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PhVWP Monthly report on safety concerns, guidelines and general matters

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The CHMP Pharmacovigilance Working Party (PhVWP) held its January 2012 plenary meeting on 16-18 January 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=.

Ethinylestradiol + drospirenone-containing oral contraceptives (YASMIN, YASMINELLE and other products) – Risk of venous thromboembolism

Findings from two new epidemiological studies are consistent with the outcome of the PhVWP review concluded in May 2011 and the current product information: The risk of venous thromboembolism (VTE) for drospirenone-containing combined oral contraceptives (COCs) is higher than for levonorgestrel-containing COCs (so-called second generation COCs) and may be similar to the risk for COCs containing desogestrel or gestodene (so-called third generation COCs).

The PhVWP completed a review of two new epidemiological studies regarding the risk of venous thromboembolism (VTE) associated with drospirenone-containing combined oral contraceptives (COCs), such as YASMIN and YASMINELLE. The findings of the new studies did not change the conclusion of the PhVWP in May 2011 that the risk of VTE with any COC (including those containing

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drospirenone) is very small and that the risk for drospirenone-containing COCs is higher than for levonorgestrel-containing COCs (so-called second generation COCs) and may be similar to the risk for COCs containing desogestrel or gestodene (so-called third generation COCs). The current product information for drospirenone-containing COCs authorised in the EU on the risk of VTE remains consistent with the latest available evidence (see Annex 1 for the Summary Assessment Report).

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 January 2012

Ethinylestradiol + drospirenone-containing oral contraceptives (YASMIN, YASMINELLE and other products) – Risk of venous thromboembolism

Key message

Findings from two new epidemiological studies are consistent with the outcome of the previous PhVWP review concluded in May 2011 and the current product information: The risk of venous thromboembolism (VTE) for drospirenone-containing combined oral contraceptives (COCs) is higher than for levonorgestrel-containing COCs (so-called second generation COCs) and may be similar to the risk for COCs containing desogestrel or gestodene (so-called third generation COCs).

Safety concern and reason for current safety review

Venous thromboembolism (VTE) has been a rare adverse reaction of combined oral contraceptives, well-known since their introduction in 1961. VTE has been reported with the use of all combined oral contraceptives (COCs; combination of the two hormone types oestrogen and progestogen), including those containing ethinylestradiol + drospirenone, such as YASMIN and YASMINELLE. Of 100,000 women who are not using a COC and are not pregnant, about 5 to 10 may have a VTE in one year. The corresponding figures for women taking COCs range from about 20 cases per 100,000 women in one year of use for levonorgestrel-containing COCs to 40 cases per 100,000 women in one year of use for desogestrel- or gestodene-containing COCs. Of 100,000 women who are pregnant around 60 may have a VTE.

Drospirenone-containing COCs have been authorised in the EU since 2000 under various product names, including YASMIN (ethinylestradiol 0.03mg + drospirenone 3mg) and YASMINELLE (ethinylestradiol 0.02mg + drospirenone 3mg). The risk of VTE has been continuously monitored since authorisation. The product information was last updated in May 2011 to reflect data from epidemiological studies on the risk of VTE [1-7] (see PhVWP monthly report May 2011).

Since then, two new epidemiological studies have been published [8, 9], which were reviewed by the PhVWP to determine whether the information on the risk of VTE in the EU product information of drospirenone-containing COCs is still adequate.

Information on the data assessed

The review comprised the following two epidemiological studies: a population-based cohort study conducted in the clinical database of Clalit, a large health service organisation in Israel [8], and a cohort study sponsored by the US Food and Drug Administration (FDA) using data from four geographically diverse health plans in the United States regarding COCs and cardiovascular disease endpoints [9].

Outcome of the assessment

The PhVWP considered that the risk of VTE with any COC (including those containing drospirenone) is very small. The findings from the two new studies [8, 9] in the context of the previously assessed

studies [1-7] are consistent with the conclusion reached by the PhVWP in May 2011 that the risk for drospirenone-containing COCs is higher than for levonorgestrel-containing COCs (so-called second generation COCs) and may be similar to the risk for COCs containing desogestrel or gestodene (so-called third generation COCs).

Given these considerations, the PhVWP concluded that the current product information for drospirenone-containing COCs authorised in the EU on the risk of VTE remains consistent with the latest available evidence.

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