Translated from ***Rev Prescrire*** **April 2008; 28 (294): 245**

pioglitazone

NEW INDICATION

No glitazones, with or without insulin, for diabetic patients!

pioglitazone
(ACTOS°)

Tablets

• **15 mg** or **30 mg** of pioglitazone per tablet

■ **New indication:**
"(…) with insulin in type 2 diabetes mellitus patients with insufficient glycaemic control on insulin for whom metformin is inappropriate because of contraindications or intolerance".
[EU marketing authorisation, centralised procedure]

oral antidiabetic; glitazone

● **No tangible clinical benefit but an increased risk of heart failure.**



NOT ACCEPTABLE

In patients with type 2 diabetes treated with insulin, adding metformin improves the glycated haemoglobin (HbA1c) level and reduces weight gain, without increasing the risk of hypoglycaemia (1). According to the Summaries of Product Characteristics (SPC), glitazone in combination with insulin used to be contraindicated because of an increased risk of heart failure. This contraindication was removed in 2007.

Yet there are still no data conclusively demonstrating that glitazones prevent clinical complications of diabetes (see right) (2-4). In contrast, an increased risk of adverse effects due to water-sodium retention, including heart failure, weight gain and peripheral oedema, has been confirmed in patients treated with pioglitazone plus insulin rather than with insulin alone (3). There have been similar reports in patients treated with rosiglitazone plus insulin (4).

There is no justification for adding a glitazone to insulin in the treatment of type 2 diabetes.

©Prescrire

Selected references from Prescrire's literature search.



In response to our request for information Takeda did not provide us with any information.

1- Prescrire Editorial Staff "Insulin in type 2 diabetes" *Prescrire Int* 2005; **14** (79): 187-193.
2- Prescrire Rédaction "Pioglitazone en prévention cardiovasculaire secondaire: pas de bénéfice clinique" *Rev Prescrire* 2005; **25** (267): 851-852.
3- European Medicines Agency - CHMP "European Public Assessment Report (EPAR) (rev. 12) - Actos. Scientific discussion HC-285-II-25" 26 January 2007: 18 pages.
4- European Medicines Agency - CHMP "European Public Assessment Report (EPAR) (rev. 14) - Avandia. Scientific discussion HC-268-II-52" 21 November 2007: 36 pages.

EDITORS' OPINION



Do not use glitazones either alone or in combination for treatment of diabetes

Since 2002 the use of thiazolidinediones (glitazones) in type 2 diabetes has expanded rapidly. The reasons include: obtaining new indications for existing drugs, such as pioglitazone combined with insulin (see left); marketing approval for fixed-dose combinations with one or two other oral antidiabetics; and the removal of certain contraindications, as in the case of insulin plus rosiglitazone (alone or in combination), and pioglitazone in fixed-dose combinations (1,2).

Many of the decisions to approve these drugs for use in diabetes look like concessions. For example, after reassessing the risk-benefit balance of glitazones the European agency considered that "*the combination of rosiglitazone and insulin should only be used in exceptional cases and under close supervision*" (2). In other cases, simple warnings, perhaps modifications made under pressure, were added to the summaries of characteristics, as in the case of rosiglitazone, after the publication of data establishing an increase in myocardial infarction (3-7).

Patients and healthcare professionals should focus on the clear evidence concerning glitazones. These drugs have no proven benefit in terms of clinical outcome, but their adverse effects include potentially serious disorders such as macular oedema (sometimes associated with a decline in visual acuity), fractures, myocardial infarction, and heart failure, and a risk of cancer (1,6).

As these regulatory decisions may not best serve patients' interests, it is better to simply avoid using glitazones.

©Prescrire

1- Prescrire Editorial Staff "Avoid prescribing glitazones, either alone or in combination" *Prescrire Int* 2007; **16** (90): 145.
2- European Medicines Agency "European Medicines Agency confirms positive benefit-risk balance for rosiglitazone and pioglitazone" 18 October 2007: 2 pages.
3- U.S. Food and Drug Administration - Center for Drug Evaluation and Research "Information for healthcare professionals-pioglitazone HCl" 22 August 2007: 3 pages.
4- U.S. Food and Drug Administration - Center for Drug Evaluation and Research "Information for healthcare professionals-rosiglitazone maleate" 19 November 2007: 4 pages.
5- U.S. Senate - Committee on Finance "Senators reveal effort by the FDA to suppress scientific dissent and downplay safety concerns" 24 July 2007: 4 pages.
6- Prescrire Rédactin "Rosiglitazone: infarctus" *Rev Prescrire* 2007; **27** (287): 670.
7- European Medicines Agency "EMEA recommends new warnings and contraindications for rosiglitazone" 24 January 2008: 2 pages.

Downloaded from english.prescrire.org on 02/11/2026
Copyright(c)Prescrire. For personal use only.