22 June 2026[1]
EMA/PRAC/98634/2026
Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 4-7 May 2026 PRAC meeting

This document provides an overview of the recommendations adopted by the Pharmacovigilance Risk Assessment Committee (PRAC) on the signals discussed during the meeting of 4-7 May 2026 (including the signal European Pharmacovigilance Issues Tracking Tool [EPITT][2] reference numbers).

PRAC recommendations to provide supplementary information are directly actionable by the concerned marketing authorisation holders (MAHs). PRAC recommendations for regulatory action (e.g. amendment of the product information) are submitted to the Committee for Medicinal Products for Human Use (CHMP) for endorsement when the signal concerns Centrally Authorised Products (CAPs), and to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) for information in the case of Nationally Authorised Products (NAPs). Thereafter, MAHs are expected to take action according to the PRAC recommendations.

When appropriate, the PRAC may also recommend the conduct of additional analyses by the Agency or Member States.

MAHs are reminded that in line with Article 16(3) of Regulation No (EU) 726/2004 and Article 23(3) of Directive 2001/83/EC, they shall ensure that their product information is kept up to date with the current scientific knowledge including the conclusions of the assessment and recommendations published on the European Medicines Agency (EMA) website (currently acting as the EU medicines webportal).

For CAPs, at the time of publication, PRAC recommendations for update of product information have been agreed by the CHMP at their plenary meeting (18-21 May 2026) and corresponding variations will be assessed by the CHMP.

For nationally authorised medicinal products, it is the responsibility of the National Competent Authorities (NCAs) of the Member States to oversee that PRAC recommendations on signals are adhered to.

Variations for CAPs are handled according to established EMA procedures. MAHs are referred to the available guidance. Variations for NAPs (including via mutual recognition and decentralised procedures) are handled at national level in accordance with the provisions of the Member States.

[1] Expected publication date. The actual publication date can be checked on the webpage dedicated to PRAC recommendations on safety signals.
[2] The relevant EPITT reference number should be used in any communication related to a signal.

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The timeline recommended by PRAC for submission of variations following signal assessment is applicable to both innovator and generic medicinal products, unless otherwise specified.

For procedural aspects related to the handling of PRAC recommendations on signals (e.g. submission requirements, contact points, etc.) please refer to the Questions and Answers on signal management.

1. Recommendations for update of the product information[3]

1.1. Pancreatin – Infection due to viral transmission

Authorisation procedure	Non-centralised
EPITT No	20205
PRAC Rapporteur	Dennis Lex
Date of adoption	7 May 2026

Recommendation *[see also section 3]*

Having considered the available evidence in EudraVigilance and literature including epidemiological studies, PRAC has agreed that all MAHs of pancreatin-containing medicinal products should submit a variation within 2 months from the publication of the PRAC recommendation, to amend the product information as described below (new text underlined):

Summary of product characteristics

4.4 Special warnings and precautions for use

The current text should be replaced with the following *(FR/IT):*

Hepatitis E virus infection

Despite measures taken during manufacturing to reduce the risk, the presence of hepatitis E virus (HEV) in medicinal products containing pancreas powder extracts of animal (porcine) origin is possible.

A cross-sectional study has suggested a higher HEV seroprevalence in patients with cystic fibrosis using pancreatic enzyme replacement therapy than in individuals who do not use pancreatin. This study is subject to important limitations including uncertainty with regards to the timing of past infection, as well as the potential for other sources of HEV. As a precaution, immunosuppressed patients receiving high daily dosing should be advised about symptoms of viral hepatitis and to seek medical attention if such symptoms occur.

Package leaflet

2. What you need to know before you take [product name]

The current text should be replaced with the following *(FR/IT):*

Hepatitis E virus infection

This medicine is of animal (pig) origin. Although steps are taken during manufacturing to reduce the risk, the presence of hepatitis E virus in this medicine is possible. Hepatitis E is a virus that can be present in pigs, which can be spread to humans and may cause infection of the liver.

A study has suggested that people with cystic fibrosis who have taken this medicine may be more likely to have had hepatitis E in the past. However, this study has important limitations. For example, it is unclear when the past infection happened or what the source of the infection was.

[3] Translations in all official EU languages of the new product information adopted by PRAC are also available to MAHs on the EMA website.

As a precaution, if you have a weakened immune system and you are also taking high doses of this medicine, your doctor will tell you about the symptoms of infection with hepatitis E. Talk to your doctor if you develop signs of an infection especially fever, nausea, unusual or changes in stomach pain, or yellowing of the skin or eyes.

2. Recommendations for submission of supplementary information

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Amoxicillin; amoxicillin / clavulanic acid	Encephalopathy (20264)	Jan Neuhauser (AT)	Amoxicillin: assess in the next PSUR (submission by 5 June 2027)	Sandoz/Novartis Ospamox
		Dennis Lex (DE)	Amoxicillin / clavulanic acid: assess in the next PSUR (submission by 5 June 2027)	GlaxoSmithKline
Dapagliflozin; dapagliflozin / metformin; dapagliflozin / saxagliptin; dapagliflozin / sitagliptin	Lichen sclerosus (20259)	Mari Thörn (SE)	Supplementary information requested (submission by 29 July 2026)	AstraZeneca AB
Exenatide; insulin icodec / semaglutide; semaglutide	Peripheral neuropathies (20270)	Mari Thörn (SE)	Exenatide: no action	Not applicable
			Semaglutide and insulin icodec / semaglutide: supplementary information requested (submission by 22 July 2026)	Novo Nordisk A/S
Ixekizumab	Behcet's syndrome (20269)	Dirk Mentzer (DE)	Supplementary information requested (submission by 29 July 2026)	Eli Lilly and Company (Ireland) Limited
Semaglutide; insulin icodec / semaglutide	Gastrointestinal volvulus (20260)	Mari Thörn (SE)	Supplementary information requested (submission by 29 July 2026)	Novo Nordisk A/S

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Tocilizumab	Cutaneous vasculitis (20261)	Dirk Mentzer (DE)	Supplementary information requested (submission by 29 July 2026)	Roche Registration GmbH, Celltrion Healthcare Hungary Kft., Fresenius Kabi Deutschland GmbH, STADA Arzneimittel AG, Gedeon Richter Plc.

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Benzodiazepines (including fixed-dose combinations)[4]	Miscarriage associated with in utero exposure to benzodiazepines (including fixed-dose combinations) (20272)	Tiphaine Vaillant (FR)	No action at this stage	Not applicable
Pancreatin	Infection due to viral transmission (20205)	Dennis Lex (DE)	· See section 1.1	· All MAHs of pancreatin-containing medicinal products
			· Review quality process and submit outcome of assessment to the relevant national competent authorities	· Concerned specific MAHs

[4] Alprazolam; bromazepam; brotizolam; chlordiazepoxide; cinolazepam; clobazam; clonazepam; clotiazepam; clorazepate; cloxazolam; delorazepam; diazepam; estazolam; ethyl loflazepate; etizolam; flunitrazepam; flurazepam; ketazolam; loprazolam; lorazepam; lormetazepam; medazepam; mexazolam; midazolam; nitrazepam; nordazepam; oxazepam; pinazepam; prazepam; remimazolam; temazepam; tofisopam; triazolam; as well as fixed-dose combinations: amitriptyline hydrochloride / medazepam; amitriptyline / chlordiazepoxide; bromazepam / propantheline bromide; chlordiazepoxide / clidinium bromide; clidinium bromide / diazepam; cyclobarbital calcium / diazepam; diazepam / gamma-amino-beta-hydroxybutyric acid; diazepam / isopropamide iodide; diazepam / octatropine methylbromide; diazepam / otilonium bromide; diazepam / sulpiride; diazepam / sulpiride / pyridoxine hydrochloride; trimebutine maleate / medazepam