



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Pharmacovigilance Risk Assessment Committee

PRAC recommendations on signals

Adopted at the PRAC meeting of 6-9 October 2014

This document provides an overview of the recommendations adopted by the Pharmacovigilance Risk Assessment Committee (PRAC) on the signals discussed during the meeting of 6-9 October 2014 (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 October 2014) 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.



The established procedures and timelines for submission of variation applications pertaining to generic medicinal products are to be followed.

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

The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a **causal relationship** between the medicine and the reported adverse event.

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Aflibercept	Higher systemic exposure compared to ranibizumab after intravitreal injection (18112)	Arnaud Batz (FR)	Supplementary information requested (submission by 13/12/2014)	Bayer Pharma AG
Amiodarone	Syndrome of inappropriate antidiuretic hormone secretion (SIADH) (18091)	Menno van der Elst (NL)	Supplementary information requested (submission by 13/12/2014)	Sanofi
Aripiprazole	Hyperprolactinaemia (18086)	Margarida Guimarães (PT)	Supplementary information requested (submission by 13/12/2014)	Otsuka Pharmaceutical Europe Ltd
Exenatide	Goitre and worsening/enlargement of goitre (18077)	Qun-Ying Yue (SE)	Assess in the next PSUR (submission by 08/06/2015)	AstraZeneca AB
Tocilizumab	Cholecystitis (18092)	Brigitte Keller-Stanislawski (DE)	Assess in the next PSUR (submission by 19/12/2014)	Roche Registration Ltd

3. Other recommendations

INN	Signal (EPITT No)	PRAC Rapporteur	Action for MAH	MAH
Atazanavir	Haemolytic anaemia (17921)	Arnaud Batz (FR)	Routine pharmacovigilance	Bristol-Myers Squibb Pharma EEIG
Sodium-containing effervescent, dispersible and soluble medicines	Cardiovascular events (17931)	Julie Williams (UK)	No action at this stage	Not applicable
Valproate and related substances	Mitochondrial toxicity (17956)	Martin Huber (DE)	No action at this stage	Sanofi-Aventis