

PRESCRIBERS GUIDE FOR USE WITH **PIOGLITAZONE** 15 MG, 30 MG AND 45 MG TABLETS

ADVICE FOR PRESCRIBERS

A recent review of pioglitazone by the European Medicines' Agency (EMA) concluded that there is a small increased risk of bladder cancer following pioglitazone treatment, although its benefits continue to outweigh its risks in a limited population of type 2 diabetic patients¹. The Medicines and Healthcare Products Regulatory Agency has requested that an Educational Pack is provided to all physicians and healthcare professionals expected to prescribe or use pioglitazone in the UK. The pack provides information on appropriate patient selection, based on the EMA review, the Summary of Product Characteristics (SmPC) and the Patient Information Leaflet.

Healthcare professionals should familiarize themselves with the SmPC provided in this pack to ensure they are fully aware of all risks involved when considering use of pioglitazone in individual patients.

Adverse events should be reported. Reporting forms and Information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to the products licence holder.

Initiation of Treatment (Section 4.1 of SmPC)

Pioglitazone should not be used as a first line therapy for the treatment of type 2 diabetes. The use of other anti-diabetic therapy should be ruled out before initiating treatment with pioglitazone. Pioglitazone is indicated in the treatment of type 2 diabetes mellitus: as **monotherapy**

- in adult patients (particularly overweight patients) inadequately controlled by diet and exercise for whom metformin is inappropriate because of contraindications or intolerance.

as **dual oral therapy** in combination with

- metformin, in adult patients (particularly overweight patients) with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin.
- a sulphonylurea, only in adult patients who show intolerance to metformin or for whom metformin is contraindicated, with insufficient glycaemic control despite maximal tolerated dose of monotherapy with a sulphonylurea.

as **triple oral therapy** in combination with

- metformin and a sulphonylurea, in adult patients (particularly overweight patients) with insufficient glycaemic control despite dual oral therapy.

Pioglitazone is also indicated for combination with insulin in type 2 diabetes mellitus adult patients with insufficient glycaemic control on insulin for whom metformin is inappropriate because of contraindications or intolerance.

After initiation of therapy with pioglitazone, patients should be reviewed after 3 to 6 months to assess their response to treatment (e.g. reduction in HbA1c). In patients who fail to show an adequate response, pioglitazone should be discontinued. In light of potential risks with prolonged therapy, prescribers should confirm at subsequent routine reviews that the benefit of pioglitazone is maintained.

Bladder Cancer (Section 4.3, 4.4 and 4.8 of SmPC)

Pioglitazone is contraindicated in patients with current bladder cancer, a history of bladder cancer and uninvestigated macroscopic haematuria.

- Risk factors for bladder cancer should be assessed before initiating pioglitazone treatment (risks include age, smoking history, exposure to some occupational or chemotherapy agents e.g. cyclophosphamide or prior radiation treatment in the pelvic region).
- Any macroscopic haematuria should be investigated before starting pioglitazone therapy.
- Patients should be advised to promptly seek the attention of their physician if macroscopic haematuria or other symptoms such as dysuria or urinary urgency develop during treatment.

Heart Failure (Section 4.3, 4.4 and 4.8 of SmPC)

Pioglitazone is contraindicated in patients with cardiac failure or history of cardiac failure (NYHA stages I to IV).

- Pioglitazone can cause fluid retention, which may exacerbate or precipitate heart failure.
- When treating patients who have at least one risk factor for development of congestive heart failure (e.g. prior myocardial infarction or symptomatic coronary artery disease or the elderly), physicians should start with the lowest available dose and increase the dose gradually.
- Patients should be observed for signs and symptoms of heart failure, weight gain or oedema; particularly those with reduced cardiac reserve and when used in combination with insulin.
- Pioglitazone should be discontinued if any deterioration in cardiac status occurs.

Treatment of the Elderly (Section 4.1, 4.2, and 4.4 of SmPC)

In light of age related risks (especially bladder cancer, fractures and heart failure), the risk to benefit ratio should be considered carefully before and during treatment in the elderly.

- Physicians should start treatment with the lowest available dose and increase the dose gradually, particularly when pioglitazone is used in combination with insulin.
- Combination use with insulin should be considered with caution in the elderly because of increased risk of serious heart failure.

Please refer to the Summary of Product Characteristics for further information before prescribing.

1. CHMP review of pioglitazone containing medicines (EMA/CHMP/562496/2011); July 2011