8 March 2021[1]
EMA/PRAC/82059/2021
Pharmacovigilance Risk Assessment Committee (PRAC)

PRAC recommendations on signals

Adopted at the 8-11 February 2021 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 8-11 February 2021 (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 (22-25 February 2021) 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[3]

1.1. Prednisolone; prednisone – Bradycardia

Authorisation procedure	Non-centralised
EPITT No	19613
PRAC rapporteur(s)	Anette Kirstine Stark (DK)
Date of adoption	11 February 2021

Recommendation

Having considered the available evidence, including the data submitted by the MAHs, the PRAC has agreed that the MAH(s) of prednisone and prednisolone containing products for systemic use 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

Cardiac disorders

Frequency 'not known': Bradycardia*

*Following high doses

Package leaflet

4. Possible side effects

Not known: Slow heart rate

[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
Ceftriaxone	Hepatitis (19603)	Zane Neikena (LV)	Supplementary information requested (submission by 7 April 2021)	MAH for the innovator of ceftriaxone containing products
Olanzapine	Cardiomyopathy (19663)	Kimmo Jaakkola (FI)	Supplementary information requested (submission by 7 April 2021)	Eli Lilly Nederland B.V.
Olaparib	Pneumocystis jirovecii pneumonia (19651)	Amelia Cupelli (IT)	Supplementary information requested (submission by 7 April 2021)	AstraZeneca AB
Remdesivir	Sinus bradycardia (19659)	Eva Jirsová (CZ)	Assess in the ongoing PSUR procedure EMEA/H/C/PSUSA/00010840/202011 (submission by 12 May 2021)	Gilead Sciences Ireland UC
Romosozumab	Renal impairment (19648)	Adrien Inoubli (FR)	Assess in the next PSUR (submission by 18 March 2021)	UCB Pharma S.A.

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins): atorvastatin; fenofibrate, simvastatin; fluvastatin; lovastatin; pitavastatin; pravastatin; pravastatin sodium, fenofibrate; rosuvastatin; simvastatin	Bullous pemphigoid (19586)	Adrien Inoubli (FR)	Monitor in PSUR	MAHs of statin-containing products
			New cumulative review in next PSUR on any atorvastatin containing products	MAH originator of atorvastatin (Viatris)
Filgrastim	Immune reconstitution inflammatory syndrome (IRIS) (19587)	Kirsti Villikka (FI)	Routine pharmacovigilance	MAHs of filgrastim-containing products
Remdesivir	Acute kidney injury (19605)	Eva Jirsová (CZ)	Monitor in PSUR	Gilead Sciences Ireland UC