverse cardiovascular event (MACE): cardiovascular death, non-fatal myocardial infarction or non-fatal stroke. The total number of the MACE was 254, including 108 (6.6%) with semaglutide and 146 (8.9%) with placebo.

The cardiovascular safety of treatment with semaglutide 0.5 or 1 mg was confirmed as the hazard ratio (HR) for semaglutide vs. placebo was 0.74, [0.58, 0.95] [95% CI], driven by a decrease in the rate of non-fatal stroke and non-fatal myocardial infarction with no difference in cardiovascular death (see Figure 5).

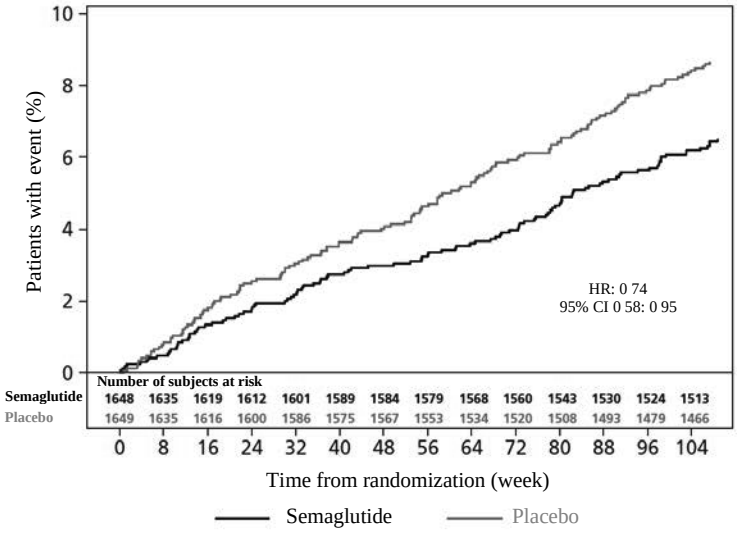


Figure 5: Kaplan-Maier plot of time to first occurrence of the composite outcome: Cardiovascular death, non-fatal myocardial infarction or non-fatal stroke (SUSTAIN 6)

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Wegovy in one or more subsets of the paediatric population in the treatment of weight management (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Compared to native GLP-1, semaglutide has a prolonged half-life of around 1 week making it suitable for once weekly subcutaneous administration. The principal mechanism of protraction is albumin binding, which results in decreased renal clearance and protection from metabolic degradation. Furthermore, semaglutide is stabilised against degradation by the DPP-4 enzyme.

Absorption

The average semaglutide steady state concentration following s.c. administration of the semaglutide maintenance dose was approximately 75 nmol/L in patients with overweight (BMI ≥27 kg/m^2 to <30 kg/m^2) or obesity (BMI ≥ 30 kg/m^2) based on data from phase 3a trials, where 90% of patients had average concentrations between 51 nmol/L and 110 nmol/L. The steady state exposure of semaglutide increased proportionally with doses from 0.25 mg up to 2.4 mg once weekly. Steady state exposure was stable with time as assessed up to week 68. Similar exposure was achieved with s.c. administration of semaglutide in the abdomen, thigh, or upper arm. The absolute bioavailability of semaglutide was 89%.

Distribution

The mean volume of distribution of semaglutide following s.c. administration in patients with overweight or obesity was approximately 12.4 L. Semaglutide is extensively bound to plasma albumin (>99%).

Metabolism/biotransformation

Prior to excretion, semaglutide is extensively metabolised through proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid side chain. The enzyme neutral endopeptidase (NEP) was identified as one of the active metabolic enzymes.

Elimination

The primary excretion routes of semaglutide-related material are via the urine and faeces. Approximately 3% of the absorbed dose was excreted in the urine as intact semaglutide.
The clearance of semaglutide in patients with overweight (BMI ≥27 kg/m^2 to <30 kg/m^2) or obesity (BMI ≥30 kg/m^2) was approximately 0.05 L/h. With an elimination half-life of approximately 1 week, semaglutide will be present in the circulation for approximately 7 weeks after the last dose of 2.4 mg.

Special populations

Elderly
Age had no effect on the pharmacokinetics of semaglutide based on data from phase 3 trials including patients 18–86 years of age.

Gender, race and ethnicity
Gender, race (White, Black or African American, Asian) and ethnicity (Hispanic or Latino, non-Hispanic or -Latino) had no effect on the pharmacokinetics of semaglutide based on data from phase 3a trials.

Body weight
Body weight had an effect on the exposure of semaglutide. Higher body weight was associated with lower exposure; a 20% difference in body weight between individuals will result in an approximate 18% difference in exposure. The 2.4 mg weekly dose of semaglutide provided adequate systemic exposures over the body weight range of 54.4−245.6 kg evaluated for exposure response in the clinical trials.

Renal impairment
Renal impairment did not impact the pharmacokinetics of semaglutide in a clinically relevant manner. This was shown with a single dose of 0.5 mg semaglutide for patients with different degrees of renal impairment (mild, moderate, severe or patients in dialysis) compared with patients with normal renal function. This was also shown for patients with overweight (BMI ≥27 kg/m^2 to <30 kg/m^2) or obesity (BMI ≥30 kg/m^2) and mild to moderate renal impairment based on data from phase 3a trials.

Hepatic impairment
Hepatic impairment did not have any impact on the exposure of semaglutide. The pharmacokinetics of semaglutide were evaluated in patients with different degrees of hepatic impairment (mild, moderate, severe) and compared with patients with normal hepatic function in a study with a single dose of 0.5 mg semaglutide.

Prediabetes and diabetes
Prediabetes and diabetes did not have any clinically relevant effect on the exposure of semaglutide based on data from phase 3 trials.

Immunogenicity
Development of anti-semaglutide antibodies when treated with semaglutide occurred infrequently (see section 4.8) and the response did not appear to influence semaglutide pharmacokinetics.

Paediatrics
Safety and efficacy of semaglutide in children and adolescents below 18 years of age have not been studied.

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeat-dose toxicity or genotoxicity.

Non-lethal thyroid C-cell tumours observed in rodents are a class effect for GLP-1 receptor agonists. In 2-year carcinogenicity studies in rats and mice, semaglutide caused thyroid C-cell tumours at clinically relevant exposures. No other treatment-related tumours were observed. The rodent C-cell tumours are caused by a non-genotoxic, specific GLP-1 receptor mediated mechanism to which rodents are particularly sensitive. The relevance for humans is considered to be low, but cannot be completely excluded.

In fertility studies in rats, semaglutide did not affect mating performance or male fertility. In female rats, an increase in oestrous cycle length and a small reduction in corpora lutea (ovulations) were observed at doses associated with maternal body weight loss.

In embryo-foetal development studies in rats, semaglutide caused embryotoxicity below clinically relevant exposures. Semaglutide caused marked reductions in maternal body weight and reductions in embryonic survival and growth. In foetuses, major skeletal and visceral malformations were observed, including effects on long bones, ribs, vertebrae, tail, blood vessels and brain ventricles. Mechanistic evaluations indicated that the embryotoxicity involved a GLP-1 receptor mediated impairment of the nutrient supply to the embryo across the rat yolk sac. Due to species differences in yolk sac anatomy and function, and due to lack of GLP-1 receptor expression in the yolk sac of non-human primates, this mechanism is considered unlikely to be of relevance to humans. However, a direct effect of semaglutide on the foetus cannot be excluded.

In developmental toxicity studies in rabbits and cynomolgus monkeys, increased pregnancy loss and slightly increased incidence of foetal abnormalities were observed at clinically relevant exposures. The findings coincided with marked maternal body weight loss of up to 16%. Whether these effects are related to the decreased maternal food consumption as a direct GLP-1 effect is unknown.

Postnatal growth and development were evaluated in cynomolgus monkeys. Infants were slightly smaller at delivery but recovered during the lactation period.

In juvenile rats, semaglutide caused delayed sexual maturation in both males and females. These delays had no impact upon fertility and reproductive capacity of either sex, or on the ability of the females to maintain pregnancy.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pre-filled pen, single-dose
Disodium phosphate, dihydrate
Sodium chloride
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

Pre-filled pen, FlexTouch
Disodium phosphate, dihydrate
Propylene glycol
Phenol
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Pre-filled pen, single-dose

2 years.

Wegovy may be stored unrefrigerated for up to 28 days at a temperature not above 30°C. Discard the pen if it has been out of the refrigerator for more than 28 days.

Pre-filled pen, FlexTouch

Before use: 3 years.
After first use: 6 weeks. Store below 30°C or in a refrigerator (2°C to 8°C).

6.4 Special precautions for storage

Store in a refrigerator (2°C-8 °C). Keep away from the cooling element.
Do not freeze.

Pre-filled pen, single-dose
Store the pen in the original carton in order to protect from light.

Pre-filled pen, FlexTouch
Keep the pen cap on when the pen is not in use in order to protect it from light.

6.5 Nature and contents of container

Pre-filled pen, single-dose

1 mL glass syringe (type I glass) with attached stainless steel needle, rigid needle shield (type II/polyisoprene) and a rubber plunger (type I/chlorobutyl).

Pre-filled pen, FlexTouch (0.25, 0.5 mg)

1.5 mL glass cartridge (type I glass) closed at the one end with a rubber plunger (chlorobutyl) and at the other end with an aluminium cap with a laminated rubber sheet (bromobutyl/polyisoprene) inserted. The cartridge is assembled into a disposable pre-filled pen made of polypropylene, polyoxymethylene, polycarbonate and acrylonitrile butadiene styrene.

Pre-filled pen, FlexTouch (1, 1.7 and 2.4 mg)

3 mL glass cartridge (type I glass) closed at the one end with a rubber plunger (chlorobutyl) and at the other end with an aluminium cap with a laminated rubber sheet (bromobutyl/polyisoprene) inserted. The cartridge is assembled into a disposable pre-filled pen made of polypropylene, polyoxymethylene, polycarbonate and acrylonitrile butadiene styrene.

Pack sizes

Pre-filled pen, single use (0.25, 0.5, 1, 1.7 and 2.4 mg)
Pack size of 4 pre-filled pens.

Pre-filled pen, FlexTouch (0.25, 0.5, 1 and 1.7 mg)
Pack size of 1 pre-filled pen and 4 disposable NovoFine Plus needles.

Pre-filled pen, FlexTouch (2.4 mg)
Pack sizes:
1 pre-filled pen and 4 disposable NovoFine Plus needles.
3 pre-filled pens and 12 disposable NovoFine Plus needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Wegovy should not be used if it does not appear clear and colourless.
The pen should not be used if it has been frozen.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Pre-filled pen, single use
The pen is for single-use only.

Pre-filled pen, FlexTouch
This pen is for multi-use. It contains 4 doses.

The patient should be advised to discard the injection needle in accordance with local requirements after each injection and store the Wegovy pen without an injection needle attached. This may prevent blocked needles, contamination, infection, leakage of solution and inaccurate dosing.

The pen is for use by one person only.

Wegovy can be administered with 30G, 31G, and 32G disposable needles up to a length of 8 mm.

7. MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

8. MARKETING AUTHORISATION NUMBERS

EU/1/21/1608/001
EU/1/21/1608/002
EU/1/21/1608/003
EU/1/21/1608/004
EU/1/21/1608/005
EU/1/21/1608/006
EU/1/21/1608/007
EU/1/21/1608/008
EU/1/21/1608/009
EU/1/21/1608/010
EU/1/21/1608/011

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Novo Nordisk A/S
Hallas Allé
DK-4400 Kalundborg
Denmark

Name and address of the manufacturer responsible for batch release

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (single-dose)

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 0.25 mg solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 0.25 mg semaglutide in 0.5 mL (0.5 mg/mL)

3. LIST OF EXCIPIENTS

Exipients: disodium phosphate dihydrate, sodium chloride, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
4 pre-filled pens (1 pen delivers 1 dose)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

For single use only

Push to open

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze
Keep the pen in the outer carton in order to protect from light
Discard pen after use

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/21/1608/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 0.25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (single-dose)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 0.25 mg injection
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL
(1 dose)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (single-dose)

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 0.5 mg solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 0.5 mg semaglutide in 0.5 mL (1 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, sodium chloride, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
4 pre-filled pens (1 pen delivers 1 dose)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

For single use only

Push to open

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze
Keep the pen in the outer carton in order to protect from light
Discard pen after use

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/21/1608/002

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 0.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (single-dose)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 0.5 mg injection
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL
(1 dose)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (single-dose)

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 1 mg solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 1 mg semaglutide in 0.5 mL (2 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, sodium chloride, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
4 pre-filled pens (1 pen delivers 1 dose)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

For single use only

Push to open

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze
Keep the pen in the outer carton in order to protect from light
Discard pen after use

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/21/1608/003

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 1 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (single-dose)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 1 mg injection
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL
(1 dose)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (single-dose)

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 1.7 mg solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 1.7 mg semaglutide in 0.75 mL (2.27 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, sodium chloride, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
4 pre-filled pens (1 pen delivers 1 dose)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

For single use only

Push to open

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze
Keep the pen in the outer carton in order to protect from light
Discard pen after use

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/21/1608/004

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 1.7 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (single-dose)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 1.7 mg injection
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.75 mL
(1 dose)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (single-dose)

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 2.4 mg solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 2.4 mg semaglutide in 0.75 mL (3.2 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, sodium chloride, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
4 pre-filled pens (1 pen delivers 1 dose)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

For single use only

Push to open

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze
Keep the pen in the outer carton in order to protect from light
Discard pen after use

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBER

EU/1/21/1608/005

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 2.4 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (single-dose)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 2.4 mg injection
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.75 mL
(1 dose)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 0.25 mg FlexTouch solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 1 mg semaglutide in 1.5 mL (0.68 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pen and 4 disposable needles (1 pen = 4 doses)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

Use Wegovy once a week

Write the weekday you choose to inject

I injected my weekly dose on the below dates

Open here

Lift here

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Do not store the pen with a needle attached.
For use by one person only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
After the first use of the pen, store below 30°C. Do not freeze.
Keep the pen cap on in order to protect from light.
Discard pen 6 weeks after first use.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBERS

EU/1/21/1608/006

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 0.25 mg FlexTouch

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 0.25 mg injection
FlexTouch
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 mL
(4 doses)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 0.5 mg FlexTouch solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 2 mg semaglutide in 1.5 mL (1.34 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pen and 4 disposable needles (1 pen = 4 doses)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

Use Wegovy once a week

Write the weekday you choose to inject

I injected my weekly dose on the below dates

Open here

Lift here

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Do not store the pen with a needle attached.
For use by one person only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
After the first use of the pen, store below 30°C. Do not freeze.
Keep the pen cap on in order to protect from light.
Discard pen 6 weeks after first use.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBERS

EU/1/21/1608/007

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 0.5 mg FlexTouch

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 0.5 mg injection
FlexTouch
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.5 mL
(4 doses)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 1 mg FlexTouch solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 4 mg semaglutide in 3 mL (1.34 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pen and 4 disposable needles (1 pen = 4 doses)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

Use Wegovy once a week

Write the weekday you choose to inject

I injected my weekly dose on the below dates

Open here

Lift here

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Do not store the pen with a needle attached.
For use by one person only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
After the first use of the pen, store below 30°C. Do not freeze.
Keep the pen cap on in order to protect from light.
Discard pen 6 weeks after first use.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBERS

EU/1/21/1608/008

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 1 mg FlexTouch

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 1 mg injection
FlexTouch
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL
(4 doses)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 1.7 mg FlexTouch solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 6.8 mg semaglutide in 3 mL (2.27 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pen and 4 disposable needles (1 pen = 4 doses)

5. METHOD AND ROUTE OF ADMINISTRATION

subcutaneous use
once weekly

Read the package leaflet before use

Use Wegovy once a week

Write the weekday you choose to inject

I injected my weekly dose on the below dates

Open here

Lift here

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Do not store the pen with a needle attached.
For use by one person only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
After the first use of the pen, store below 30°C. Do not freeze.
Keep the pen cap on in order to protect from light.
Discard pen 6 weeks after first use.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBERS

EU/1/21/1608/009

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 1.7 mg FlexTouch

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 1.7 mg injection
FlexTouch
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL
(4 doses)

6. OTHER

Novo Nordisk A/S

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT

Wegovy 2.4 mg FlexTouch solution for injection in pre-filled pen
semaglutide

2. STATEMENT OF ACTIVE SUBSTANCE

Each pre-filled pen contains 9.6 mg semaglutide in 3 mL (3.2 mg/mL)

3. LIST OF EXCIPIENTS

Excipients: disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

solution for injection
1 pen and 4 disposable needles (1 pen = 4 doses)
3 pens and 12 disposable needles (1 pen = 4 doses)

5. METHOD AND ROUTE OF ADMINISTRATION

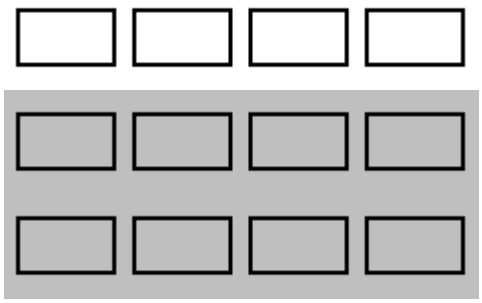
subcutaneous use
once weekly

Read the package leaflet before use

Use Wegovy once a week

Write the weekday you choose to inject

I injected my weekly dose on the below dates



Open here

Lift here

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Do not store the pen with a needle attached.
For use by one person only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
After the first use of the pen, store below 30°C. Do not freeze.
Keep the pen cap on in order to protect from light.
Discard pen 6 weeks after first use.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

12. MARKETING AUTHORISATION NUMBERS

EU/1/21/1608/010 1 pen and 4 disposable needles
EU/1/21/1608/011 3 pens and 12 disposable needles

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Wegovy 2.4 mg FlexTouch

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED PEN LABEL (multi-dose pre-filled pen (FlexTouch))

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Wegovy 2.4 mg injection
FlexTouch
semaglutide
SC

2. METHOD OF ADMINISTRATION

Subcutaneous use
once weekly

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mL
(4 doses)

6. OTHER

Novo Nordisk A/S

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Wegovy 0.25 mg solution for injection in pre-filled pen
Wegovy 0.5 mg solution for injection in pre-filled pen
Wegovy 1 mg solution for injection in pre-filled pen
Wegovy 1.7 mg solution for injection in pre-filled pen
Wegovy 2.4 mg solution for injection in pre-filled pen
semaglutide

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
– Keep this leaflet. You may need to read it again.
– If you have any further questions, ask your doctor, pharmacist or nurse.
– This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
– If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Wegovy is and what it is used for

What Wegovy is
Wegovy is a medicine for weight loss and weight maintenance that contains the active substance semaglutide. It is similar to a natural hormone called glucagon-like peptide-1 (GLP-1) that is released from the intestine after a meal. It works by acting on targets (receptors) in the brain that control your appetite, causing you to feel fuller and less hungry and experience less craving for food. This will help you eat less food and reduce your body weight.

What Wegovy is used for
Wegovy is used together with diet and physical activity for weight loss and to help keep the weight under control. It is used in adults, who have
• a BMI of 30 kg/m² or greater (obesity) or
• a BMI of at least 27 kg/m² but less than 30 kg/m² (overweight) who have weight-related health problems (such as diabetes, high blood pressure, abnormal levels of fats in the blood, breathing problems during sleep called ‘obstructive sleep apnoea’ or a history of heart attack, stroke or blood vessel problems).

BMI (Body Mass Index) is a measure of your weight in relation to your height.

2. What you need to know before you use Wegovy

Do not use Wegovy
- if you are allergic to semaglutide or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Wegovy.

The use of Wegovy is not recommended if you:
- use other products for weight loss,
- have type 1 diabetes,
- have severely reduced kidney function,
- have severely reduced liver function,
- have severe heart failure,
- have diabetic eye disease (retinopathy).

There is little experience with Wegovy in patients:
- of 75 years and older,
- with liver problems,
- with severe stomach or gut problem which results in delayed stomach emptying (called gastroparesis), or if you have an inflammatory bowel disease.

Please consult your doctor if one of the above applies to you.

- **Dehydration**
  During treatment with Wegovy, you may feel sick (nausea) or be sick (vomiting), or have diarrhoea. These side effects can cause dehydration (loss of fluids). It is important that you drink enough fluids to prevent dehydration. This is especially important if you have kidney problems. Talk to your doctor if you have any questions or concerns.

- **Inflammation of the pancreas**
  If you have severe and on-going pain in the stomach area (see section 4) – see a doctor straight away as this could be a sign of inflamed pancreas (acute pancreatitis).

- **People with type 2 diabetes**
  Wegovy cannot be used as a substitute for insulin. Do not use Wegovy in combination with other medicines that contain GLP-1 receptor agonists (such as liraglutide, dulaglutide, exenatide or lixisenatide).

- **Low blood sugar (hypoglycaemia)**
  Taking a sulfonylurea or an insulin with Wegovy might increase the risk of getting low blood sugar levels (hypoglycaemia). Please see section 4 for the warning signs of low blood sugar levels. Your doctor may ask you to test your blood sugar levels. This will help your doctor decide if the dose of the sulfonylurea or insulin needs to be changed to reduce the risk of low blood sugar.

- **Diabetic eye disease (retinopathy)**
  If you have diabetic eye disease and are using insulin, this medicine may lead to a worsening of your vision, and this may require treatment. Fast improvements in blood sugar control may lead to a temporary worsening of diabetic eye disease. If you have diabetic eye disease and experience eye problems while taking this medicine, talk to your doctor.

Children and adolescents
This medicine is not recommended in children and adolescents under 18 years as the safety and effectiveness in this age group have not been established.

Other medicines and Wegovy
Tell your doctor, pharmacist or nurse if you are using, have recently used or might use any other medicines.

In particular, tell your doctor, pharmacist or nurse if you are using medicines containing the following:
- Warfarin or other similar medicines taken by mouth to reduce blood clotting (oral anti-coagulants). When you start treatment with e.g. wafarin or similar medicines, frequent blood testing to determine the ability of your blood to clot may be required.

Pregnancy and breast-feeding
This medicine should not be used during pregnancy, as it is not known if it may affect your unborn child. Therefore, it is recommended to use contraception while using this medicine. If you wish to become pregnant, you should stop using this medicine at least two months in advance. If you become or are pregnant, think you may be pregnant or are planning to have a baby when using this medicine, talk to your doctor straight away, as your treatment will need to be stopped.

Do not use this medicine if you are breast-feeding, as it is unknown if it passes into breast milk.

Driving and using machines
Wegovy is unlikely to affect your ability to drive and use machines. Some patients may feel dizzy when taking Wegovy mainly during the first 4 months of treatment (see section 4). If you feel dizzy be extra careful while driving or using machines. If you need any further information, talk to your doctor, pharmacist or nurse.

People with type 2 diabetes
If you use this medicine in combination with a sulfonylurea or insulin, low blood sugar (hypoglycaemia) may occur which may reduce your ability to concentrate. Avoid driving or using machines if you get any signs of low blood sugar. See section 2, ‘Warnings and precautions’ for information on increased risk of low blood sugar and section 4 for the warning signs of low blood sugar. Talk to your doctor for further information.

Wegovy contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Wegovy

Always use this medicine exactly as your doctor has told you. Check with your doctor, pharmacist or nurse if you are not sure.

How much to use
The recommended dose is 2.4 mg once weekly.
Your treatment will start at a low dose which will be gradually increased over 16 weeks of treatment.
- When you first start using Wegovy, the starting dose is 0.25 mg once weekly.
- Your doctor will instruct you to gradually increase your dose every 4 weeks until you reach the recommended dose of 2.4 mg once weekly.
- Once you reach the recommended dose of 2.4 mg, do not increase this dose further.
- In case you are feeling very bothered by sickness (nausea) or by being sick (vomiting) talk with your doctor about delaying dose escalation or lowering to the previous dose until symptoms have improved.

Usually, you will be told to follow the table below.

Dose escalation	Weekly dose
Week 1–4	0.25 mg
Week 5–8	0.5 mg
Week 9–12	1 mg
Week 13–16	1.7 mg
From week 17	2.4 mg

Your doctor will assess your treatment on a regular basis.

How Wegovy is given

Wegovy is given as an injection under the skin (subcutaneous injection). Do not inject it into a vein or muscle.

- The best places to give the injection are the front of your upper arm, upper legs or stomach.
- Before you use the pen for the first time, your doctor, pharmacist or nurse will show you how to use it.

Detailed instructions on how to use the pen are on the other side of this leaflet.

People with type 2 diabetes
Tell your doctor if you have type 2 diabetes. Your doctor may adjust the dose of your diabetes medicines to prevent you from getting low blood sugar.

When to use Wegovy

- You should use this medicine once a week and if possible, on the same day each week.
- You can give yourself the injection at any time of the day – regardless of meals.

If necessary, you can change the day of your weekly injection of this medicine as long as it has been at least 3 days since your last injection. After selecting a new dosing day, continue with once a week dosing.

If you use more Wegovy than you should
Talk to your doctor straight away. You may get side effects such as feeling sick (nausea), being sick (vomiting) or have diarrhoea, which may cause dehydration (loss of fluids).

If you forget to use Wegovy
If you forgot to inject a dose and:

- it is 5 days or less since you should have used Wegovy, use it as soon as you remember. Then inject your next dose as usual on your scheduled day.
- it is more than 5 days since you should have used Wegovy, skip the missed dose. Then inject your next dose as usual on your next scheduled day.

Do not use a double dose to make up for a forgotten dose.

If you stop using Wegovy
Do not stop using this medicine without talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

Common (may affect up to 1 in 10 people)
- Complications of diabetic eye disease (diabetic retinopathy). If you have diabetes you should inform your doctor if you experience eye problems, such as changes in vision, during treatment with this medicine.

Uncommon (may affect up to 1 in 100 people)
- Inflamed pancreas (acute pancreatitis). Signs of inflamed pancreas may include severe and long-lasting pain in your stomach, the pain may move to your back. You should see your doctor immediately if you experience such symptoms.

Rare (may affect up to 1 in 1,000 people)
- Severe allergic reactions (anaphylactic reactions, angioedema). You should seek immediate medical help and inform your doctor straight away if you get symptoms such as breathing difficulty, swelling, light-headedness, fast heartbeat, sweating and loss of consciousness or rapid swelling under the skin in areas such as the face, throat, arms and legs, which can be life threatening if throat swelling blocks the airway.

Other side effects

Very common (may affect more than 1 in 10 people)
- headache
- feeling sick (nausea)
- being sick (vomiting)
- diarrhoea
- constipation
- stomach pain
- feeling weak or tired

– these are mainly seen during dose escalation and usually go away over time.

Common (may affect up to 1 in 10 people)
- feeling dizzy
- upset stomach or indigestion
- burping
- gas (flatulence)
- bloating of the stomach
- inflamed stomach (‘gastritis’) – the signs include stomach-ache, feeling sick (nausea) or being sick (vomiting)
- reflux or heartburn – also called ‘gastro-oesophageal reflux disease’
- gallstones
- hair loss
- injection site reactions
- low blood sugar (hypoglycaemia) in patients with type 2 diabetes.

The warning signs of low blood sugar may come on suddenly. They can include: cold sweat, cool pale skin, headache, fast heartbeat, feeling sick (nausea) or very hungry, changes in vision, feeling sleepy or weak, feeling nervous, anxious or confused, difficulty concentrating or shaking.
Your doctor will tell you how to treat low blood sugar and what to do if you notice these warning signs.
Low blood sugar is more likely to happen if you also take a sulfonylurea or insulin. Your doctor may reduce your dose of these medicines before you start using this medicine.

Uncommon (may affect up to 1 in 100 people)
- low blood pressure
- feeling dizzy or lightheaded on standing or sitting up because of a drop in blood pressure
- fast heartbeat
- increase of pancreatic enzymes (such as lipase and amylase) shown in blood tests.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Wegovy

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the pen label and carton after 'EXP'. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep away from the cooling element. Always store the pen in the original carton in order to protect from light.
Wegovy may be stored unrefrigerated for up to 28 days at a temperature not above 30°C.
Discard the pen if it has been exposed to light or temperatures above 30°C, has been out of the refrigerator for more than 28 days, or has been frozen.

Do not use this medicine if you notice that the solution is not clear and colourless.

After use: The pen is for single use and contains one dose only. Discard pen after use.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Wegovy contains
– The active substance is semaglutide.
Wegovy 0.25 mg solution for injection
Each pre-filled pen contains 0.25 mg semaglutide in 0.5 mL (0.5 mg/mL).

Wegovy 0.5 mg solution for injection
Each pre-filled pen contains 0.5 mg semaglutide in 0.5 mL (1 mg/mL).

Wegovy 1 mg solution for injection
Each pre-filled pen contains 1 mg semaglutide in 0.5 mL (2 mg/mL).

Wegovy 1.7 mg solution for injection
Each pre-filled pen contains 1.7 mg semaglutide in 0.75 mL (2.27 mg/mL).

Wegovy 2.4 mg solution for injection
Each pre-filled pen contains 2.4 mg of semaglutide in 0.75 mL (3.2 mg/mL).

– The other ingredients are disodium phosphate dihydrate, sodium chloride, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See also section 2 'Wegovy contains sodium' for information on sodium.

What Wegovy looks like and contents of the pack
Wegovy is a clear and colourless solution for injection in a pre-filled disposable pen.

Each pen contains one dose only.

Pack size of 4 pre-filled pens.

Marketing Authorisation Holder and Manufacturer
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

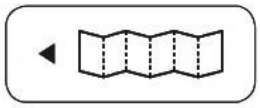
Package leaflet: Information for the patient

Wegovy

0.25 mg **0.5 mg** **1 mg** **1.7 mg** **2.4 mg**

Wegovy 0.25 mg solution for injection in pre-filled pen
Wegovy 0.5 mg solution for injection in pre-filled pen
Wegovy 1 mg solution for injection in pre-filled pen
Wegovy 1.7 mg solution for injection in pre-filled pen
Wegovy 2.4 mg solution for injection in pre-filled pen
semaglutide

Pull out to get started



Use Wegovy one time each week

Instructions on how to use Wegovy pen

Important information before you start

The package contains one package leaflet and four Wegovy pre-filled pens.

This part of the package leaflet instructs on how to use the pen. For further information regarding your medicine please refer to the other side of this package leaflet.

Each pen is only to be used once.
It comes with:

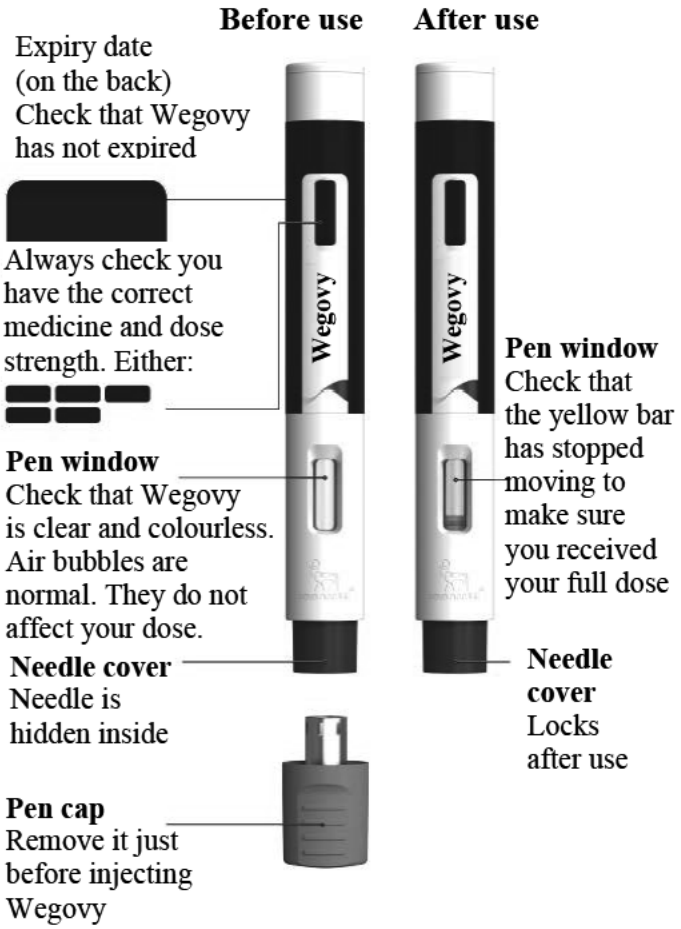
- **one pre-set dose**.
- **a needle cover** that hides the built-in needle before, during and after use.
- **an automatic dosing** mechanism that starts when the needle cover is pressed against your skin as described by your doctor or nurse.

When injecting the dose, a yellow bar will appear in the pen window. Do not lift the pen before the yellow bar has stopped moving. If you do, the automatic dosing will continue, but you may not receive your full dose.

The needle cover will lock when the pen is removed from your skin. You cannot pause the injection and restart it later.

People who are blind or have vision problems should not use Wegovy pen without help from a person trained to use Wegovy.

Always follow these user instructions and any directions given by your doctor or nurse.



EXP/ XX/XXXX
Batch: AB1234

0.25 mg | 0.5 mg | 1 mg | 1.7 mg | 2.4 mg

How to use your Wegovy

1. Prepare for your injection.

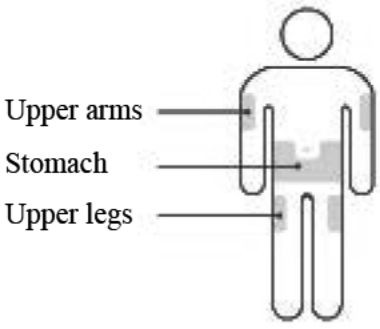
Check your Wegovy pen and be careful not to use your pen if:

1. it has expired
2. it appears to have been used or damaged, e.g. if it has been dropped or stored incorrectly
3. the medicine looks cloudy.

Choose your injection site

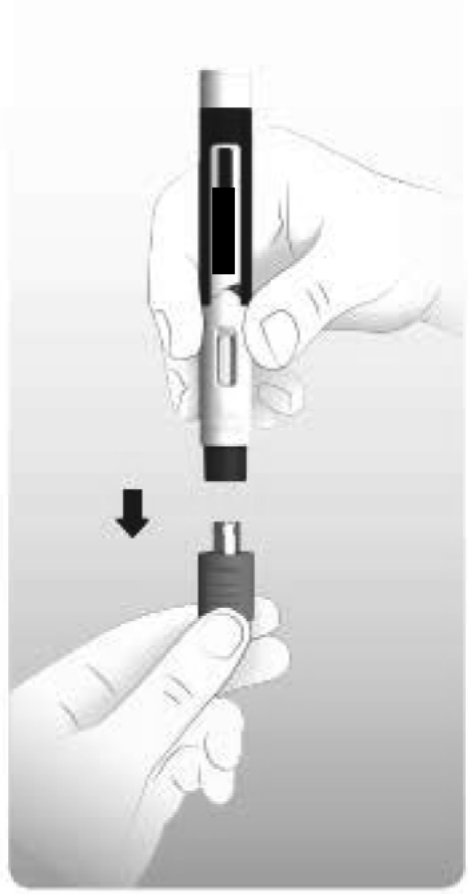
Choose an injection site in one of the body areas marked below. You can choose your upper arms, upper legs or stomach (keep a 5 cm distance from your belly button).

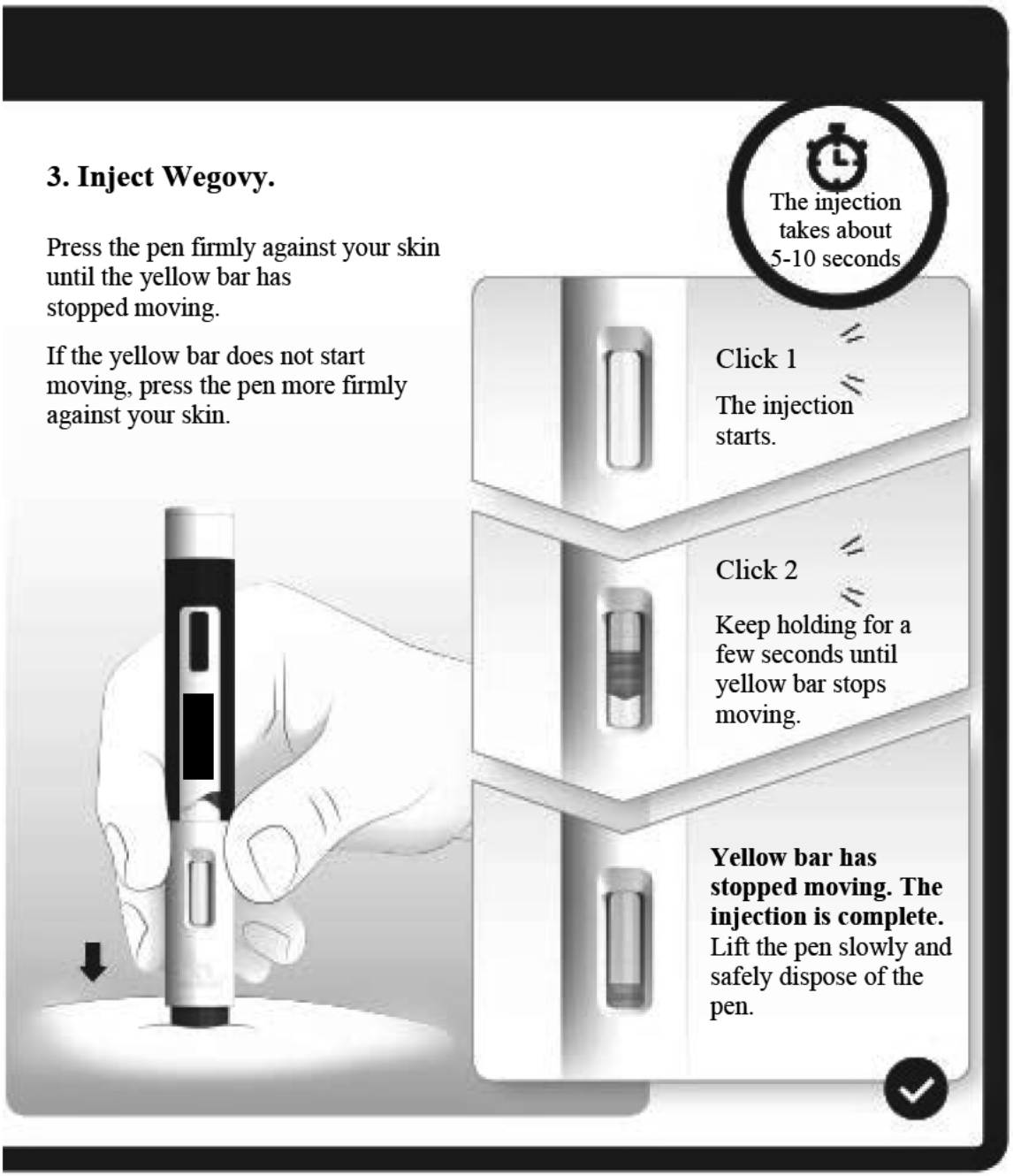
You may inject in the same body area each week, but make sure it is not in the same spot as used the last time.



2. Remove pen cap.

Pull the pen cap straight off your pen.





How do I handle my pen safely?

For information regarding your medicine please refer to the other side of this package leaflet.

- The pen is for a single injection of Wegovy under the skin once a week and should be used by one person only.
- Always refer to the instructions on the other side of this package leaflet and ensure you have been shown how to use these pens by your doctor or nurse.
- Always keep Wegovy pens out of sight and reach of children. Also, keep the pen cap away from children to prevent them from swallowing it.
- Treat your pen with care and do not expose it to any kind of liquid. Rough handling or misuse may cause your pen to give less than the full dose or no dose at all.

- Keep the pen cap on until you are ready to inject. Your pen will no longer be sterile if you store an unused pen without the cap, if you pull the pen cap off and put it on again, or if the pen cap is missing. This could lead to an infection.

- Be careful when handling your pen before use and do not touch the needle or the needle cover. The hidden needle can cause needle stick injuries.

- Each pen contains one weekly dose and cannot be reused. Dispose of it after use.

How do I store my unused pens?

For information regarding storage see section 5 on the other side of this package leaflet.

How do I dispose of my pens?

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Package leaflet: Information for the patient

Wegovy 0.25 mg FlexTouch solution for injection in pre-filled pen
Wegovy 0.5 mg FlexTouch solution for injection in pre-filled pen
Wegovy 1 mg FlexTouch solution for injection in pre-filled pen
Wegovy 1.7 mg FlexTouch solution for injection in pre-filled pen
Wegovy 2.4 mg FlexTouch solution for injection in pre-filled pen
semaglutide

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
– Keep this leaflet. You may need to read it again.
– If you have any further questions, ask your doctor, pharmacist or nurse.
– This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
– If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Wegovy is and what it is used for

What Wegovy is
Wegovy is a medicine for weight loss and weight maintenance that contains the active substance semaglutide. It is similar to a natural hormone called glucagon-like peptide-1 (GLP-1) that is released from the intestine after a meal. It works by acting on targets (receptors) in the brain that control your appetite, causing you to feel fuller and less hungry and experience less craving for food. This will help you eat less food and reduce your body weight.

What Wegovy is used for
Wegovy is used together with diet and physical activity for weight loss and to help keep the weight under control. It is used in adults, who have
• a BMI of 30 kg/m² or greater (obesity) or
• a BMI of at least 27 kg/m² but less than 30 kg/m² (overweight) who have weight-related health problems (such as diabetes, high blood pressure, abnormal levels of fats in the blood, breathing problems during sleep called ‘obstructive sleep apnoea’ or a history of heart attack, stroke or blood vessel problems).

BMI (Body Mass Index) is a measure of your weight in relation to your height.

2. What you need to know before you use Wegovy

Do not use Wegovy
- if you are allergic to semaglutide or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Wegovy.

The use of Wegovy is not recommended if you:
- use other products for weight loss,
- have type 1 diabetes,
- have severely reduced kidney function,
- have severely reduced liver function,
- have severe heart failure,
- have diabetic eye disease (retinopathy).

There is little experience with Wegovy in patients:
- of 75 years and older,
- with liver problems,
- with severe stomach or gut problem which results in delayed stomach emptying (called gastroparesis), or if you have an inflammatory bowel disease.

Please consult your doctor if one of the above applies to you.

- **Dehydration**
  During treatment with Wegovy, you may feel sick (nausea) or be sick (vomiting), or have diarrhoea. These side effects can cause dehydration (loss of fluids). It is important that you drink enough fluids to prevent dehydration. This is especially important if you have kidney problems. Talk to your doctor if you have any questions or concerns.

- **Inflammation of the pancreas**
  If you have severe and on-going pain in the stomach area (see section 4) – see a doctor straight away as this could be a sign of inflamed pancreas (acute pancreatitis).

- **People with type 2 diabetes**
  Wegovy cannot be used as a substitute for insulin. Do not use Wegovy in combination with other medicines that contain GLP-1 receptor agonists (such as liraglutide, dulaglutide, exenatide or lixisenatide).

- **Low blood sugar (hypoglycaemia)**
  Taking a sulfonylurea or an insulin with Wegovy might increase the risk of getting low blood sugar levels (hypoglycaemia). Please see section 4 for the warning signs of low blood sugar levels. Your doctor may ask you to test your blood sugar levels. This will help your doctor decide if the dose of the sulfonylurea or insulin needs to be changed to reduce the risk of low blood sugar.

- **Diabetic eye disease (retinopathy)**
  If you have diabetic eye disease and are using insulin, this medicine may lead to a worsening of your vision, and this may require treatment. Fast improvements in blood sugar control may lead to a temporary worsening of diabetic eye disease. If you have diabetic eye disease and experience eye problems while taking this medicine, talk to your doctor.

Children and adolescents
This medicine is not recommended in children and adolescents under 18 years as the safety and effectiveness in this age group have not been established.

Other medicines and Wegovy
Tell your doctor, pharmacist or nurse if you are using, have recently used or might use any other medicines.

In particular, tell your doctor, pharmacist or nurse if you are using medicines containing the following:
- Warfarin or other similar medicines taken by mouth to reduce blood clotting (oral anti-coagulants). When you start treatment with e.g. wafarin or similar medicines, frequent blood testing to determine the ability of your blood to clot may be required.

Pregnancy and breast-feeding
This medicine should not be used during pregnancy, as it is not known if it may affect your unborn child. Therefore, it is recommended to use contraception while using this medicine. If you wish to become pregnant, you should stop using this medicine at least two months in advance. If you become or are pregnant, think you may be pregnant or are planning to have a baby when using this medicine, talk to your doctor straight away, as your treatment will need to be stopped.

Do not use this medicine if you are breast-feeding, as it is unknown if it passes into breast milk.

Driving and using machines
Wegovy is unlikely to affect your ability to drive and use machines. Some patients may feel dizzy when taking Wegovy mainly during the first 4 months of treatment (see section 4). If you feel dizzy be extra careful while driving or using machines. If you need any further information, talk to your doctor, pharmacist or nurse.

People with type 2 diabetes
If you use this medicine in combination with a sulfonylurea or insulin, low blood sugar (hypoglycaemia) may occur which may reduce your ability to concentrate. Avoid driving or using machines if you get any signs of low blood sugar. See section 2, ‘Warnings and precautions’ for information on increased risk of low blood sugar and section 4 for the warning signs of low blood sugar. Talk to your doctor for further information.

Wegovy contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Wegovy

Always use this medicine exactly as your doctor has told you. Check with your doctor, pharmacist or nurse if you are not sure.

How much to use
The recommended dose is 2.4 mg once weekly.
Your treatment will start at a low dose which will be gradually increased over 16 weeks of treatment.
- When you first start using Wegovy, the starting dose is 0.25 mg once weekly.
- Your doctor will instruct you to gradually increase your dose every 4 weeks until you reach the recommended dose of 2.4 mg once weekly.
- Once you reach the recommended dose of 2.4 mg, do not increase this dose further.
- In case you are feeling very bothered by sickness (nausea) or by being sick (vomiting) talk with your doctor about delaying dose escalation or lowering to the previous dose until symptoms have improved.

Usually, you will be told to follow the table below.

Dose escalation	Weekly dose
Week 1–4	0.25 mg
Week 5–8	0.5 mg
Week 9–12	1 mg
Week 13–16	1.7 mg
From week 17	2.4 mg

Your doctor will assess your treatment on a regular basis.

How Wegovy is given

Wegovy is given as an injection under the skin (subcutaneous injection). Do not inject it into a vein or muscle.
- The best places to give the injection are the front of your upper arm, upper legs or stomach.
- Before you use the pen for the first time, your doctor, pharmacist or nurse will show you how to use it.

Detailed instructions on how to use the pen are on the other side of this leaflet.

People with type 2 diabetes
Tell your doctor if you have type 2 diabetes. Your doctor may adjust the dose of your diabetes medicines to prevent you from getting low blood sugar.

When to use Wegovy
- You should use this medicine once a week and if possible, on the same day each week.
- You can give yourself the injection at any time of the day – regardless of meals.

If necessary, you can change the day of your weekly injection of this medicine as long as it has been at least 3 days since your last injection. After selecting a new dosing day, continue with once a week dosing.

If you use more Wegovy than you should
Talk to your doctor straight away. You may get side effects such as feeling sick (nausea), being sick (vomiting) or have diarrhoea, which may cause dehydration (loss of fluids).

If you forget to use Wegovy
If you forgot to inject a dose and:
- it is 5 days or less since you should have used Wegovy, use it as soon as you remember. Then inject your next dose as usual on your scheduled day.
- it is more than 5 days since you should have used Wegovy, skip the missed dose. Then inject your next dose as usual on your next scheduled day.

Do not use a double dose to make up for a forgotten dose.

If you stop using Wegovy
Do not stop using this medicine without talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

Common (may affect up to 1 in 10 people)
- Complications of diabetic eye disease (diabetic retinopathy). If you have diabetes you should inform your doctor if you experience eye problems, such as changes in vision, during treatment with this medicine.

Uncommon (may affect up to 1 in 100 people)
- Inflamed pancreas (acute pancreatitis). Signs of inflamed pancreas may include severe and long-lasting pain in your stomach, the pain may move to your back. You should see your doctor immediately if you experience such symptoms.

Rare (may affect up to 1 in 1,000 people)
- Severe allergic reactions (anaphylactic reactions, angioedema). You should seek immediate medical help and inform your doctor straight away if you get symptoms such as breathing difficulty, swelling, light-headedness, fast heartbeat, sweating and loss of consciousness or rapid swelling under the skin in areas such as the face, throat, arms and legs, which can be life threatening if throat swelling blocks the airway.

Other side effects

Very common (may affect more than 1 in 10 people)
- headache
- feeling sick (nausea)
- being sick (vomiting)
- diarrhoea
- constipation
- stomach pain
- feeling weak or tired

– these are mainly seen during dose escalation and usually go away over time.

Common (may affect up to 1 in 10 people)
- feeling dizzy
- upset stomach or indigestion
- burping
- gas (flatulence)
- bloating of the stomach
- inflamed stomach (‘gastritis’) – the signs include stomach-ache, feeling sick (nausea) or being sick (vomiting)
- reflux or heartburn – also called ‘gastro-oesophageal reflux disease’
- gallstones
- hair loss
- injection site reactions
- low blood sugar (hypoglycaemia) in patients with type 2 diabetes.

The warning signs of low blood sugar may come on suddenly. They can include: cold sweat, cool pale skin, headache, fast heartbeat, feeling sick (nausea) or very hungry, changes in vision, feeling sleepy or weak, feeling nervous, anxious or confused, difficulty concentrating or shaking.
Your doctor will tell you how to treat low blood sugar and what to do if you notice these warning signs.
Low blood sugar is more likely to happen if you also take a sulfonylurea or insulin. Your doctor may reduce your dose of these medicines before you start using this medicine.

Uncommon (may affect up to 1 in 100 people)
- low blood pressure
- feeling dizzy or lightheaded on standing or sitting up because of a drop in blood pressure
- fast heartbeat

- increase of pancreatic enzymes (such as lipase and amylase) shown in blood tests.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Wegovy

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the pen label and carton after 'EXP'. The expiry date refers to the last day of that month.

Before opening
Store in a refrigerator (2°C – 8°C). Do not freeze. Keep away from the cooling element.

During use
- You can keep the pen for 6 weeks when stored at a temperature below 30°C or in a refrigerator (2°C – 8°C) away from the cooling element. Do not freeze Wegovy and do not use it if it has been frozen.
- When you are not using the pen, keep the pen cap on in order to protect from light.

Do not use this medicine if you notice that the solution is not clear and colourless.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment

6. Contents of the pack and other information

What Wegovy contains
– The active substance is semaglutide.
Wegovy 0.25 mg FlexTouch solution for injection
Each pre-filled pen contains 1 mg semaglutide in 1.5 mL (0.68 mg/mL).

Wegovy 0.5 mg FlexTouch solution for injection
Each pre-filled pen contains 2 mg semaglutide in 1.5 mL (1.34 mg/mL).

Wegovy 1 mg FlexTouch solution for injection
Each pre-filled pen contains 4 mg semaglutide in 3 mL (1.34 mg/mL).

Wegovy 1.7 mg FlexTouch solution for injection
Each pre-filled pen contains 6.8 mg semaglutide in 3 mL (2.27 mg/mL).

Wegovy 2.4 mg FlexTouch solution for injection
Each pre-filled pen contains 9.6 mg of semaglutide in 3 mL (3.2 mg/mL).

– The other ingredients are disodium phosphate dihydrate, propylene glycol, phenol, hydrochloric acid/sodium hydroxide (for pH adjustment), water for injections. See also section 2 'Wegovy contains sodium' for information on sodium.

What Wegovy looks like and contents of the pack
Wegovy is a clear and colourless solution for injection in a pre-filled pen.

Each pre-filled pen contains 4 doses.

Wegovy 0.25, 0.5, 1 and 1.7 mg FlexTouch solution for injection is available in the following pack size:
1 pre-filled pen and 4 disposable NovoFine Plus needles.

Wegovy 2.4 mg FlexTouch solution for injection is available in the following pack sizes:
1 pre-filled pen and 4 disposable NovoFine Plus needles.
3 pre-filled pens and 12 disposable NovoFine Plus needles

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsværd
Denmark

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

Instructions on how to use Wegovy

Before you begin using your once-weekly Wegovy FlexTouch pen, **always read these instructions carefully,** and talk to your doctor, nurse or pharmacist about how to inject Wegovy correctly.

Wegovy pen is a dial-a-dose pen that **contains four of your prescribed doses of Wegovy, corresponding to four times of once-weekly use**.

Please use the table inside the lid of the carton to keep track of how many injections you have used and how many doses remain in your pen.

Wegovy comes in five different pens, each containing one of the following prescribed doses of semaglutide:

0.25 mg | **0.5 mg** | **1 mg** | **1.7 mg** | **2.4 mg**

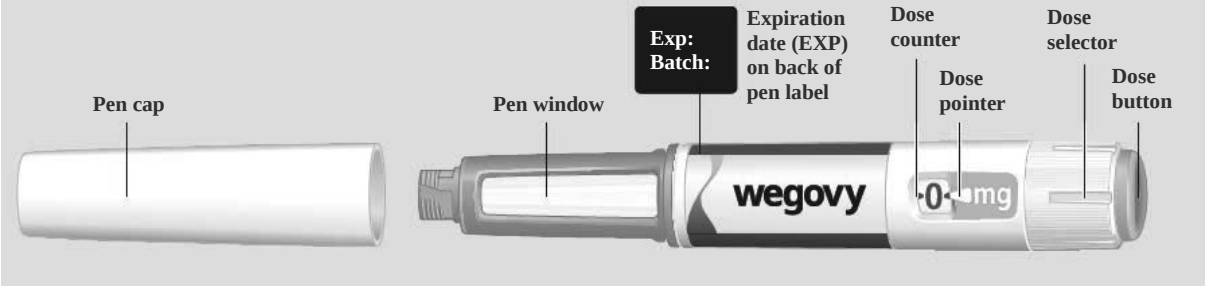
Always start by checking your pen label to make sure that it contains your prescribed dose of Wegovy.

Your pen is designed to be used with 30G, 31G, and 32G disposable needles up to a length of 8 mm.

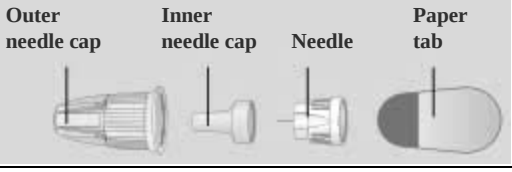
The pack contains:
- Wegovy pen
- 4 NovoFine Plus needles
- Package leaflet

Wegovy FlexTouch pen (example)

Please note: Your pen may differ in size and your pen label may differ in colour from the example shown in the pictures.
These instructions apply to all Wegovy FlexTouch pens



NovoFine Plus needle (example)

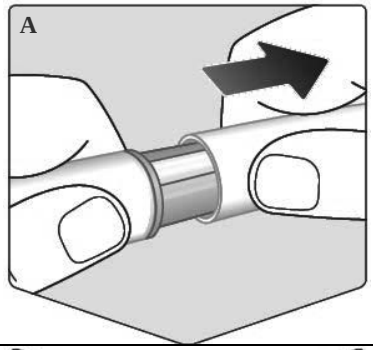


1 Prepare your pen with a new needle

Check the name and dose of your pen to make sure it contains your prescribed dose of Wegovy.

Pull off the pen cap.

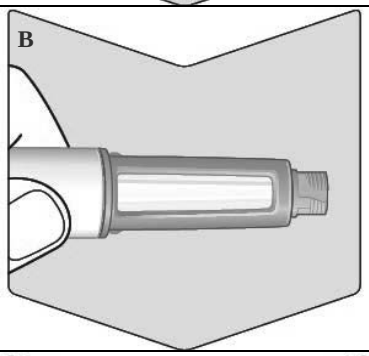
(See figure A).



Check that the solution in your pen is clear and colourless.

Look through the pen window. If Wegovy looks cloudy or coloured, do not use the pen.

(See figure B).

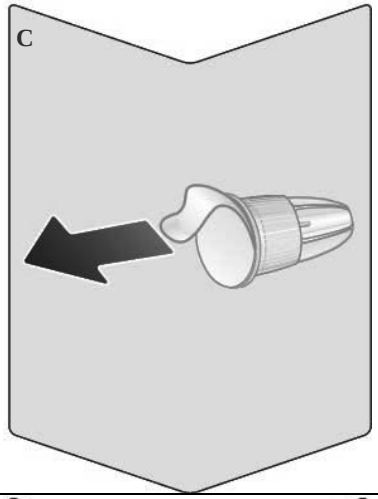


Always use a new needle for each injection.

Take a needle when you are ready to take your injection. Check the paper tab and the outer needle cap for damages that could affect sterility. If any damage is seen, use a new needle.

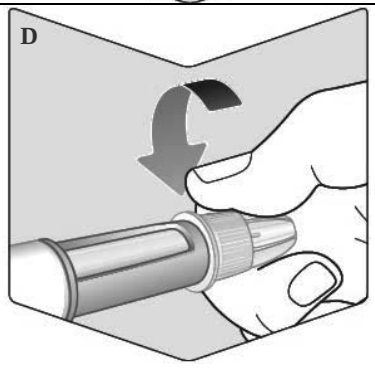
Tear off the paper tab.

(See figure C).



Push the needle straight onto the pen. Turn until it is on tight.

(See figure D).



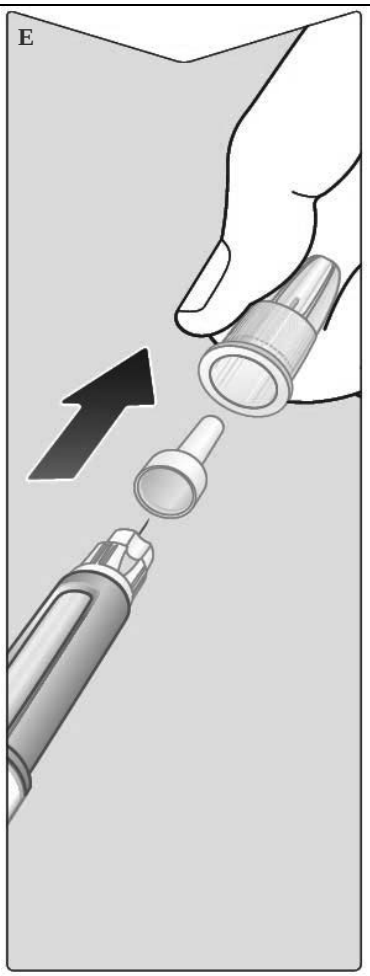
The needle is covered by two caps. You must remove both caps. If you forget to remove both caps you will not inject any Wegovy.

Pull off the outer needle cap and keep it for later. You will need it to safely remove the needle from the pen after the injection.

Pull off the inner needle cap and dispose of it. A drop of Wegovy may appear at the needle tip. You must still check the Wegovy flow if you use a new pen for the first time. See **'Check the flow with each new pen'.**

Never use a bent or damaged needle. For more information about needle handling, see **'About your needles'** below these instructions.

(See figure E).



Check the flow with each new pen

If your Wegovy pen is already in use, go to **'2 Set your dose'.**

Only check the Wegovy flow before your **first injection with each new pen.**

Turn the dose selector until you see the flow check symbol (▪ ▪ ▬).

(See figure F).

Make sure the flow check symbol lines up with the dose pointer.

(See figure G).

G

Check the flow

Hold the pen with the needle pointing up.

Press and hold in the dose button until the dose counter returns to 0. The 0 must line up with the dose pointer.

A drop of Wegovy should appear at the needle tip. This drop indicates that your pen is ready for use.

If a drop does not appear, check the flow again. **This should only be done twice.**

If there is still no drop, **change the needle and check the flow once more.**

Do not use the pen if a drop of Wegovy still does not appear.

(See figure H).

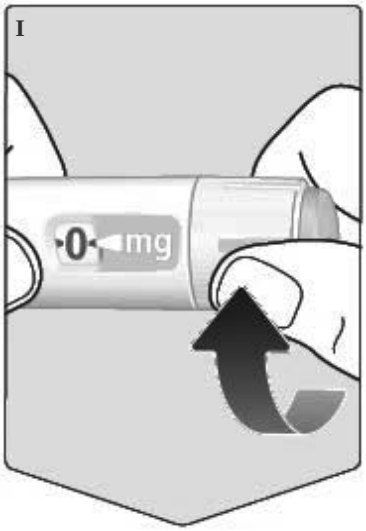
H

2 Set your dose

Turn the dose selector until the **dose counter stops,** and it **shows your prescribed dose.**

(See figure I).

I

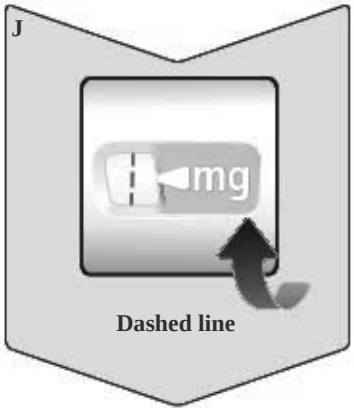


The dashed line ( ) in the dose counter will guide you to your dose.

The dose selector clicks differently when turned forward, backwards or past your dose. You will hear a 'click' every time you turn the dose selector. Do not set the dose by counting the number of clicks you hear.

(See figure J).

J

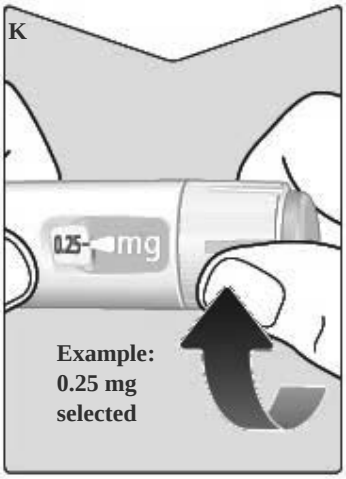


When your prescribed dose lines up with the dose pointer, you have selected your dose. In this picture, the dose **0.25 mg** is shown as an example.

If the dose counter stops before you reach your prescribed dose, see the section **'Do you have enough Wegovy?'** below these instructions.

(See figure K).

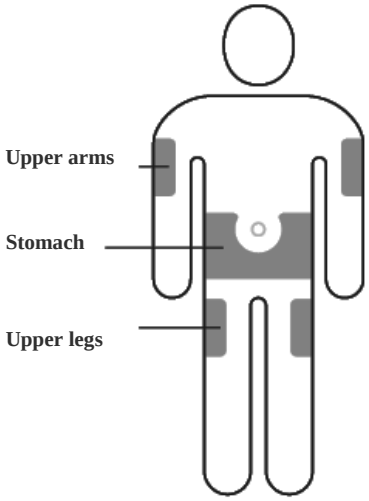
K



Choose your injection site

Choose your upper arms, upper legs or stomach (keep a 5 cm distance from your belly button).

You may inject in the same body area each week, but make sure it is not in the same spot as used the last time.



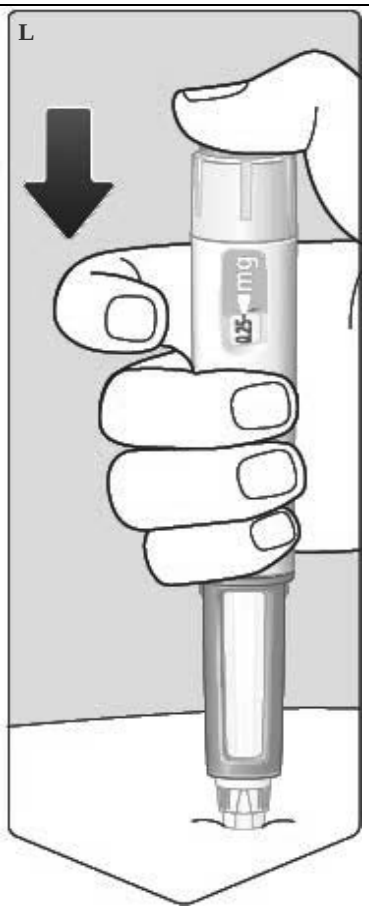
3 Inject your dose

Insert the needle into your skin.

Make sure you can see the dose counter. Do not cover it with your fingers. This could interrupt the injection.

(See figure L).

L



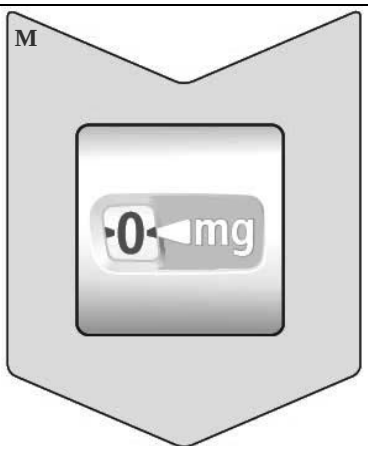
Press and hold down the dose button until the dose counter shows -0-.

(See figure M).

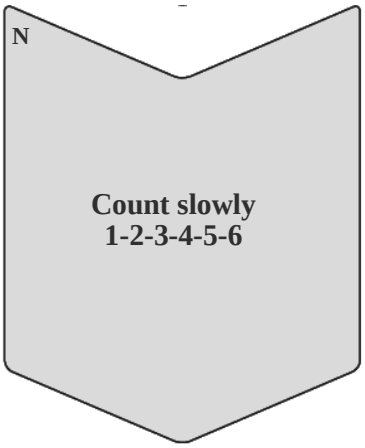
Keep pressing the dose button with the needle in your skin and slowly count to 6. The -0- must line up with the dose pointer. You may hear or feel a click when the dose counter returns to -0-.

(See figure N).

M



N



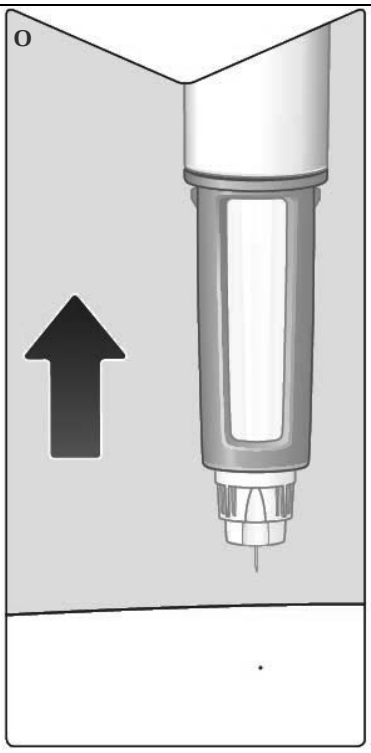
Remove the needle from your skin. If the needle is removed earlier, a stream of Wegovy may come from the needle tip and the full dose will not be delivered.

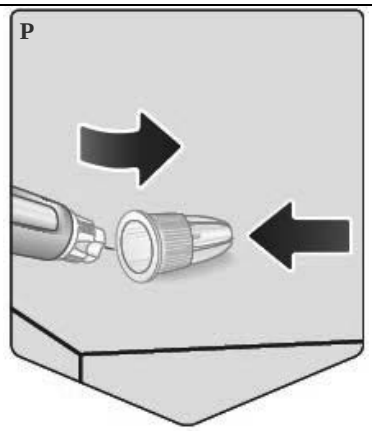
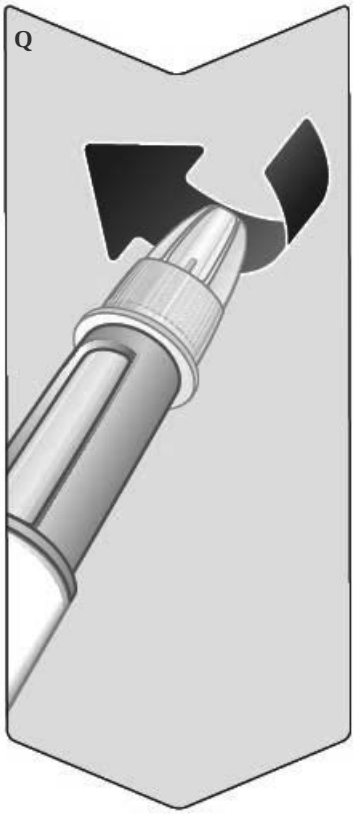
If blood appears at the injection site, press lightly on the area to stop the bleeding.

You may see a drop of Wegovy at the needle tip after injecting. This is normal and does not affect your dose.

(See figure O).

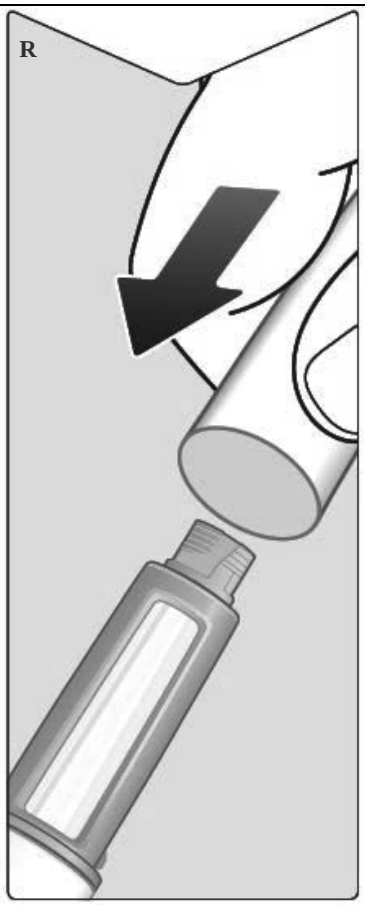
O



4 After your injection	
Lead the needle tip into the outer needle cap on a flat surface without touching the needle or the outer needle cap. **Once the needle is covered,** carefully push the outer needle cap completely on. (See figure P).	
Unscrew the needle and dispose of it carefully as instructed by your doctor, nurse, pharmacist or local authorities. **Never try to put the inner needle cap back on the needle.** You may stick yourself with the needle. **Always dispose of the needle immediately after each injection** to prevent blocked needles, contamination, infection, and inaccurate dosing. **Never store your pen with the needle attached.** (See figure Q).	

Put the pen cap on your pen after each use to protect Wegovy from light.

(See figure R).



When the pen is empty, dispose of the pen without a needle on as instructed by your doctor, nurse, pharmacist, or local authorities.

The pen cap and the empty carton can be disposed of in your household waste.

About your needles

How to identify a blocked or damaged needle

- If ·0· does not appear in the dose counter after continuously pressing the dose button, you may have used a blocked or damaged needle.
- In this case, you have **not** received any Wegovy – even though the dose counter has moved from the original dose that you have set.

How to handle a blocked needle

- Change the needle as instructed in **'1 Prepare your pen with a new needle'** and go to **'2 Set your dose'**.

Caring for your pen

Treat your pen with care. Rough handling or misuse may cause inaccurate dosing. If this happens, you might not get the intended effect of Wegovy.

- See the back of this leaflet to read the storage conditions for your pen.
- **Do not inject Wegovy that has been exposed to direct sunlight.**
- **Do not subject Wegovy to frost and never inject Wegovy that has been frozen.** Dispose of the pen.

- **Do not drop your pen** or knock it against hard surfaces.
- **Do not try to refill your pen.** Once empty, it must be disposed of.
- **Do not try to repair your pen** or pull it apart.
- **Do not expose your pen to dust, dirt or liquid.**
- **Do not wash, soak or lubricate your pen.** If necessary, clean it with a mild detergent on a moistened cloth.

Do you have enough Wegovy?

If the dose counter stops before you reach your prescribed dose, there is not enough Wegovy left for a full dose. Dispose of the pen and use a new Wegovy pen.

Important information

- **Only inject one dose of Wegovy once weekly.** If you do not use your Wegovy as prescribed, you may not get the intended effect of this medicine.
- If you use more than one type of injectable medicine, it is very **important to check the name and dose** of your pen label **before use.**
- **Do not use this pen without help if you have poor eyesight and cannot follow these instructions.** Get help from a person with good eyesight who is trained to use the Wegovy pen.
- Always keep pen and needles **out of sight and reach of others, especially children.**
- **Never share** your pen or your needles with other people.
- **Needles are for single use only. Never reuse your needles** as it may lead to blocked needles, contamination, infection and inaccurate dosing.
- Caregivers must **be very careful when handling used needles** to prevent accidental needle stick injuries and infection.

Company Core Data Sheet

Wegovy®

CCDS

Author

[redacted]

Novo Nordisk A/S

次ページ以降108 of 108までは
公表を省略する