4 May 2026[1]
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Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 7-10 April 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 7-10 April 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 (20-23 April 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. Axicabtagene ciloleucel; lisocabtagene maraleucel – Increased risk of brain oedema in primary mediastinal large B-cell lymphoma (PMBCL) patients

Authorisation procedure	Centralised
EPITT No	20224
PRAC Rapporteur	Karin Erneholm (DK)
Date of adoption	10 April 2026

Recommendation *[see also section 3]*

PRAC recommendation for Yescarta:

Having considered the cumulative review submitted by the Marketing Authorisation Holder (MAH), the PRAC has agreed that the MAH of Yescarta (Kite Pharma EU. B.V.) 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

Neurologic adverse reactions

Fatal and serious cases of cerebral oedema have been reported in patients treated with Yescarta~~.~~ with most cases occurring in patients with ICANS. The risk for cerebral oedema may be higher in PMBCL patients (see section 4.8).

4.8 Undesirable effects

Table 1: Adverse drug reactions identified with Yescarta

Under SOC nervous system disorders with frequency "Uncommon"

Cerebral oedema##

[Footnote to cerebral oedema] ## Most cases of cerebral oedema occurred in patients with ICANS

4.8 Undesirable effects

Description of selected adverse reactions

……

Neurologic adverse reactions

……

Other neurologic adverse reactions have been reported less frequently in clinical trials and included dysphagia (3%), myelitis (0.2%), and quadriplegia (0.1%).

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

In registries, the cerebral oedema event rate in the PMBCL indication was 1.6% overall (2 cases in 129 exposed) compared with 0.7% overall in DLBCL and other lymphoma indications (28 cases in 3876 exposed).

See section 4.4 for monitoring and management guidance.

Package leaflet

4. Possible side effects

Serious side effects

Uncommon (may affect up to 1 in 100 people)

- Condition of severe systemic inflammation which symptoms may include fever, rash, enlarged liver, spleen and lymph nodes.
- Improper functioning of at least 2 organs (eg, liver, lungs and kidneys) that requires medical treatment and/or procedures to restore normal organ function.
- Swelling of the brain (cerebral oedema).

[…]

1.2. Ponatinib – Congenital megacolon, maternal exposure during pregnancy

Authorisation procedure	Centralised
EPITT No	20231
PRAC Rapporteur	Mari Thörn (SE)
Date of adoption	**10 April 2026**

Recommendation *[see also section 3]*

Having considered the available evidence in EudraVigilance including the cumulative review submitted by the Marketing Authorisation Holder (MAH), the PRAC has agreed that the MAH of ICLUSIG (INCYTE BIOSCIENCES DISTRIBUTION B.V.) 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, text to be removed in ~~strike-through~~):

Summary of product characteristics

4.6 Fertility, pregnancy and lactation

[…]

Pregnancy:

Based on limited human data (less than 50 known pregnancy outcomes), cases of congenital megacolon (Hirschsprung's disease) have been reported in children born to women exposed to ponatinib during the first trimester. ~~There are no adequate data from the use of Iclusig in pregnant women.~~ Studies in animals have shown reproductive toxicity (see section 5.3). ~~The potential risk for humans is unknown.~~ Iclusig should not be used during pregnancy unless the clinical condition of the woman requires treatment with ponatinib ~~should be used during pregnancy only when clearly necessary~~. If it is used during pregnancy, the patient must be informed of the potential risk to the

foetus.

Package leaflet

2. What you need to know before you take Iclusig

[…]

Pregnancy and breast-feeding

[…]

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

- **Contraceptive advice for men and women**
  Women of childbearing age being treated with Iclusig should avoid becoming pregnant. Men receiving treatment with Iclusig are advised not to father a child during treatment. Effective contraception must be used during treatment.
  Only use Iclusig during pregnancy if your doctor tells you it is absolutely necessary, as potential risks exist for the unborn child.
  Cases of congenital megacolon, also known as Hirschsprung's disease (a birth defect where nerve cells are missing from part of the baby's large intestine, resulting in bowel blockage) have been reported in children born to women treated with Iclusig in early pregnancy.

[…]

2. Recommendations for submission of supplementary information

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Binimetinib; encorafenib	Neutropenia, febrile neutropenia (20255)	Carla Torre (PT)	Supplementary information requested (submission by 24 June 2026)	Pierre Fabre Medicament
Tirzepatide; warfarin and other coumarin derivatives	Drug interaction with warfarin and other coumarin derivatives leading to international normalised ratio decreased (20198)	Bianca Mulder (NL)	Tirzepatide: monitor in the PSUR	Eli Lilly Nederland B.V.
			Warfarin: assess in the next PSUR (submission by 1 May 2033)	Orifarm, Teofarma, Therabel
			Acenocoumarol: assess in the next PSUR (submission by 29 September 2027)	Merus Labs Luco

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Axicabtagene ciloleucel; lisocabtagene maraleucel	Increased risk of brain oedema in primary mediastinal large B-cell lymphoma (PMBCL) patients (20224)	Karin Erneholm (DK)	Axicabtagene ciloleucel: · See section 1.1 · Assess tumour flare syndrome and tumour pseudoprogression in the next PSUR (submission by 26 December 2026)	Kite Pharma EU B.V.
			Lisocabtagene maraleucel: monitor in the PSUR	Bristol-Myers Squibb Pharma EEIG
Ponatinib	Congenital megacolon, maternal exposure during pregnancy (20231)	Mari Thörn (SE)	· See section 1.2 · Assess use during pregnancy in the next PSUR (submission by 13 March 2027)	Incyte Biosciences Distribution B.V.