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Patient Health Protection

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Pharmacovigilance Working Party (PhVWP)

January 2011 plenary meeting

The CHMP Pharmacovigilance Working Party (PhVWP) held its January 2011 plenary meeting on 17-19 January 2011.

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 CHMP monthly report (http://www.ema.europa.eu, go to: about us/Committees/CHMP/Committees meeting reports).

Insulin products – Consistent product information regarding the risk of heart failure with concomitant use of pioglitazone

Product information regarding the risk of heart failure with concomitant use of pioglitazone should be consistent for all insulin products.

Given recent agreement to implement warnings in the product information for pioglitazone and centrally authorised insulin products with regard to the risk of heart failure in causal association with their combined use, the PhVWP reviewed the product information for nationally authorised insulin products and concluded that the warning and advice for centrally authorised insulin products with regard to this risk should also be implemented in the product information for nationally authorised insulin products (see Annex 1 for the Summary Assessment Report).

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The PhVWP informed the CMD(h) accordingly. For the final wording to be included in the summaries of product characteristics (SmPCs) and package leaflets (PLs), as well as practical information on implementation, interested readers are advised to consult the HMA website (http://www.hma.eu/cmdh.html) for upcoming information.

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.

New legislation for pharmacovigilance in the European Union

The PhVWP noted that, on 31 December 2010, the European Commission published new legislation to strengthen pharmacovigilance in the EU in their Official Journal (interested readers are referred to http://ec.europa.eu/health/human-use/pharmacovigilance/index_en.htm). The PhVWP will contribute to the implementation of the new legal provisions. Most of the provisions will apply from July 2012.

Regulatory abbreviations

CHMP – Committee for Medicinal Products for Human Use

CMD(h) – Co-ordination Group for Mutual Recognition and Decentralised Procedures for Human Medicines

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 January 2011

Insulin products – Consistent product information regarding the risk of heart failure with concomitant use of pioglitazone

Key message

Product information regarding the risk of heart failure with concomitant use of pioglitazone should be consistent for all insulin products.

Safety concern and reason for current safety review

Combined use of an insulin product and a thiazolidinedione is associated with an increased incidence of heart failure, as documented in the medical literature and by study data. This information was implemented by the CHMP as a warning in the summary of product characteristics (SmPC) for the thiazolidinedione pioglitazone, and subsequently the CHMP agreed to implement a warning for all centrally authorised insulin products.

The PhVWP therefore reviewed the product information for nationally authorised insulin products, including those authorised through the mutual recognition and decentralised procedures.

Clinical setting

Insulin is a hormone naturally produced by the pancreas to regulate the glucose metabolism in the body. In diabetic patients, the glucose metabolism is impaired and they may require insulin products, which contain insulin or an insulin analogue.

Pioglitazone is the only thiazolidinedione authorised in the EU and is a medicine to control diabetes. It may either be used on its own or in combination with other antidiabetic medicines. In specific situations it may be added to insulin therapy[1].

Information on the data assessed

The data derive from clinical studies in patients with type 2 diabetes using various insulin products and thiazolidinediones, including pioglitazone, as well as other antidiabetic medicines.

Outcome of the assessment

The PhVWP considered the risk to be relevant for the entire class of insulin products. A survey in Member States revealed that in the EU there are almost 200 nationally authorised insulin products, including products authorised through the mutual recognition procedure, and currently none of these products contain information relating to the concomitant use of pioglitazone in their product information.

Therefore, the PhVWP concluded that the same information as for centrally authorised insulin products should be implemented in the SmPCs for nationally authorised insulin products. The SmPC, in its section 4.4 on special warnings and precautions for use, should provide the information:

[1] For the product information of pioglitazone, interested readers are referred to http://www.ema.europa.eu, search: pioglitazone.

- that cases of heart failure have been reported when thiazolidinediones are used in combination with an insulin product, especially in patients with risk factors for development of heart failure, and that this should be kept in mind if combination therapy is considered; and
- that, if the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema and that pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs.

The package leaflets should be amended to reflect the information in the SmPCs.