

June 9th 2011

Press Release

Use of Medications Containing Pioglitazone (Actos®, Competact®) Suspended

The Afssaps decided today to suspend use in France of medications containing pioglitazone (Actos® and Competact®), based on an opinion from the French Marketing Authorisation Committee (MA) and the French National Pharmacovigilance Committee [Commission Nationale de Pharmacovigilance]. Thus, the results from a study conducted by the CNAMTS at the request of Afssaps, which have just been made public, confirm that there is a slight increase in the risk of bladder cancer in patients treated with pioglitazone.

The Afssaps recommends that patients currently being treated with a medication containing pioglitazone not suspend their treatment but consult with their physician in order to adapt their diabetes therapy. Physicians must no longer prescribe medications containing pioglitazone.

Pioglitazone was indicated as a second-line treatment (after failure or intolerance of metformin, combined with metformin and/or sulfonylureas, or combined with insulin) for controlling glycaemia in diabetic patients. This medication was authorised through the centralised European procedure involving Actos® (pioglitazone) in 2000, and Competact® (a combination of pioglitazone and metformin) in 2006. These are currently the only medications on the French market for this class of anti-diabetics. To date, some 230,000 patients in France have been treated with pioglitazone.

Analysis of the preclinical, clinical, epidemiological and drug safety data indicated a potential risk of bladder cancer in diabetic patients treated with pioglitazone and led the French National Pharmacovigilance Committee to issue an opinion and solicit the MA commission for further investigation. On 7th April, the latter asked to see the results from a broad-scale cohort study conducted by the CNAMTS at Afssaps request before issuing an opinion. In the meantime, on 19th April, the Afssaps issued an advisory to healthcare professionals concerned with the use of pioglitazone in long-term treatment of diabetes patients.

The available drug safety data, along with the new results from the study presented to the members of the MA commission to date by the National Health Insurance System (CNAMTS), confirm that the use of pioglitazone carries a slight risk of bladder cancer. The MA commission ruled that the risk/benefit ratio for this product was now unfavourable.

Analysis of all these data led the Afssaps to suspend the use of medications containing pioglitazone. Healthcare professionals concerned will receive a letter in the next few days informing them of this decision.

The Afssaps requests that patients currently being treated with a medication containing pioglitazone not suspend their treatment but consult with their physician on adapting their diabetes treatment. Physicians must no longer prescribe medications containing pioglitazone.

The Afssaps reiterates that healthcare professionals must declare serious and/or unexpected side effects to their regional drug safety centres (CRPV).

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Summary of the Study Conducted by the National Health Insurance Agency

**Risk of bladder cancer in diabetics treated with pioglitazone in France:
A Cohort Study Using Data from the SNIRAM and PMSI**

This is the broadest study ever done on this subject. Its main objective is to identify, in diabetics treated in France, the existence of any eventual correlation between exposure to pioglitazone and the risk of occurrence of bladder cancer.

This study was done on a cohort of 1,491,060 diabetics on special drug therapy, ages 40 - 79. It covers the period of 2006-2009.

The group exposed to pioglitazone included 155,535 people with diabetes and the group not exposed contained 1,335,525 persons.

Analysis of this cohort of diabetes patients monitored in France between 2006 and 2009 supports the hypothesis that there is a statistically significant correlation between exposure to pioglitazone and the occurrence of bladder cancer. The results found are similar to those obtained in the United States for the cohort in the *Kaiser Permanente Northern California* study.