



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Press Office

Press release

European Medicines Agency recommends new contra-indications and warnings for pioglitazone to reduce small increased risk of bladder cancer

Benefit-risk balance remains positive in a limited population of type 2 diabetics

Finalising its review on antidiabetic pioglitazone-containing medicines and the occurrence of bladder cancer, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) confirmed that these medicines remain a valid treatment option for certain patients with type 2 diabetes but that there is a small increased risk of bladder cancer in patients taking these medicines. However, the CHMP also concluded that the small increased risk could be reduced by appropriate patient selection and exclusion, including a requirement for periodic review of the efficacy and safety of the individual patient's treatment.

Prescribers are advised not to use these medicines in patients with current or a history of bladder cancer or in patients with uninvestigated macroscopic haematuria. Risk factors for bladder cancer should be assessed before initiating pioglitazone treatment. In light of age-related risks, the balance of benefits and risks should be considered carefully both before initiating and during treatment in the elderly. Prescribers should review the treatment of patients on pioglitazone after three to six months (and regularly afterwards) to ensure that only patients who are deriving sufficient benefit continue to take it.

The CHMP reviewed all available data on the occurrence of bladder cancer, including results of preclinical studies, clinical studies, epidemiological studies and spontaneous reports. The Committee also considered the advice from its Scientific Advisory Group (SAG) on Diabetes/Endocrinology.

The CHMP concluded that the evidence from different sources shows that there is a small increased risk of bladder cancer with pioglitazone. Recently available data from epidemiological studies (Kaiser Permanente Northern California cohort study, French CNAMTS cohort study, GPRD case control study) point to a small increased risk (relative risk ranging from 1.12-1.33) of bladder cancer in diabetic patients treated with pioglitazone, in particular in patients treated for the longest durations and with the highest cumulative doses.



Furthermore, in a meta-analysis of randomised controlled clinical studies, 19 out of 12,506 patients taking pioglitazone had bladder cancer (0.15%) compared with 7 out of 10,212 patients not taking pioglitazone (0.07%). A possible risk after short term treatment cannot be excluded.

In line with the recommendations of the SAG, the CHMP concluded that there are some patients who cannot be adequately treated by other treatments and who will benefit from treatment with pioglitazone. The CHMP agreed that it was not possible to further restrict the current indications of pioglitazone. Instead, prescribers are advised to carefully select patients and monitor response to treatment. In patients responding to treatment, the CHMP concluded that the benefits outweigh the risks.

The CHMP agreed that there is a need for further analysis of the types, evolution and severity of bladder cancer in patients treated with pioglitazone compared to diabetics not treated with pioglitazone. It remains unclear as to whether it is an early effect or a risk with prolonged use/high cumulative dose. Therefore, the CHMP has asked the marketing authorisation holder to conduct a pan-European epidemiological study focussing on more robust characterisation of the risk, in particular the risk period and risk with increasing age, to inform the evidence-base for risk minimisation measures.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. The European review of the centrally authorised pioglitazone-containing medicines Actos, Glustin, Competact, Glubrava and Tandemact and the occurrence of bladder cancer was conducted in the context of a formal review, initiated at the request of the European Commission under Article 20 of Regulation (EC) No 726/2004, on 16 March 2011.
3. A European Commission Decision on this opinion will be issued in due course.
4. Actos and Glustin were authorised in the EU in October 2000, Competact in July 2006, Tandemact in January 2007 and Glubrava in December 2007. The medicines are marketed by Takeda. More information about these medicines can be found in the European public assessment reports available on the Agency's website.
5. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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