ANNEX II

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

Name and address of the manufacturer(s) of the biological active substance(s)
Immunex Rhode Island Corporation
40 Technology Way
West Greenwich
Rhode Island, 02817
United States

Name and address of the manufacturer(s) responsible for batch release
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Amgen Technology Ireland
Pottery Road
Dun Laoghaire
Co Dublin
Ireland

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

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**

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation. Subsequently, the marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

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

- **Risk Management Plan (RMP)**

The 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.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Repatha 140 mg solution for injection in pre-filled syringe
evolocumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 140 mg of evolocumab in 1 mL of solution.

3. LIST OF EXCIPIENTS

Proline, glacial acetic acid, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
1 pre-filled syringe.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.

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 WARNING(S), IF NECESSARY

Contains latex, read the package leaflet before use.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original carton in order to protect from light.

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

Amgen Europe B.V.
Minervum 7061,
NL-4817 ZK Breda,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1016/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Repatha 140 syringe

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

PRE-FILLED SYRINGE BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Repatha 140 mg solution for injection
evolocumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Amgen Europe B.V.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Repatha 140 mg injection
evolocumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON PRE-FILLED PEN

1. NAME OF THE MEDICINAL PRODUCT

Repatha 140 mg solution for injection in pre-filled pen
evolocumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 140 mg of evolocumab in 1 mL of solution.

3. LIST OF EXCIPIENTS

Proline, glacial acetic acid, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
1 SureClick pre-filled pen.
2 SureClick pre-filled pens.
3 SureClick pre-filled pens.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.

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 WARNING(S), IF NECESSARY

Contains latex, read the package leaflet before use.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original carton in order to protect from light.

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

Amgen Europe B.V.
Minervum 7061,
NL-4817 ZK Breda,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1016/002
EU/1/15/1016/003
EU/1/15/1016/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Repatha 140 pen

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON PRE-FILLED PEN (without blue box)

1. NAME OF THE MEDICINAL PRODUCT

Repatha 140 mg solution for injection in pre-filled pen
evolocumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 140 mg of evolocumab in 1 mL of solution.

3. LIST OF EXCIPIENTS

Proline, glacial acetic acid, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
2 SureClick pre-filled pens. Component of a multi-pack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.

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 WARNING(S), IF NECESSARY

Contains latex, read the package leaflet before use.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original carton in order to protect from light.

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

Amgen Europe B.V.
Minervum 7061,
NL-4817 ZK Breda,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1016/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Repatha 140 pen

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

MULTIPACK LABEL PRE-FILLED PEN (with blue box)

1. NAME OF THE MEDICINAL PRODUCT

Repatha 140 mg solution for injection in pre-filled pen
evolocumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each SureClick pre-filled pen contains 140 mg of evolocumab in 1 mL of solution.

3. LIST OF EXCIPIENTS

Proline, glacial acetic acid, polysorbate 80, sodium hydroxide, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.
Multipack: 6 (3 packs of 2) single use SureClick pre-filled pens.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.

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 WARNING(S), IF NECESSARY

Contains latex, read the package leaflet before use.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Store in the original carton in order to protect from light.

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

Amgen Europe B.V.
Minervum 7061,
NL-4817 ZK Breda,
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1016/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Repatha 140 pen

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL PRE-FILLED PEN

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Repatha 140 mg injection
evolocumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Repatha 140 mg solution for injection in pre-filled syringe
evolocumab

▼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 Repatha is and what it is used for
2. What you need to know before you use Repatha
3. How to use Repatha
4. Possible side effects
5. How to store Repatha
6. Contents of the pack and other information

1. What Repatha is and what it is used for

What Repatha is and how it works

Repatha is a medicine that lowers levels of 'bad' cholesterol, a type of fat, in the blood.

Repatha contains the active substance evolocumab, a monoclonal antibody (a type of specialised protein designed to attach to a target substance in the body). Evolocumab is designed to attach to a substance called PCSK9 that affects the liver's ability to take in cholesterol. By attaching to, and mopping up PCSK9, the medicine increases the amount of cholesterol entering the liver and so lowers the level of cholesterol in the blood.

Repatha is used in patients who cannot control their cholesterol levels with a cholesterol lowering diet alone. You should stay on your cholesterol lowering diet while taking this medicine.

What Repatha is used for

Repatha is used in addition to your cholesterol lowering diet if you are:
- an adult with a high cholesterol level in your blood (primary hypercholesterolaemia [heterozygous familial and non-familial] or mixed dyslipidaemia). It is given:
  - together with a statin or other cholesterol lowering medication, if the maximum dose of a statin does not lower levels of cholesterol sufficiently.
  - alone or together with other cholesterol lowering medications when statins do not work well or cannot be used.
- 12 years and older with a high cholesterol level in your blood because of a condition that runs in your family (homozygous familial hypercholesterolaemia or HoFH). It is given:
  - together with other cholesterol lowering treatments.

2. What you need to know before you use Repatha

Do not use Repatha if you are allergic to evolocumab 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 Repatha if you have:
- liver disease,
- severe kidney problems.

The needle cover of the glass pre-filled syringe is made from dry natural rubber (a derivative of latex), which may cause allergic reactions.

Children and adolescents

The use of Repatha has not been studied in children under 18 years of age being treated for primary hypercholesterolaemia and mixed dyslipidaemia.

The use of Repatha has not been studied in children under 12 years of age being treated for homozygous familial hypercholesterolaemia.

Other medicines and Repatha

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding

Repatha has not been tested in pregnant women. It is not known if Repatha will harm your unborn baby.

Inform your doctor if you are trying to get pregnant, think you may be pregnant or become pregnant taking Repatha.

It is not known whether Repatha is found in breast milk.

It is important to tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding, or whether to stop taking Repatha, considering the benefit of breast-feeding to the baby and the benefit of Repatha to the mother.

Driving and using machines

Repatha has no or negligible influence on the ability to drive and use machines.

Repatha contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium- free' and should not affect a sodium-controlled diet.

3. How to use Repatha

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

Repatha is given as an injection under the skin (subcutaneous).

The recommended dose depends on the underlying condition:

- for primary hypercholesterolaemia and mixed dyslipidaemia the dose is either 140 mg every two weeks or 420 mg once monthly.
- for homozygous familial hypercholesterolaemia the recommended starting dose is 420 mg once monthly. After 12 weeks your doctor may decide to increase the dose to 420 mg every two weeks. If you also receive apheresis, a procedure similar to dialysis where cholesterol and other fats are removed from the blood, your doctor may decide to start you on a dose of 420 mg every two weeks to coincide with your apheresis treatment.

If your doctor prescribes a dose of 420 mg you must use three pre-filled syringes because each pre-filled syringe only contains 140 mg of medicine. After reaching room temperature, all injections should be given within a 30 minute period.

If your doctor decides that you or a caregiver can give the injections of Repatha, you or your caregiver should receive training on how to prepare and inject Repatha correctly. Do not try to inject Repatha until you have been shown how to do it by your doctor or nurse.

See the detailed "Instructions for Use" at the end of this leaflet for instructions about how to store, prepare, and give your Repatha injections at home.

Before starting Repatha, you should be on a diet to lower your cholesterol. You should keep on this cholesterol lowering diet while taking Repatha.

If your doctor has prescribed Repatha along with another cholesterol lowering medicine, follow your doctor's instructions on how to take these medicines together. In this case, please read the dosage instructions in the package leaflet of that particular medicine as well.

If you use more Repatha than you should

Contact your doctor or pharmacist immediately.

If you forget to take Repatha

Take Repatha as soon as you can after the missed dose. Then, contact your doctor who will tell you when you should schedule your next dose, and follow the new schedule exactly as your doctor has told you.

4. Possible side effects

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

Common: may affect up to 1 in 10 people

- Flu (high temperature, sore throat, runny nose, cough and chills)
- Common cold, such as runny nose, sore throat or sinus infections (nasopharyngitis or upper respiratory tract infections)
- Feeling sick (nausea)
- Back pain
- Joint pain (arthralgia)
- Injection site reactions, redness, bruising or pain
- Rash

Uncommon: may affect up to 1 in 100 people

- Hives, red itchy bumps on your skin (urticaria)

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 Repatha

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 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.
Store in the original carton in order to protect from light.

Your pre-filled syringe may be left outside the refrigerator to reach room temperature (up to 25°C) before injection. This will make the injection more comfortable. After removal from the refrigerator, Repatha may be stored at room temperature (up to 25°C) in the original carton and must be used within 1 week.

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 Repatha contains

- The active substance is evolocumab. Each pre-filled syringe contains 140 mg of evolocumab in 1 mL of solution.
- The other ingredients are proline, glacial acetic acid, polysorbate 80, sodium hydroxide, water for injections.

What Repatha looks like and contents of the pack

Repatha is a solution which is clear to opalescent, colourless to yellowish, and practically free from particles. Do not use this medicine if you notice it is discoloured or contains large lumps, flakes or coloured particles.

Each pack contains one single use pre-filled syringe.

Marketing Authorisation Holder and Manufacturer:
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Marketing Authorisation Holder:
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Manufacturer:
Amgen Technology Ireland
Pottery Road
Dun Laoghaire
Co Dublin
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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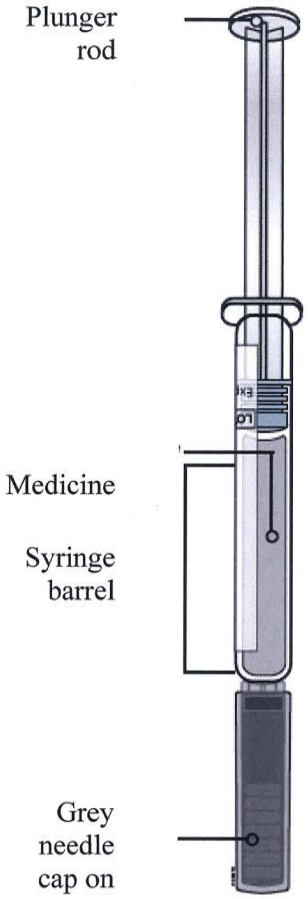
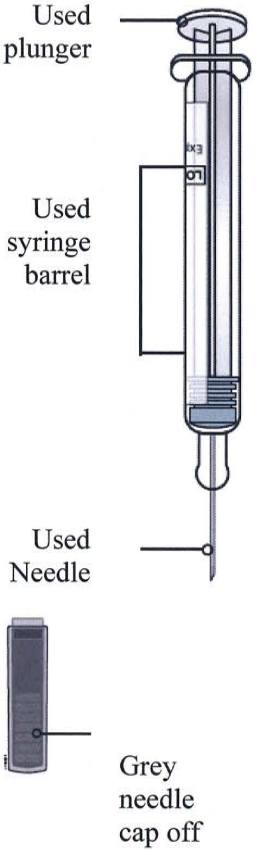
This leaflet was last revised in.

Other sources of information

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

Instructions for use: Repatha single use pre-filled syringe

Guide to parts

Before use	After use
	

	Needle is inside

Important

Before you use a single use Repatha pre-filled syringe, read this important information:

- Your healthcare provider will tell you how many Repatha pre-filled syringes are needed for your dose. If injecting more than one Repatha pre-filled syringe, after reaching room temperature, all injections should be given within a 30 minute period.
- Keep the Repatha pre-filled syringe in the original carton in order to protect it from light.
- The Repatha pre-filled syringe is to be stored in the refrigerator (2°C to 8°C).
- It is important that you do not try to give yourself the injection unless you have received training from your healthcare provider.
- The grey needle cap on the Repatha pre-filled syringe is composed of dry natural rubber, which is made from latex. Tell your healthcare provider if you are allergic to latex.
- Keep the Repatha pre-filled syringe out of the sight and reach of children.

⊘ **DO NOT**:

- ✘ Use the Repatha pre-filled syringe if the packaging is open or damaged.
- ✘ Freeze the Repatha pre-filled syringe or use one that has been frozen.
- ✘ Use the Repatha pre-filled syringe if it has been dropped onto a hard surface. Part of the syringe may be broken even if you cannot see the break. Use a new Repatha pre-filled syringe.
- ✘ Remove the grey needle cap from the Repatha pre-filled syringe until you are ready to inject.

Step 1: Prepare	
A	**Remove the Repatha pre-filled syringe carton from the refrigerator and wait 30 minutes.**

Wait at least 30 minutes for the pre-filled syringe in the carton to naturally reach room temperature before injecting.

Check that the name Repatha appears on the carton label.

⊘ **DO NOT**:

- ✘ Try to warm the Repatha pre-filled syringe by using a heat source such as hot water or microwave.
- ✘ Leave the Repatha pre-filled syringe exposed to direct sunlight.
- ✘ Shake the Repatha pre-filled syringe.

B	**Gather all materials needed for your injection.**

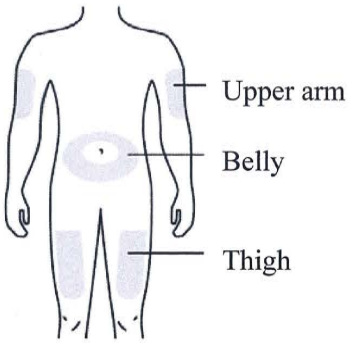
Wash your hands thoroughly with soap and water.

On a clean, well-lit, flat work surface, place:

- One Repatha pre-filled syringe in its tray.
- Alcohol wipes.
- Cotton ball or gauze pad.
- Plaster.
- Sharps disposal container.

⊘ **DO NOT** use if expiry date on the Repatha pre-filled syringe carton has passed.

C	**Choose your injection site.**



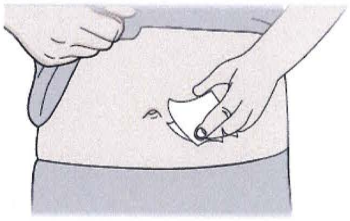
You can use:

- Thigh.
- Belly, except for the 2 inches (5 centimetres) around the belly button.
- Outer area of upper arm (only if someone else is giving you the injections).

⊘ **DO NOT** choose an area where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used last time.

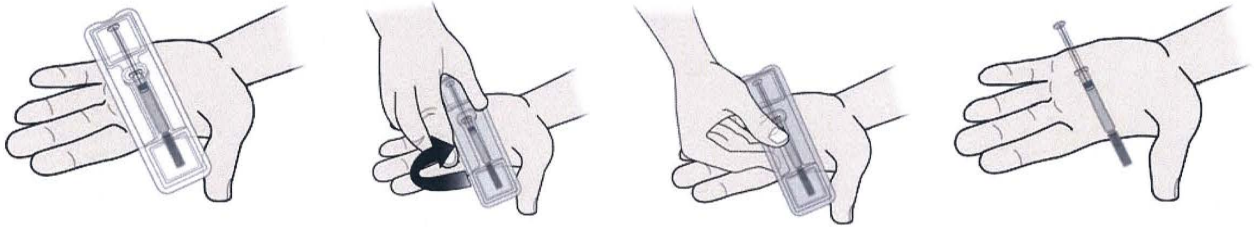
D	**Clean your injection site.**



Clean your injection site with an alcohol wipe. Let your skin dry before injecting.

⊘ **DO NOT** touch this area of skin again before injecting.

E	**Remove the pre-filled syringe from the tray.**



To remove:

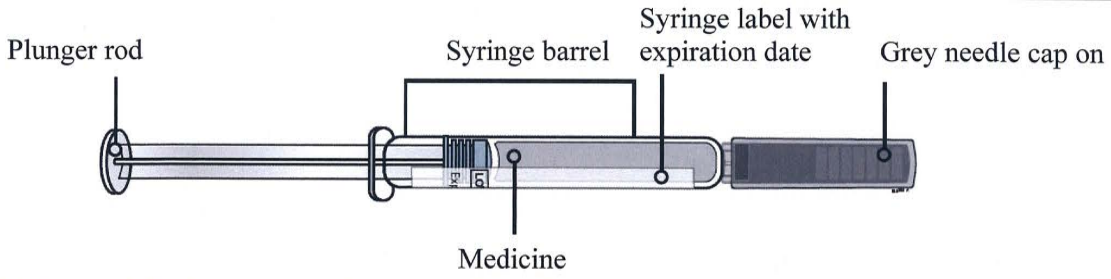
- Peel the paper off of the tray.
- Place the tray on your hand.
- Turn the tray over and gently press the middle of the tray's back to release the syringe into your palm.
- If the pre-filled syringe does not release from the tray, gently press on the back of tray.

⊘ **DO NOT**:

- ✘ Pick up or pull the pre-filled syringe by the plunger rod or grey needle cap. This could damage the syringe.
- ✘ Remove the grey needle cap from the pre-filled syringe until you are ready to inject.

Always hold the pre-filled syringe by the syringe barrel.

F	**Inspect medicine and syringe.**

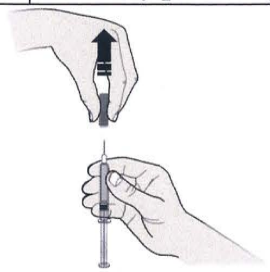


Always hold the pre-filled syringe by the syringe barrel.
Check that:

- The name Repatha appears on the pre-filled syringe label.
- The medicine in the pre-filled syringe is clear and colourless to slightly yellow.

⊘ **DO NOT** use the pre-filled syringe if:

- ✘ any part of the pre-filled syringe appears cracked or broken.
- ✘ the grey needle cap is missing or not securely attached.
- ✘ the medicine is discoloured or contains large lumps, flakes or coloured particles.
- ✘ the expiration date on the pre-filled syringe has passed.

Step 2: Get ready	
A	**Carefully pull the grey needle cap straight out and away from your body.**
1.  It is normal to see a drop of medicine at the end of the needle.	2.  Immediately place the cap in the sharps disposal container.

⊘ **DO NOT:**

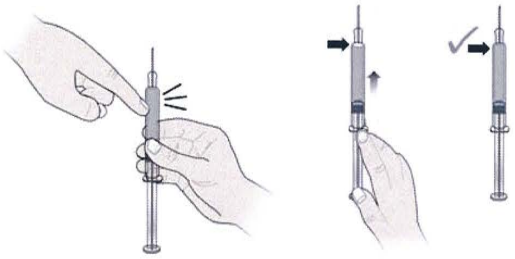
- ✘ twist or bend the grey needle cap. This can damage the needle.
- ✘ put the grey needle cap back onto the pre-filled syringe.

B	**Remove the air bubble / gap.**

You may notice an air bubble/gap in the Repatha pre-filled syringe.

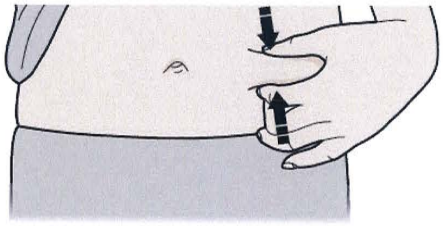
If you notice an air bubble/gap:

- Hold the pre-filled syringe with the needle facing up.
- Gently tap the syringe barrel with your fingers until the air bubble/gap rises to the top of the syringe.
- Slowly and gently push the plunger rod up to get the air out of the pre-filled syringe. Be very careful not to push out any medicine.



⊘ **DO NOT** tap the syringe needle.

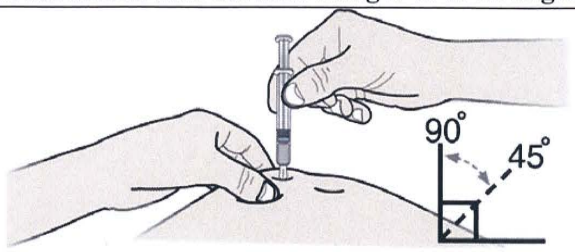
C	**PINCH your injection site to create a firm surface.**



Pinch skin firmly between your thumb and fingers, creating an area about 2 inches (5 centimetres) wide.

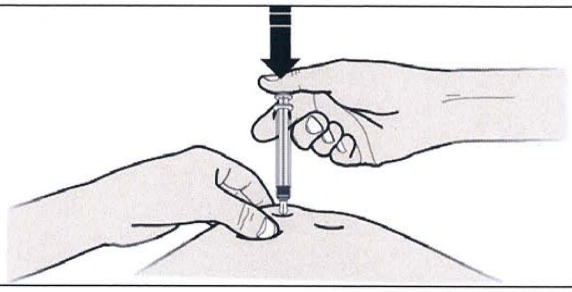
It is important to keep the skin pinched while injecting.

Step 3: Inject	
A	**Hold the PINCH. Insert the needle into the skin using a 45 to 90 degree angle.**

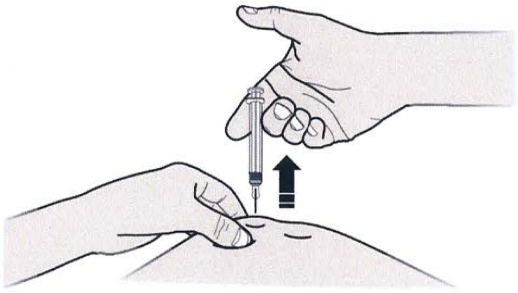


⊘ **DO NOT** place your finger on the plunger rod while inserting the needle.

B	**Using slow and constant pressure, PUSH the plunger rod all the way down until the syringe is empty.**



C	**When done, RELEASE your thumb, and gently lift the syringe off skin.**



⊘ **DO NOT** put the grey needle cap back onto the used syringe.

Step 4: Finish	
A	**Immediately place the used syringe in a sharps disposal container.**



Talk with your healthcare provider about proper disposal. There may be local guidelines for disposal.

⊘ **DO NOT** reuse the used syringe.

⊘ **DO NOT** use any medicine that is left in the used syringe.

⊘ **DO NOT** recycle the syringe or the sharps disposal container or throw it into household rubbish.

Keep the used syringe and sharps container out of the sight and reach of children.

B	**Examine the injection site.**

If there is blood, press a cotton ball or gauze pad on your injection site. Apply a plaster if needed.

⊘ **DO NOT** rub the injection site.

Package leaflet: Information for the user

Repatha 140 mg solution for injection in pre-filled pen
evolocumab

▼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 Repatha is and what it is used for
2. What you need to know before you use Repatha
3. How to use Repatha
4. Possible side effects
5. How to store Repatha
6. Contents of the pack and other information

1. What Repatha is and what it is used for

What Repatha is and how it works

Repatha is a medicine that lowers levels of 'bad' cholesterol, a type of fat, in the blood.

Repatha contains the active substance evolocumab, a monoclonal antibody (a type of specialised protein designed to attach to a target substance in the body). Evolocumab is designed to attach to a substance called PCSK9 that affects the liver's ability to take in cholesterol. By attaching to, and mopping up PCSK9, the medicine increases the amount of cholesterol entering the liver and so lowers the level of cholesterol in the blood.

Repatha is used in patients who cannot control their cholesterol levels with a cholesterol lowering diet alone. You should stay on your cholesterol lowering diet while taking this medicine.

What Repatha is used for

Repatha is used in addition to your cholesterol lowering diet if you are:
- an adult with a high cholesterol level in your blood (primary hypercholesterolaemia [heterozygous familial and non-familial] or mixed dyslipidaemia). It is given:
  - together with a statin or other cholesterol lowering medication, if the maximum dose of a statin does not lower levels of cholesterol sufficiently.
  - alone or together with other cholesterol lowering medications when statins do not work well or cannot be used.
- 12 years and older with a high cholesterol level in your blood because of a condition that runs in your family (homozygous familial hypercholesterolaemia or HoFH). It is given:
  - together with other cholesterol lowering treatments.

2. What you need to know before you use Repatha

Do not use Repatha if you are allergic to evolocumab 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 Repatha if you have:
- liver disease,
- severe kidney problems.

The needle cover of the glass pre-filled pen is made from dry natural rubber (a derivative of latex), which may cause allergic reactions.

Children and adolescents

The use of Repatha has not been studied in children under 18 years of age being treated for primary hypercholesterolaemia and mixed dyslipidaemia.

The use of Repatha has not been studied in children under 12 years of age being treated for homozygous familial hypercholesterolaemia.

Other medicines and Repatha

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding

Repatha has not been tested in pregnant women. It is not known if Repatha will harm your unborn baby.

Inform your doctor if you are trying to get pregnant, think you may be pregnant or become pregnant taking Repatha.

It is not known whether Repatha is found in breast milk.

It is important to tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding, or whether to stop taking Repatha, considering the benefit of breast-feeding to the baby and the benefit of Repatha to the mother.

Driving and using machines

Repatha has no or negligible influence on the ability to drive and use machines.

Repatha contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium- free' and should not affect a sodium-controlled diet.

3. How to use Repatha

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

Repatha is given as an injection under the skin (subcutaneous).

The recommended dose depends on the underlying condition:

- for primary hypercholesterolaemia and mixed dyslipidaemia the dose is either 140 mg every two weeks or 420 mg once monthly.
- for homozygous familial hypercholesterolaemia the recommended starting dose is 420 mg once monthly. After 12 weeks your doctor may decide to increase the dose to 420 mg every two weeks. If you also receive apheresis, a procedure similar to dialysis where cholesterol and other fats are removed from the blood, your doctor may decide to start you on a dose of 420 mg every two weeks to coincide with your apheresis treatment.

If your doctor prescribes a dose of 420 mg you must use three pre-filled pens because each pre-filled pen only contains 140 mg of medicine. After reaching room temperature, all injections should be given within a 30 minute period.

If your doctor decides that you or a caregiver can give the injections of Repatha, you or your caregiver should receive training on how to prepare and inject Repatha correctly. Do not try to inject Repatha until you have been shown how to do it by your doctor or nurse.

See the detailed "Instructions for Use" at the end of this leaflet for instructions about how to store, prepare, and give your Repatha injections at home.

Before starting Repatha, you should be on a diet to lower your cholesterol. You should keep on this cholesterol lowering diet while taking Repatha.

If your doctor has prescribed Repatha along with another cholesterol lowering medicine, follow your doctor's instructions on how to take these medicines together. In this case, please read the dosage instructions in the package leaflet of that particular medicine as well.

If you use more Repatha than you should

Contact your doctor or pharmacist immediately.

If you forget to take Repatha

Take Repatha as soon as you can after the missed dose. Then, contact your doctor who will tell you when you should schedule your next dose, and follow the new schedule exactly as your doctor has told you.

4. Possible side effects

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

Common: may affect up to 1 in 10 people

- Flu (high temperature, sore throat, runny nose, cough and chills)
- Common cold, such as runny nose, sore throat or sinus infections (nasopharyngitis or upper respiratory tract infections)
- Feeling sick (nausea)
- Back pain
- Joint pain (arthralgia)
- Injection site reactions, redness, bruising or pain
- Rash

Uncommon: may affect up to 1 in 100 people

- Hives, red itchy bumps on your skin (urticaria)

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 Repatha

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 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.
Store in the original carton in order to protect from light.

Your pre-filled pen may be left outside the refrigerator to reach room temperature (up to 25°C) before injection. This will make the injection more comfortable. After removal from the refrigerator, Repatha may be stored at room temperature (up to 25°C) in the original carton and must be used within 1 week.

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 Repatha contains
- The active substance is evolocumab. Each SureClick pre-filled pen contains 140 mg of evolocumab in 1 mL of solution.
- The other ingredients are proline, glacial acetic acid, polysorbate 80, sodium hydroxide, water for injections.

What Repatha looks like and contents of the pack

Repatha is a solution which is clear to opalescent, colourless to yellowish, and practically free from particles. Do not use this medicine if you notice it is discoloured or contains large lumps, flakes or coloured particles.

Each pack contains one, two, three or six single use SureClick pre-filled pens.

Marketing Authorisation Holder and Manufacturer:
Amgen Europe B.V.
Minervum 7061
4817 ZK Breda
The Netherlands

Marketing Authorisation Holder:
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Minervum 7061
4817 ZK Breda
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Manufacturer:
Amgen Technology Ireland
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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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 for use:
Repatha single use SureClick pre-filled pen

Guide to parts

Before use



After use



Needle is inside

Important

Before you use the Repatha pre-filled pen, read this important information:

- Your healthcare provider will tell you how many Repatha pre-filled pens are needed for your dose. If injecting more than one Repatha pre-filled pen, after reaching room temperature, all injections should be given within a 30 minute period.
- Keep the Repatha pre-filled pen in original carton to protect it from light.
- The Repatha pre-filled pen is to be stored in the refrigerator (2°C to 8°C).
- It is important that you do not try to give yourself the injection unless you have received training from your healthcare provider.
- The orange cap on a Repatha pre-filled pen contains a needle cover (located inside the cap) that is composed of dry natural rubber, which is made from latex. Tell your healthcare provider if you are allergic to latex.
- Keep the Repatha pre-filled pen out of the sight and reach of children.

⊘ **DO NOT**:

- ✘ freeze or use the Repatha pre-filled pen if it has been frozen.
- ✘ shake the Repatha pre-filled pen.
- ✘ remove the orange cap from the Repatha pre-filled pen until you are ready to inject.
- ✘ use the Repatha pre-filled pen if it has been dropped on a hard surface. Part of the Repatha pre-filled pen may be broken even if you cannot see the break.
- ✘ use the Repatha pre-filled pen after the expiration date.

Step 1: Prepare	
A	**Remove one Repatha pre-filled pen from the package.**
1.	Carefully lift the pre-filled pen straight up out of the box.
2.	Put the original package with any unused pre-filled pens back in the refrigerator.
3.	Wait at least 30 minutes for the pre-filled pen to naturally reach room temperature before injecting.
⊘	**DO NOT**:
	✘ try to warm the pre-filled pen by using a heat source such as hot water or microwave.
	✘ leave the pre-filled pen in direct sunlight.
	✘ shake the pre-filled pen.
	✘ remove the orange cap from the pre-filled pen yet.

B	**Inspect the Repatha pre-filled pen.**



Make sure the medicine in the window is clear and colourless to slightly yellow.
Check the expiration date.

⊘ **DO NOT** use pre-filled pen if:

- ✘ medicine is cloudy or discoloured or contains large lumps, flakes, or particles.
- ✘ any part appears cracked or broken.
- ✘ the pre-filled pen has been dropped.
- ✘ the orange cap is missing or not securely attached.
- ✘ the expiration date has passed.

In all cases, use a new pre-filled pen.

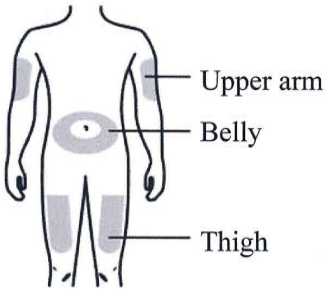
C	**Gather all materials needed for your injection.**

Wash your hands thoroughly with soap and water.

On a clean, well-lit work surface, place the:

- New pre-filled pen.
- Alcohol wipes.
- Cotton ball or gauze pad.
- Plaster.
- Sharps disposal container.

D	**Prepare and clean your injection site.**



You can use:

- Thigh.
- Belly, except for a 2 inch (5 centimetres) area around your belly button.
- Outer area of upper arm (only if someone else is giving you the injection).

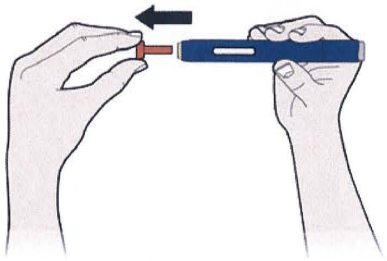
Clean the injection site with an alcohol wipe. Let your skin dry.

⊘ **DO NOT** touch this area again before injecting.

Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used last time.

DO NOT inject into areas where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

Step 2: Get ready	
A	**Pull the orange cap straight off when you are ready to inject.**



It is normal to see a drop of liquid at the end of the needle or yellow safety guard.

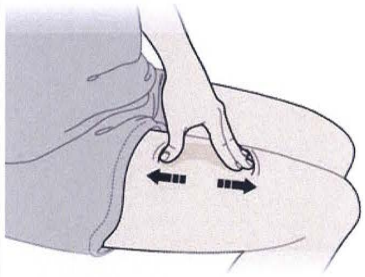
⊘ **DO NOT**:

- ✘ twist, bend or wiggle the orange cap.
- ✘ put the orange cap back onto the pre-filled pen.
- ✘ put fingers into the yellow safety guard.

DO NOT remove the orange cap from the pre-filled pen until you are ready to inject.

B	**Stretch or pinch your injection site to create a firm surface.**

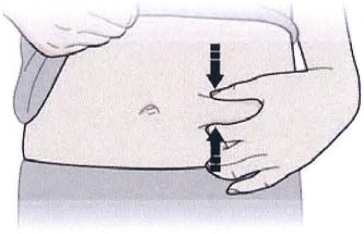
Stretch method



Stretch skin firmly by moving your thumb and fingers in the opposite direction, creating an area about 2 inches (5 centimetres) wide.

OR

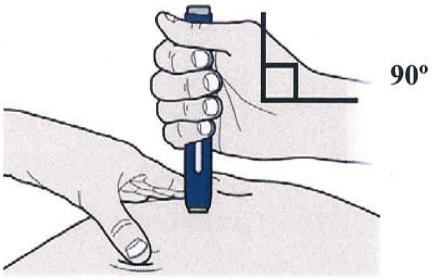
Pinch method



Pinch skin firmly between your thumb and fingers, creating an area about 2 inches (5 centimetres) wide.

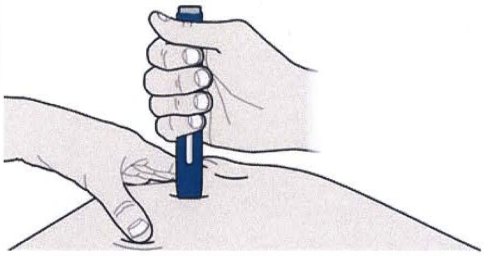
It is important to keep skin stretched or pinched while injecting.

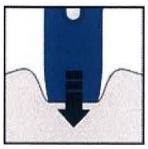
Step 3: Inject	
A	**Hold the stretch or pinch. With the orange cap off, PLACE the pre-filled pen on the skin at 90 degrees.**



DO NOT touch the grey start button yet.

B	**Firmly PUSH down the pre-filled pen onto the skin until it stops moving.**





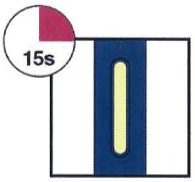
You must push all the way down but **DO NOT** touch the grey start button until you are ready to inject.

C	**When you are ready to inject, PRESS the grey start button. You will hear a click.**

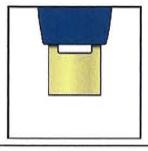


D	**Keep PUSHING down on the skin. Then LIFT thumb. Your injection could take about 15 seconds.**





Window turns yellow when the injection is done



NOTE: After you remove the pre-filled pen from your skin, the needle will be automatically covered.

Step 4: Finish	
A	**Discard the used pre-filled pen and orange needle cap.**



Discard the used pre-filled pen and the orange cap in a sharps disposal container.

Talk with your healthcare provider about proper disposal. There may be local guidelines for disposal.

Keep the pre-filled pen and the sharps disposal container out of the sight and reach of children.

⊘ **DO NOT**:

- ✘ reuse the pre-filled pen.
- ✘ recap the pre-filled pen or put fingers into the yellow safety guard.
- ✘ recycle the pre-filled pen or sharps disposal container or throw them into household rubbish.

B	**Examine the injection site.**

If there is blood, press a cotton ball or gauze pad on your injection site. **DO NOT** rub the injection site. Apply a plaster if needed.