4 March 2024[1]
EMA/PRAC/54558/2024
Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 5-8 February 2024 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 February 2024 (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 February 2024) 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.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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

Not applicable

2. Recommendations for submission of supplementary information

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Adagrasib	Serious cutaneous adverse reactions (SCARs) (20051)	Kimmo Jaakkola (FI)	Supplementary information requested (submission by 7 March 2024)	Mirati Therapeutics B.V.
Ceftriaxone	Precipitation when administered with calcium-containing solutions in infants between 29 days and 1 year (1964)	Zane Neikena (LV)	Supplementary information requested (submission by 10 April 2024)	Roche
Medroxyprogesterone acetate	Meningioma (20030)	Bianca Mulder (NL)	Supplementary information requested (submission by 10 April 2024)	Pfizer Limited
Methotrexate	Hyperhomocysteinaemia (20031)	Martin Huber (DE)	Assess in the ongoing PSUR (submission of data within the MAH comments to the PSUR preliminary assessment report by 15 May 2024)	MAHs of methotrexate-containing products with obligation to submit PSURs
Valaciclovir	Acute hepatitis (20047)	Jana Lukačišinová (CZ)	Supplementary information requested (submission by 10 April 2024)	MAHs of valaciclovir-containing products with obligation to submit PSURs

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Atezolizumab; avelumab; cemiplimab; dostarlimab; durvalumab; ipilimumab; nivolumab; nivolumab, relatlimab; pembrolizumab; tislelizumab; tremelimumab	Coeliac disease (19958)	Bianca Mulder (NL)	Provide ADR frequency and comments on the proposed amendments to the product information (submission by 7 March 2024)	Bristol-Myers Squibb Pharma EEIG, Merck Sharp & Dohme B.V., Merck Europe B.V., AstraZeneca AB, Roche Registration GmbH, Regeneron Ireland Designated Activity Company, GlaxoSmithKline (Ireland) Limited, Beigene Ireland Limited
Atezolizumab; avelumab; cemiplimab; dostarlimab; durvalumab; ipilimumab; nivolumab; nivolumab, relatlimab; pembrolizumab; tislelizumab; tremelimumab	Pancreatic failure (19955)	Martin Huber (DE)	Provide ADR frequency and comments on the proposed amendments to the product information (submission by 7 March 2024)	Bristol-Myers Squibb Pharma EEIG, Merck Sharp & Dohme B.V., Merck Europe B.V., AstraZeneca AB, Roche Registration GmbH, Regeneron Ireland Designated Activity Company, GlaxoSmithKline (Ireland) Limited, Beigene Ireland Limited
Chlorhexidine for cutaneous use and other relevant fixed-	Persistent corneal injury and significant visual impairment (19970)	Lina Šeibokienė (LT)	Provide comments on the proposed amendments to the product information	Becton Dickinson France, 3M Deutschland GmbH, Mölnlycke Health Care

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
dose combinations[3]			(submission by 7 March 2024)	

[3] Chlorhexidine, chlorocresol, hexamidine; chlorhexidine gluconate, chlorocresol, hexamidine; chlorocresol, hexamidine, chlorhexidine digluconate; benzalkonium chloride, chlorhexidine gluconate; chlorhexidine gluconate, benzoxonium chloride, retinol; benzalkonium chloride, chlorhexidine gluconate, benzyl alcohol; chlorhexidine gluconate; chlorhexidine gluconate, cetrimonium; chlorhexidine gluconate, chlorocresol, hexamidine; chlorhexidine gluconate, dexpanthenol; chlorhexidine gluconate, hydrocortisone; chlorhexidine gluconate, hydrogen peroxide, isopropyl alcohol; chlorhexidine gluconate, isopropyl alcohol; chlorhexidine gluconate, ethanol; chlorhexidine gluconate, phenol; benzalkonium chloride, chlorhexidine gluconate; benzalkonium chloride, chlorhexidine digluconate; chlorhexidine digluconate; chlorhexidine digluconate, ethanol; chlorhexidine digluconate, isopropyl alcohol; chlorhexidine dihydrochloride; benzalkonium chloride, chlorhexidine dihydrochloride, isopropyl myristate, liquid paraffin; chlorhexidine dihydrochloride, dexpanthenol; chlorhexidine dihydrochloride, nystatin; chlorhexidine dihydrochloride, nystatin, dexamethasone; chlorhexidine dihydrochloride, nystatin, hydrocortisone; chlorhexidine dihydrochloride, zinc oxide, pramocaine hydrochloride;, triamcinolone acetonide; chlorhexidine dihydrochloride, dexpanthenol, alphatocopherol acetate, vitamin A; chlorhexidine gluconate; cetrimide, chlorhexidine digluconate; chlorhexidine acetate; cetrimide, chlorhexidine acetate; retinol palmitate, chlorhexidine acetate; retinol palmitate, benzocaine, retinol, chlorhexidine acetate; bacitracin zinc, chlorhexidine acetate; nystatin, hydrocortisone, chlorhexidine acetate