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Patient Health Protection

PhVWP Monthly report on safety concerns, guidelines and general matters

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The CHMP Pharmacovigilance Working Party (PhVWP) held its February 2012 plenary meeting on 13-15 February 2012.

Safety concerns

Discussions on non-centrally authorised medicinal products are summarised below in accordance with the PhVWP publication policy. The positions agreed by the PhVWP for non-centrally authorised products form recommendations to Member States. For the publication policy, readers are referred to http://www.ema.europa.eu/docs/en_GB/document_library/Report/2009/10/WC500006181.pdf.

The PhVWP also provides advice to the Committee for Medicinal Products for Human Use (CHMP) on centrally authorised products and products subject to ongoing CHMP procedures at the request of the CHMP. For safety updates concerning these products, readers are referred to the meeting highlights from the CHMP published under http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/landing/news_and_events.jsp&mid=.

DOCETAXEL ACTAVIS – Risk of infusion site reactions

Care should be taken when preparing docetaxel infusions in order to minimise the risk of infusion site reactions. Further evaluation of this signal will be achieved through continued close monitoring and careful evaluation of any further cases with DOCETAXEL ACTAVIS.

Given a cluster of case reports of infusion site reactions with the docetaxel-containing medicinal product DOCETAXEL ACTAVIS in Finland, the PhVWP reviewed these cases. The PhVWP agreed with the proposal from the marketing authorisation holder to carry out detailed follow-up of any reports of infusion site reaction, including collection of information on when the reaction occurred in relation to the time of infusion and whether the patient had previously been treated with docetaxel. In addition, the marketing authorisation holder will prepare monthly safety update reports with a focus on infusion

European Medicines Agency
7 Westferry Circus ● Canary Wharf
London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

HMA Management Group
Kevin O'Malley House ● Earlsfort Centre
Earlsfort Terrace ● Dublin 2 ● Ireland
Telephone +353 1 634 3453 **Facsimile** +353 1 661 4764
E-mail hma-ps@imb.ie **Website** www.hma.eu

site reactions to obtain more information and ensure close monitoring of the issue (see Annex 1 for the Summary Assessment Report).

Guidelines and general matters

Below is a summary of the main discussions on guidelines and other general matters of an organisational, regulatory or methodological nature.

Good Pharmacovigilance Practices (GVP) for the EU – Release for public consultation

The PhVWP noted that the first seven draft modules of good pharmacovigilance practices (GVP) will be released for public consultation in the following week. GVP is a set of guidelines for the conduct of pharmacovigilance in the EU, drawn up by the European Medicines Agency in cooperation with the competent authorities in Member States and interested parties based on Article 108a of Directive 2001/83/EC as amended by the new pharmacovigilance legislation (see PhVWP Monthly Report 1101). GVP will apply to marketing authorisation holders in the EU, the Agency and competent authorities in Member States. Experts from the PhVWP contributed to the development of these GVP modules, and the PhVWP was consulted on all modules as part of the development process. The first seven modules provide guidance on pharmacovigilance systems and their quality systems, the pharmacovigilance system master file, risk management systems, reporting of adverse reaction cases, periodic safety update reports, post-authorisation safety studies and signal management. Interested readers and those wanting to participate in the public consultation are referred to the EMA website (http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/02/news_detail_001451.jsp&mid=WC0b01ac058004d5c1).

Regulatory abbreviations

CHMP – Committee for Medicinal Products for Human Use

CMDh – Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human

EU – European Union

HMA – Heads of Medicines Agencies

PASS – post-authorisation safety study

PhVWP – CHMP Pharmacovigilance Working Party

PL – package leaflet

PSUR – periodic safety update report

RMP – risk management plan

SmPC – summary of product characteristics

Annex 1

Summary Assessment Report of the PhVWP February 2012

DOCETAXEL ACTAVIS – Risk of infusion site reactions

Key message

Care should be taken when preparing docetaxel infusions in order to minimise the risk of infusion site reactions. Further evaluation of this signal will be achieved through continued close monitoring and careful evaluation of any further cases with DOCETAXEL ACTAVIS.

Safety concern and reason for current safety review

A cluster of case reports of infusion site reactions with the docetaxel-containing medicinal product DOCETAXEL ACTAVIS was observed by the Finnish competent authority. These were reported from three hospitals where supply had been switched to DOCETAXEL ACTAVIS from another docetaxel-containing product.

The occurrence of infusion site reactions with docetaxel-containing medicinal products is known, and the reactions are generally mild, consisting of hyperpigmentation, inflammation, redness or dryness of the skin, phlebitis or extravasation and swelling of the vein.

The adverse reactions reported in Finland were described as 'burn like' lesions that appeared most frequently about 7 to 10 days after the infusion. The reactions were most often non-serious but since they were distressing to the patient they were reviewed by the PhVWP.

Clinical setting

Docetaxel is an antineoplastic active substance used as an infusion in the treatment of different types of cancer, e.g. breast cancer, lung cancer, prostate cancer, gastro-intestinal cancer and head and neck cancers.

Information on the data assessed

After an initial review of the Finnish case reports, the PhVWP considered that although this information constituted a safety signal, it was observed only in Finland and no other Member State. The available data did not provide an explanation for this adverse reaction cluster, and in order to evaluate the signal further, the marketing authorisation holder ACTAVIS was requested to submit an updated overview on this type of adverse reactions and an evaluation of the quality aspects of the batches of DOCETAXEL ACTAVIS.

Outcome of the assessment

The assessment of the information provided did not show any quality defect and it was demonstrated that the stability of the DOCETAXEL ACTAVIS solution in the recommended diluents was no different to that of the docetaxel-containing originator product. Confirmation was obtained that the solutions for infusion had been prepared in the hospitals in accordance with the summary of product characteristics and local protocols. The PhVWP noted that since December 2011 no further cases of infusion site reactions have been observed, suggesting that the issue may have been related to the introduction of the product to clinical use.

The PhVWP agreed with the proposal from the marketing authorisation holder for DOCETAXEL ACTAVIS to carry out detailed follow-up of any reports of infusion site reaction, including collection of information on when the reaction occurred in relation to the time of infusion and whether the patient had previously been treated with docetaxel. In addition, the marketing authorisation holder will prepare monthly safety update reports with a focus on infusion site reactions to obtain more information and ensure close monitoring of the issue.