7 January 2020[1]
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Pharmacovigilance Risk Assessment Committee (PRAC)

# PRAC recommendations on signals

## Adopted at the 25-28 November 2019 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 25-28 November 2019 (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 (9-12 December 2019) 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] Intended 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

None

# 2. Recommendations for submission of supplementary information

| INN | Signal (EPITT No) | PRAC Rapporteur | Action for MAH | MAH |
|---|---|---|---|---|
| Andexanet alfa | Erroneous assay results for levels of anti-factor Xa activity with use of andexanet alfa (19493) | Menno van der Elst (NL) | Supplementary information requested (submission by 10 February 2020) | Portola Netherlands B.V. |
| Idelalisib | Drug reaction with eosinophilia and systemic symptoms (DRESS) (19500) | Martin Huber (DE) | Supplementary information requested (submission by 10 February 2020) | Gilead Sciences Ireland UC |
| Nilotinib | Anaphylactic reaction (19497) | Hans Christian Siersted (DK) | Assess in the next PSUR (submission by 10 April 2020) | Novartis Europharm Limited |

# 3. Other recommendations

| INN | Signal (EPITT No) | PRAC Rapporteur | Action for MAH | MAH |
|---|---|---|---|---|
| Ifosfamide | Increased risk of encephalopathy (19433) | Annika Folin (SE) | No action at this stage | Not applicable |
| Insulin[3] | Cutaneous amyloidosis (19499) | Hans Christian Siersted (DK) | Provide comments on the proposed updates to the product information (submission by 10 February 2020) | Novo Nordisk, Eli Lilly, Sanofi-Aventis, Wockhardt UK LTD |
| Thiazide, thiazide-like diuretics and combinations | Choroidal effusion (19468) | Martin Huber (DE) | Provide comments on the proposed updates to the product information (submission by 8 January 2020) | Innovator MAHs of thiazide and thiazide-like diuretics[4] |

[3] Insulin aspart; insulin aspart/insulin degludec; insulin bovine; insulin degludec; insulin degludec/liraglutide; insulin determir; insulin glulisine; insulin human; insulin lispro; insulin glargine; insulin porcine

[4] Waymade Plc, Alliance Pharmaceuticals Ltd, Ipsen Consumer Healthcare, Pharmaswiss Česká Republika S.R.O., Mercury Pharmaceuticals Ltd, Chiesi España S.A.U., Chelonia Healthcare Limited, Lestral S.A., Zentiva K.S., Desma Laboratorio Farmacéutico SL, BGP Products Unipessoal Lda