25 September 2023[1]
EMA/PRAC/359902/2023
Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 28-31 August 2023 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 28-31 August 2023 (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 (11-14 September 2023) 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. Acetazolamide – Choroidal effusion and choroidal detachment

Authorisation procedure	Non-centralised
EPITT No	19924
PRAC Rapporteur	Ulla Wändel Liminga (SE)
Date of adoption	31 August 2023

Recommendation

Having considered the available evidence from case reports in EudraVigilance and literature, the PRAC has agreed that Marketing Authorisation Holders of acetazolamide containing 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

Cases of choroidal effusion/detachment have been reported after the use of acetazolamide. Symptoms include acute onset of decreased visual acuity or ocular pain and can occur within hours after initiation of acetazolamide treatment. If choroidal effusion/detachment is suspected, acetazolamide should be discontinued as rapidly as possible.

4.8 – Undesirable effects

Eye disorders

Frequency 'not known': Choroidal effusion, choroidal detachment

Package leaflet

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

Warnings and precautions

[This information should be added as separate paragraph, after issues that should be assessed before treatment.]
A decrease in vision or eye pain could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion or choroidal detachment). This can happen within hours of taking [product name]. Talk to your doctor promptly if you experience these symptoms.

4 - Possible side effects
Frequency 'not known': Decrease in vision or pain in your eyes due to accumulation of fluid in the vascular layer of the eye (choroidal effusion or choroidal detachment).

[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
Amphotericin B	Hyperkalaemia (19966)	Maria del Pilar Rayon (ES)	Supplementary information requested (submission by 30 October 2023)	Teva, Gilead, Cheplapharm Arzneimittel GmbH
Atezolizumab; avelumab; cemiplimab; dostarlimab; durvalumab; ipilimumab; nivolumab; pembrolizumab; tislelizumab; tremelimumab	Coeliac disease (19958)	Menno van der Elst (NL)	Supplementary information requested (submission by 8 November 2023)	Roche Registration GmbH, Merck Europe B.V., Regeneron Ireland Designated Activity Company, GlaxoSmithKline (Ireland) Limited, AstraZeneca AB, Bristol-Myers Squibb Pharma EEIG, Merck Sharp & Dohme B.V., Novartis Europharm Limited
Atezolizumab; avelumab; cemiplimab; dostarlimab; durvalumab; ipilimumab; nivolumab; pembrolizumab; tislelizumab; tremelimumab	Pancreatic failure (19955)	Martin Huber (DE)	Supplementary information requested (submission by 8 November 2023)	Roche Registration GmbH, Merck Europe B.V., Regeneron Ireland Designated Activity Company, GlaxoSmithKline (Ireland) Limited, AstraZeneca AB, Bristol-Myers Squibb Pharma EEIG, Merck Sharp & Dohme B.V., Novartis Europharm Limited

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Avatrombopag	Antiphospholipid syndrome (19954)	Monica Martinez Redondo (ES)	Supplementary information requested (submission by 30 October 2023)	Swedish Orphan Biovitrum AB
Cefotaxime	Drug reaction with eosinophilia and systemic symptoms (DRESS) (19960)	Jan Neuhauser (AT)	Supplementary information requested (submission by 30 October 2023)	Sanofi Aventis
Cobimetinib; vemurafenib	Aphthous ulcer, mouth ulceration, stomatitis (19961)	Ulla Wändel Liminga (SE)	Supplementary information requested (submission by 30 October 2023)	Roche Registration GmbH
Minoxidil (topical formulation)	Hypertrichosis in children following accidental exposure via patients (19951)	Eamon O'Murchu (IE)	Assess in the next PSUR (submission by 29 January 2024)	MAHs of minoxidil for cutaneous use with obligation to submit PSURs
Osimertinib	Anaphylactic reaction (19959)	Menno van der Elst (NL)	Assess in the next PSUR (submission by 10 February 2024)	AstraZeneca AB
Palbociclib	Rhabdomyolysis by interaction with statins (19963)	Marie Louise Schougaard Christiansen (DK)	Assess in the next PSUR (submission by 11 October 2023)	Pfizer Europe MA EEIG

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Megestrol	Meningioma (19923)	Eamon O'Murchu (IE)	Monitor in PSUR	MAHs of megestrol containing medicinal products