

PMDA Alert for Proper Use of Drugs

Pharmaceuticals and Medical Devices Agency



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This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Request for Proper Use of GLP-1 Receptor Agonists and GIP/GLP-1 Receptor Agonists

- It has been confirmed that GLP-1 receptor agonists and GIP/GLP-1 receptor agonists (hereinafter referred to as GLP-1 receptor agonists, etc.) are currently being prescribed in some medical institutions for aesthetic and slimming purposes other than for the treatment of type 2 diabetes mellitus and obesity. The Ministry of Health, Labour and Welfare issued notifications regarding the proper use of these drugs on June 16, 2026 and October 14, 2026.
- For GLP-1 receptor agonists, etc., caution has been raised regarding the development of adverse reactions such as hypoglycaemia, acute pancreatitis, nausea, vomiting, and diarrhoea, and similar health hazards may occur when they are used off-label for aesthetic and slimming purposes.
- There have been several reported cases of adverse reactions when these drugs were used for aesthetic or slimming purposes, which include serious cases requiring transportation by ambulance. Therefore, note again that the following precautions should be taken.

- The safety and efficacy of GLP-1 receptor agonists, etc. have not been established when used off-label for aesthetic or slimming purposes. Adhere to the indications and dosage and administration stipulated in the electronic package insert for each product.**
- There have been several reports of patients who were diagnosed with ketosis*, were unable to move due to frequent vomiting, and were transported by ambulance while using GLP-1 receptor agonists, etc. and following excessive dietary restrictions.** *Ketosis is a condition in which ketone bodies increase in the body due to extreme dietary restrictions, etc. Worsening of ketosis may progress to ketoacidosis, which may result in disturbed consciousness and life-threatening conditions, requiring urgent treatment.
- Adverse reactions, such as nausea/vomiting, hypoglycaemia, and pancreatitis, have been reported in addition to ketosis.**
- Instruct patients to discontinue the drug immediately and seek medical attention if they experience symptoms such as vomiting or an inability to consume food/water during use.**

Related information:

- Ministry of Health, Labour and Welfare Notifications (June 16 and October 14, 2026)
https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iyakuhin/kojinyunyu/index_00003.html
- Japan Society for the Study of Obesity "Statement on safe weight loss - Alert for ketosis-related events due to weight loss with incretin-related drugs"

For information on GLP-1 receptor agonists and GIP/GLP-1 receptor agonists, refer to the latest electronic package inserts on the PMDA's website (<https://www.pmda.go.jp/>) > Package Inserts etc. > Prescription Drugs.

● Major adverse reactions reported when drugs are used for aesthetic or slimming

	Reported events (PT)	Tirzepatide		Semaglutide		Liraglutide	Total
		<u>Mounjaro Subcutaneous Injection</u>	Zepbound Subcutaneous Injection	<u>Rybelsus tablets, Ozempic Subcutaneous Injection</u>	Wegovy Subcutaneous Injection	<u>Victoza Subcutaneous Injection</u>	
Gastrointestinal symptoms	Vomiting, nausea, abdominal pain, gastritis, gastrointestinal disorder, diarrhoea, abdominal pain upper	19	0	8	0	1	28
Ketosis	Ketosis, ketoacidosis, starvation ketoacidosis	17	0	0	0	0	17
Hypoglycemia	Hypoglycemia	13	0	0	0	1	14
Pancreatitis	Pancreatitis acute, pancreatitis, obstructive pancreatitis	7	0	4	0	0	11

*The data are based on reports from marketing authorization holders, healthcare institutions, and others, and do not represent the incidence of adverse reactions.
*Underlines indicate drugs to treat type 2 diabetes mellitus
*Data collected between April 2004 and May 2026 (via the Japanese Adverse Drug Event Report database as of September 2026)

● Reported cases (Patients transported by ambulance to the emergency department due to ketosis-related events occurring during **off-label use**)

Case 1. Ketosis

Sex Age	Reason for use	Clinical course and management
Female in 20s	Weight control (weight loss)	The patient obtained the drug through an online healthcare service and started self-injection of the drug (BMI about 18). Approximately 4 weeks after the start of administration, the dose was increased. Approximately 2 months after the start of administration, the patient developed severe nausea (BMI about 16). The patient experienced repeated bilious vomiting and presyncope, which made it difficult to maintain an upright posture, resulting in emergency hospitalization. The patient was diagnosed with starvation ketosis.
Comorbidities/Past medical history, anorexia nervosa; Concomitant drugs, unknown; Outcome, recovered		

Case 2. Ketoacidosis

Sex Age	Reason for use	Clinical course and management
Female in 20s	Weight control (diet)	After the start of administration of the drug, the patient developed a decreased appetite. On the day after the second dose (Day 9 of administration), the patient developed pyrexia, frequent vomiting, and malaise. The patient could not take meals. On Day 10 of administration, because of persistent vomiting, the patient called an ambulance and was hospitalized (BMI about 20). The patient was diagnosed with starvation ketoacidosis.
Comorbidities/Past medical history, none; Concomitant drugs, pills; Outcome, recovered		

Case 3. Ketoacidosis

Sex Age	Reason for use	Clinical course and management
Female in 20s	Weight control (weight loss)	The patient was reducing carbohydrates to decrease weight. Since the patient obtained the drug online, she did not receive nutritional counseling before starting administration of the drug (BMI about 30 at baseline). One month after the start of administration, the patient developed persistent nausea and vomiting, which gradually limited oral intake. Because the symptoms did not improve and general fatigue worsened, the patient visited the emergency department. The patient was diagnosed with starvation ketoacidosis and hospitalized (BMI about 22 on admission).
Comorbidities/Past medical history, obesity; Concomitant drugs, metoclopramide, vonoprazan fumarate; Outcome, recovered		

About this information
“PMDA Alert for Proper Use of Drugs” communicates to healthcare providers with clear information from the perspective of promoting the proper use of drugs. The information presented here includes such cases where the reporting frequencies of similar reports have not decreased despite relevant alerts provided in package inserts, among Adverse Drug Reaction/infection cases reported in accordance with the Pharmaceutical and Medical Device Act.
*We have tried to ensure the accuracy of this information at the time of its compilation but do not guarantee its accuracy in the future.
*This information is not intended to impose constraints on the discretion of healthcare professionals or to impose obligations and responsibilities on them, but is provided to promote the proper use of drugs.

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