European Medicines Agency

London, 9 October 2009
EMEA/599450/2009

ISSUE NUMBER: 0909

MONTHLY REPORT

PHARMACOVIGILANCE WORKING PARTY (PHVWP)

SEPTEMBER 2009 PLENARY MEETING

The CHMP Pharmacovigilance Working Party (PhVWP) held its September 2009 plenary meeting on 21-23 September 2009.

PhVWP DISCUSSIONS ON SAFETY CONCERNS

Below is a summary of the discussions regarding non-centrally authorised medicinal products in accordance with the PhVWP publication policy (see under http://www.emea.europa.eu/htms/general/contacts/CHMP/CHMP_PhVWP.html). Positions agreed by the PhVWP for non-centrally authorised products are recommendations to Member States.

For safety updates concerning centrally authorised products and products subject to ongoing CHMP procedures, readers are referred to the CHMP Monthly Report (see under http://www.emea.europa.eu/whatsnewp.htm). The PhVWP provides advice on these products to the Committee of Medicinal Products for Human Use (CHMP) upon its request.

Apomorphine - Risk of QT interval prolongation

Exercise caution when using apomorphine in patients at risk for torsades de pointes and avoid concomitant use with other QT interval prolonging medicines

Apomorphine is a dopamine agonist used to treat motor fluctuations ("on-off" phenomena) in Parkinson's disease. Some evidence from preclinical and clinical studies suggested that apomorphine, especially at high doses, may have the potential to prolong the QT interval in humans. The PhVWP considered that increased awareness of the issue would promote safer prescribing. The PhVWP therefore recommended that the product information should contain warnings to exercise caution when treating patients at risk for torsades de pointes and to avoid the concomitant use of apomorphine with other medicines known to prolong the QT interval.

The PhVWP informed the CMD(h) accordingly, and for the final wording to be included in the Summary of Product Characteristics (SmPCs) and Package Leaflet (PLs) as well as practical information on the implementation, interested readers are asked to visit the HMA website (http://www.hma.eu/cmdh.html) for upcoming information.

Further clinical trials are ongoing and the results will be reviewed when available.

EMEA
7 Westferry Circus, Canary Wharf
London, E14 4HB, UK
Tel. (44-20) 74 18 84 00
Fax (44-20) 75 23 71 29
E-mail: mail@emea.europa.eu
Internet: http://www.emea.europa.eu

HMA Management Group
Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace
Dublin 2, Ireland
Tel: (353-1) 63 43 453
E-mail: hma-ps@imb.ie
Internet: http://www.hma.eu

Ceftriaxone - Harmonisation of contraindications in newborns and risk of calcium-ceftriaxone precipitation when administered/mixed with solutions containing calcium

Ceftriaxone and calcium-containing solutions contraindicated in newborns in certain conditions and not to be mixed or administered simultaneously for intravenous use in patients of any age

A review of the risk of precipitation of the antibiotic ceftriaxone and calcium with intravenous co-administration was conducted because of differences in the product information across Member States in this respect.

The PhVWP discussed a small number of case reports of fatal reactions due to calcium-ceftriaxone precipitates in lungs and kidneys in premature newborns and full-term newborns aged less than 28 days after intravenous (IV) medication. In at least one case, ceftriaxone and calcium were given at different times and through different intravenous lines. In vitro studies requested from the marketing authorisation holder by the PhVWP demonstrated that newborns may have an increased risk of precipitation of ceftriaxone-calcium compared to other age groups due to their lower blood volume and longer elimination half-life of ceftriaxone compared with adults. The available data do not contain reports of confirmed intravascular precipitates in patients other than newborns.

As a result, the PhVWP recommended harmonising, across the EU, the wording in the product information in terms of contraindicating ceftriaxone in premature newborns and, in certain conditions, full-term newborns. Furthermore, the PhVWP recommended that in patients of any age ceftriaxone must not be mixed or administered simultaneously IV with any calcium-containing solution, even via different infusion lines or at different infusion sites. However, in patients older than 28 days sequential administration may be feasible when following certain preventive measures. Likewise, preventive measures are considered necessary in patients requiring continuous total parenteral nutrition (TPN).

The PhVWP informed the CMD(h) accordingly, and for the final wording to be included in the Summary of Product Characteristics (SmPCs) and Package Leaflet (PLs) as well as practical information on the implementation, interested readers are asked to visit the HMA website (http://www.hma.eu/cmdh.html) for upcoming information.

Vigabatrin - Risk of movement disorders with or without abnormalities shown in brain magnetic resonance imaging (MRI)

Evaluate benefit/risk balance of vigabatrin for each patient and consider dose reduction or a gradual discontinuation of treatment if unusual movement disorders occur during treatment

Vigabatrin is an antiepileptic and is also indicated for the treatment of infantile spasms (West's syndrome). West’s syndrome is a rare, severe disease in children with very few treatment options other than vigabatrin. Spontaneous reports from healthcare professionals on movement disorders and cerebral abnormalities shown by magnetic resonance imaging (MRI) in patients treated with vigabatrin triggered a review of data, including a literature review.

With regard to abnormal brain MRI findings, the PhVWP considered that these have been reported, in particular in young infants treated for infantile spasms with high doses of vigabatrin, but that the clinical significance of these findings is currently unknown. In some cases, the abnormal MRI findings may resolve even if vigabatrin is continued.

Concerning movement disorders, the PhVWP concluded that disorders such as dystonia, dyskinesia and hypertonia have been reported in patients treated for infantile spasms, either alone or in association with abnormalities in MRI. Therefore, the PhVWP recommended that the treating physician should evaluate the benefit/risk balance of vigabatrin for each patient at individual level. If new movement disorders occur during treatment with vigabatrin, consideration should be given to dose reduction or a gradual discontinuation of treatment. Parents/carers should be advised to consult the physician in case unusual movements are seen in a treated child.

The PhVWP recommended that the Summary of Product Characteristics (SmPC) and Package Leaflet (PL) should provide adequate information about these observations.

The PhVWP informed the CMD(h) accordingly, and for the final SmPC and PL wording as well as practical information on the implementation, interested readers are asked to visit the HMA website (http://www.hma.eu/cmdh.html) for upcoming information.

GUIDELINES AND GENERAL MATTERS

Below readers will find a summary of the principal discussions on guidelines and other general matters of organisational, regulatory or methodological nature.

Pharmacovigilance for medicinal products used against novel swine-origin Influenza A (H1N1) virus in humans

Medicines used to treat or prevent influenza belong to the group of antivirals and vaccines. The EMEA is engaged, in close co-operation with European and international partners, in ensuring the availability and safety surveillance of medicines effective against the pandemic A (H1N1) influenza. The activities undertaken by the EMEA in this respect are reported to the public via the EMEA website under http://www.emea.europa.eu/htms/human/pandemicinfluenza/novelflu.htm.

The PhVWP supports these activities, and at this meeting, the PhVWP provided input to further revisions of the CHMP Recommendations for the Pharmacovigilance Plan as part of the Risk Management Plan to be submitted with the Marketing Authorisation Application for a Pandemic Influenza Vaccine and to the European Pharmacovigilance Strategy for (A) H1N1 Vaccines Benefit-Risk Surveillance. The PhVWP also welcomed further activities by the EMEA currently under development, and provided comments from their perspective.

Guideline on the Conduct of Pharmacovigilance for Vaccines for Pre- and Post-Exposure Prophylaxis against Infectious Diseases (EMEA/CHMP/PhVWP/503449/2007)

The PhVWP, and subsequently the CHMP, adopted this Guideline in July 2009, taking into account comments received during the public consultation. The final Guideline is now available on the EMEA website under http://www.emea.europa.eu/htms/human/phv/phvwp.htm, together with the comments received during the public consultation and the responses agreed by the PhVWP and the CHMP. The Guideline will be included in the revised Volume 9A of the Rules Governing Medicinal Products in the European Union scheduled for publication later in 2009.

Worksharing between Member States for the assessment of periodic safety update reports

This worksharing scheme relates to periodic safety update reports (PSURs) submitted by marketing authorisation holders to the competent authorities in Member States for nationally authorised products, including those authorised through the mutual recognition and decentralised procedures. The objective is to avoid multiplication of assessment by allocating review of PSURs for particular substances to single Member States. The assessment report on the world-wide safety data summarised in a PSUR is then considered by all other Member States for EU-wide agreement on a final assessment report. Where the preliminary assessment report identifies a safety concern that may significantly alter the risk-benefit evaluation of the active substance, the issue will be referred to the PhVWP for advice. Based on the recommendations of the final assessment reports, Member States update the national product information (Summaries of Product Characteristics and Package Leaflets) as applicable.

After a development and pilot phase, the scheme entered its operational phase in October 2008. The PSUR Worksharing Group meets every month, in the margins of the PhVWP meeting, for the purpose of further developing the scheme in the light of the experience gained. A meeting with industry associations was organised on 24 September 2009 to discuss practical issues and the revision of guidance documents.

For more information on the worksharing scheme, interested readers are referred to http://www.hma.eu/80.html, where updates are published as they become available.

REGULATORY ABBREVIATIONS

CHMP – Committee of Medicinal Products for Human Use
CMD(h) – Co-ordination Group for Mutual Recognition and Decentralised Procedures for Human Medicines
EMEA – European Medicines Agency
EU – European Union
HMA – Heads of Medicines Agencies
PhVWP – CHMP Pharmacovigilance Working Party
PL – Package Leaflet
PASS – Post-Authorisation Safety Study
PSUR – Period Safety Update Report
RMP – Risk Management Plan
SmPC – Summary of Product Characteristics