EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EMA/CHMP/566874/2013
Committee for Medicinal Products for Human Use

Tandemact

International non-proprietary name: pioglitazone / glimepiride

Procedure No. EMEA/H/C/000680/PSUV/0033

Period covered by the PSUR: 1 August 2012 – 31 January 2013

Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSURs for Actos, Glustin, Competact, Tandemact and Glubrava, the scientific conclusions of PRAC are as follows:

PRAC considered that the product information should be updated to reflect that some of the observational studies have also shown an increased risk of fractures in men. While this is not a consistent finding in these studies, it may be that the inconsistency relates to a difference in baseline bone density, rather than a gender specific risk. Furthermore no clear mechanism for gender specific differences has been confirmed.

The fluid retentive effects of both pioglitazone and the non-steroidal anti-inflammatory class of medicines are well established. PRAC considered that the prescriber should take this into account when prescribing such agents and, consistent with the post-marketing cases of cardiac failure and peripheral oedema reported with pioglitazone with concomitant use of nonsteroidal anti-inflammatory drugs (NSAID/COXIBs), the product information should be updated accordingly.

A benefit-risk analysis of pioglitazone in elderly patients using insulin was provided as part of the PSUR. Overall it was found that the risk of heart failure is increased in elderly patients and increased in those using insulin. According to the recent Drug Utilisation Studies use with insulin has been decreasing over the last number of years and represents a small proportion of pioglitazone users, perhaps reflecting increasing awareness of the increased risk of heart failure in this population. It is considered that the current risk minimisation activities, both routine (product information) and additional (educational materials) are adequate and the benefit-risk remains positive in this population. The PRAC was of the view that the product information should be updated to inform about the incidence of heart failure in patients $\geq$ 65 years receiving insulin concomitantly.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds recommending the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for Actos, Glustin, Competact, Tandemact and Glubrava the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing the active substance pioglitazone is favourable subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisations should be varied.