NHS
South West London

Thiazolidinedione – Pioglitazone

Pioglitazone is the only licensed thiazolidinedione in the UK (also known as glitazones).

Indication

For treatment of type 2 diabetes mellitus (T2DM) as a 2nd or 3rd line treatment:

- Monotherapy if metformin is contraindicated or not tolerated
- Dual oral therapy with metformin or another antidiabetic medication
- Triple oral therapy with metformin and another antidiabetic medication
- Combined with insulin if metformin is not appropriate

Mechanism of action

The thiazolidinediones reduce peripheral insulin resistance, leading to a reduction of blood-glucose concentration.

Dosing and titration

Initially 15 to 30 mg once daily, with or without food, adjusted according to response to 45 mg once daily. In elderly patients, initiate with lowest possible dose and increase gradually. Review the safety and efficacy after 3 to 6 months of treatment to ensure that only patients who are deriving benefit continue to be treated. Pioglitazone should be stopped in patients who do not respond adequately to treatment (e.g., reduction in glycosylated haemoglobin (HbA1c) according to agreed individual plan).

Contraindications

Do NOT start or continue pioglitazone in people who have:

- A higher risk of fracture
- A history of bladder cancer
- Diabetic ketoacidosis
- Heart failure (NYHA class I-IV) or history of heart failure
- Hepatic impairment or failure
- Macula oedema
- Uninvestigated macroscopic or microscopic haematuria

Cautions

- No adjustment is necessary in patients with impaired renal function (creatinine clearance more than 4 ml/min). Avoid in dialysis
- No dose adjustment is necessary for elderly patients. Start with the lowest available dose and increase gradually, particularly when used in combination with insulin

Monitoring

- Due to rare reports of hepatocellular dysfunction during post-marketing experience it is recommended that patients treated with pioglitazone have liver enzymes checked prior to initiation and then periodic monitoring
- There is evidence of dose related weight gain, in some cases weight increase may be a symptom of cardiac failure, therefore weight should be closely monitored

MHRA/Safety alerts

- Insulin combined with pioglitazone: risk of cardiac failure (December 2014)
- Risk of bladder cancer (December 2014)
- Risk of cardiac failure when combined with insulin (December 2014)

Information on adverse effects (Individual product license contains full list)

- Dose related weight gain has been seen in clinical trials with pioglitazone; may be due to fat accumulation and in some cases associated with fluid retention
- Monitor weight and dietary control
- Fluid retention, which may exacerbate or precipitate heart failure. Discuss the potential benefits and risks of treatment with pioglitazone with the person to enable them to make an informed decision
- Numbness, visual impairment, weight increase, insomnia
- Increased risk of bone fractures
- Increased risk of infection
- Bladder cancer
- Hepatic impairment (rare) — stop pioglitazone if jaundice occurs. Seek immediate medical advice if symptoms such as nausea, vomiting, abdominal pain, fatigue, and dark urine develop

Prescribing information

Pioglitazone may be preferable to a dipeptidyl peptidase-4 (DPP-4) inhibitor (gliptin) if:

- the person has marked insulin insensitivity, or
- a gliptin is contraindicated, or
- the person has previously had a poor response to, or did not tolerate, a gliptin

In light of age-related risks (especially bladder cancer, fractures and heart failure), the balance of benefits and risks should be considered carefully both before and during treatment in the elderly.

Sick Day Rules

No specific requirements for pioglitazone. Follow general sick day rules for patients with T2DM.

References

- NICE guideline [NG28] Type 2 diabetes in adults: management (Last accessed 05/09/2022)
- SPC – Pioglitazone 30mg tablets (Last accessed 05/09/2022)

Document History

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Author: **Insert the name of the network OR working group**

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