17 March 2025[1]
EMA/PRAC/43844/2025
Pharmacovigilance Risk Assessment Committee (PRAC)

# PRAC recommendations on signals

## Adopted at the 10-13 February 2025 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 10-13 February 2025 (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 (24-27 February 2025) 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. Mogamulizumab – Colitis*

| | |
|---|---|
| **Authorisation procedure** | Centralised |
| **EPITT No** | 20113 |
| **PRAC Rapporteur** | Marie Louise Schougaard Christiansen (DK) |
| **Date of adoption** | 13 February 2025 |

## Recommendation

Having considered the available evidence in EudraVigilance and the literature, and the cumulative review submitted by the Marketing Authorisation Holder (MAH), the PRAC has agreed that the MAH of POTELIGEO (Kyowa Kirin Holdings 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**

4.8 Undesirable effects

Under the SOC Gastrointestinal disorders with a frequency 'common'

Colitis

Under 'Description of selected adverse reactions'

*Gastrointestinal disorders*

Colitis was mainly characterized by watery diarrhoea, in some cases excessive.

**Package leaflet**

4. Possible side effects

**Serious side effects**

**Common side effects (may affect up to 1 in 10 people):**

- Watery diarrhoea, more bowel movements than usual, severe abdominal pain or tenderness which are possible signs of inflammation of the large bowel (colitis).

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

## 2. Recommendations for submission of supplementary information

| INN | Signal (EPITT No) | PRAC Rapporteur | Action for MAH | MAH |
|---|---|---|---|---|
| Ciltacabtagene autoleucel; idecabtagene vicleucel; tisagenlecleucel | Progressive multifocal leukoencephalopathy (20153) | Gabriele Maurer (DE) | Supplementary information requested (submission by 11 April 2025) | Bristol-Myers Squibb Pharma EEIG, Janssen-Cilag International NV, Novartis Europharm Limited |
| Clozapine | Haematological malignant tumours (20150) | Amelia Cupelli (IT) | Assess in the next PSUR (submission by 1 June 2025) | MAHs of clozapine containing products with the obligation to submit PSURs |
| Idecabtagene vicleucel | Sarcoidosis (20154) | Mari Thörn (SE) | Assess in the next PSUR (submission by 3 June 2025) | Bristol-Myers Squibb Pharma EEIG |
| Vortioxetine | Hallucinations, not related to serotoninergic syndrome (20152) | Jo Robays (BE) | Supplementary information requested (submission by 2 April 2025) | H. Lundbeck A/S |

## 3. Other recommendations

| INN | Signal (EPITT No) | PRAC Rapporteur | Action for MAH | MAH |
|---|---|---|---|---|
| Adagrasib | Thrombocytopenia (20112) | Kimmo Jaakkola (FI) | Monitor in PSUR | Bristol-Myers Squibb Pharma EEIG |
| Regorafenib | Hyperammonaemia, hyperammonaemic encephalopathy (20147) | Bianca Mulder (NL) | Comment on proposed product information update (submission by 7 March 2025) | Bayer AG |