4 July 2022
EMA/PRAC/407574/2022
Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 7-10 June 2022 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 June 2022 (including the signal European Pharmacovigilance Issues Tracking Tool [EPITT][1] 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 June 2022) 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] 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

Not applicable.

2. Recommendations for submission of supplementary information

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Adalimumab; etanercept; infliximab	Menstrual disorder (19812)	Ulla Wändel Liminga (SE)	Supplementary information requested (submission by 31 August 2022)	Abbvie, Pfizer Europe MA EEIG, Janssen Biologics B.V.
Durvalumab	Myelitis transverse (19815)	David Olsen (NO)	Supplementary information requested (submission by 24 August 2022)	AstraZeneca AB
Elasomeran (COVID-19 mRNA vaccine) – Spikevax	Amenorrhoea (19781)	Brigitte Keller-Stanislawski (DE)	Assess in the PSUR with data lock point 18 December 2022	Moderna Biotech Spain, S.L.
Elasomeran (COVID-19 mRNA vaccine) – Spikevax	Heavy menstrual bleeding (19780)	Brigitte Keller-Stanislawski (DE)	Supplementary information requested (submission by 24 August 2022)	Moderna Biotech Spain, S.L.
Gemtuzumab ozogamicin	Atypical haemolytic reactions (19788)	Márcia Silva (PT)	Supplementary information requested (submission by 27 July 2022)	Pfizer Europe MA EEIG
Ipilimumab; nivolumab	Pure red cell aplasia and aplastic anaemia (19804)	Brigitte Keller-Stanislawski (DE)	Supplementary information requested (submission by 24 August 2022)	Bristol-Myers Squibb Pharma EEIG
Temozolomide	Progressive multifocal leukoencephalopathy (PML) (19814)	Martin Huber (DE)	Supplementary information requested (submission by 27 July 2022)	Merck Sharp & Dohme B.V.
Tildrakizumab	Herpes zoster (19801)	Adam Przybylkowski (PL)	Supplementary information requested (submission by 24 August 2022)	Almirall S.A

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Tozinameran (COVID-19 mRNA vaccine) – Comirnaty	Amenorrhoea (19784)	David Olsen (NO)	Assess in the PSUR with data lock point 18 December 2022	BioNTech Manufacturing GmbH
Tozinameran (COVID-19 mRNA vaccine) – Comirnaty	Heavy menstrual bleeding (19783)	David Olsen (NO)	Supplementary information requested (submission by 24 August 2022)	BioNTech Manufacturing GmbH

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Codeine, ibuprofen	Renal tubular acidosis and hypokalaemia (19820)	Rhea Fitzgerald (IE)	· Respond to list of questions · Provide comments to the proposed updates to the product information · Submit a draft DHPC · Discuss inclusion of a warning on the outer label packaging (submission by 27 July 2022 for all bullet points)	Innovator MAHs of codeine/ ibuprofen (Reckitt Benckiser and Mylan)
Human normal immunoglobulin for intravenous use	Thrombocytopenia (19764)	Brigitte Keller-Stanislawski (DE)	Routine pharmacovigilance	MAHs of all approved intravenous immunoglobulins