2 June 2025[1]
EMA/PRAC/143099/2025
Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 5-8 May 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 5-8 May 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 (19-22 May 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. Sertraline – Multiple acyl-coenzyme A dehydrogenase deficiency (MADD)

Authorisation procedure	Non-centralised
EPITT No	20125
PRAC Rapporteur	Liana Martirosyan (NL)
Date of adoption	8 May 2025

Recommendation

Having considered the available evidence from literature and the EudraVigilance database, including the cumulative review submitted by the Marketing Authorisation Holder (MAH), the PRAC has agreed that the MAHs of all sertraline-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 (taking into account the already existing wording in some nationally authorised products the text needs to be adapted by MAHs to individual products) (new text underlined):

Summary of product characteristics

4.8 Undesirable effects

Table 1: Adverse reactions

Under SOC "Musculoskeletal and connective tissue disorders", with frequency "Not known":

Multiple acyl-coenzyme A dehydrogenase deficiency (MADD)-like disorder*

* ADR identified post-marketing

Package leaflet

4. Possible side effects

Under frequency ''Not known'':

Muscle weakness and severe muscle pain, which can be a sign of multiple acyl-coenzyme A dehydrogenase deficiency (MADD)-like disorder.

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

1.2. Sulfamethoxazole, trimethoprim (cotrimoxazole) – Circulatory shock

Authorisation procedure	Non-centralised
EPITT No	20135
PRAC Rapporteur	Barbara Kovačić Bytyqi (HR)
Date of adoption	8 May 2025

Recommendation

Having considered the available evidence from literature and the EudraVigilance database, including the cumulative review submitted by the Marketing Authorisation Holder (MAH), the PRAC has agreed that the MAHs of all sulfamethoxazole + trimethoprim (co-trimoxazole)-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 (taking into account the already existing wording in some nationally authorised products the text needs to be adapted by MAHs to individual products) (new text underlined):

Summary of product characteristics

4.8 Undesirable effects

Under SOC "Vascular disorders", with frequency "Not known":

Circulatory shock

Description of selected adverse reactions

...

Circulatory shock

Cases of circulatory shock, often accompanied by fever and not responding to standard treatment for hypersensitivity, have been reported with sulfamethoxazole + trimethoprim, mainly in immunocompromised patients.

Package leaflet

4. Possible side effects

Serious side effects

Call the emergency department immediately if you experience multiple symptoms such as fever, very low blood pressure or increased heart rate after taking this drug as it may be a sign of shock.

2. Recommendations for submission of supplementary information

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Adalimumab	Morphoea (20166)	Karin Bolin (SE)	Supplementary information requested (submission by 23 July 2025)	AbbVie Deutschland GmbH & Co. KG
Dabigatran	Splenic rupture (20164)	Marie Louise Schougaard Christiansen (DK)	Supplementary information requested (submission by 27 June 2025)	Boehringer Ingelheim International GmbH
Desogestrel; etonogestrel	Meningioma (20167)	Karin Bolin (SE)	Supplementary information requested (submission by 27 August 2025)	Organon
Dinutuximab beta	Atypical haemolytic uraemic syndrome (20169)	Gabriele Maurer (DE)	Supplementary information requested (submission by 27 June 2025)	Recordati Netherlands B.V.
Osimertinib	Hepatitis B reactivation (20172)	Bianca Mulder (NL)	Supplementary information requested (submission by 27 June 2025)	AstraZeneca AB
Polatuzumab vedotin	Infusion site extravasation (20171)	Mari Thörn (SE)	Assess in the next PSUR (submission by 18 August 2025)	Roche Registration GmbH
Somatrogon	Lipoatrophy (20173)	Liana Martirosyan (NL)	Supplementary information requested (submission by 27 June 2025)	Pfizer Europe MA EEIG

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Adalimumab	Paradoxical hidradenitis (20126)	Karin Bolin (SE)	Monitor in PSUR	MAHs of adalimumab containing products with an obligation to submit PSURs
Chikungunya virus (CHIKV) Δ5nsP3 strain (live, attenuated)	Adverse events requiring hospitalisation in elderly patients (20178)	Gabriele Maurer (DE)	Review under Article 20 of Regulation (EC) No 726/2004	Valneva Austria GmbH