

Pioglitazone – a glitazone (Pizaccord®)

Pioglitazone is an oral anti-diabetic agent which increases insulin sensitivity, by acting on muscle and adipose tissue to increase glucose utilization. It lowers hepatic glucose production. Pioglitazone is indicated as third-line treatment of Type 2 diabetes mellitus due to its potential associated risks. It can be used as monotherapy, as dual therapy or triple therapy in combination with either metformin and/or a sulphonylurea, or in combination with insulin in Type 2 diabetes.

Key Messages: not first line, consider potential risks and review regularly

- Pioglitazone should not be used as first-line therapy in the treatment of Type 2 diabetes mellitus
- Prior to initiation, and during treatment patients must be assessed for contraindications and potential risk of harm from being treated with pioglitazone (see below)
- Liver function should be assessed prior to treatment and monitored every 2 months for the first year and periodically thereafter
- Review patients at least 3 months after initiation to assess adequacy of response to treatment
- Pioglitazone should only be continued beyond 6 months in patients who have achieved a reduction in HbA1c of $\geq 5\text{mmol/mol}$ (0.5%)
- In light of potential risks with prolonged therapy, prescribers should confirm at subsequent routine reviews that the benefit of pioglitazone is maintained

Assess and review regularly for risk of:

Fluid Retention and Congestive Heart Failure

Pioglitazone is contraindicated in patients with heart failure or a history of heart failure, NYHA stages I to IV. Patients with at least one risk factor for development of congestive heart failure e.g. previous MI, coronary artery disease or elderly, should be started on the lowest dose and dose increased gradually. Patients should be observed for signs and symptoms of heart failure, weight gain or oedema regularly. Concomitant administration of pioglitazone and insulin may increase the risk of oedema. Use should be discontinued if cardiac status of patient deteriorates.

Bladder Cancer

Pioglitazone is contraindicated in patients with current bladder cancer, a history of bladder cancer and uninvestigated macroscopic haematuria. Risk factors for bladder cancer (age, smoking, exposure to some occupational/chemotherapy agents, history of chronic bladder infections) should be assessed prior to initiating pioglitazone treatment. Patients should be advised to report macroscopic haematuria, dysuria, or urinary urgency during treatment.

Fractures

The long-term use of glitazones is associated with an increased risk of bone fractures in women. Pioglitazone should not be initiated in patients who are at increased risk of bone fracture e.g. osteoporosis.

Use in Older Patients

In view of age-related risks especially bladder cancer, fracture and heart failure, the risks and benefits must be carefully considered prior to initiating treatment with pioglitazone in the older patient. It should be used cautiously in combination with insulin in the older person because of an increased risk of serious heart failure.

References

1. MHRA Guidance: Pioglitazone Prescriber's Guide: Patient Selection and Risk Minimisation
<http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con143511.pdf>
2. Best Practice Journal, 2013, Issue 53: Improving glycaemia control in people with type 2 diabetes: Expanding the primary care toolbox <http://www.bpac.org.nz/BPJ/2013/June/diabetes.aspx>
3. MHRA Drug Safety Advice, August 2011, Pioglitazone: risk of bladder cancer
<http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON125962>
4. MHRA Drug Safety Advice, January 2011, Insulin combined with pioglitazone: risk of cardiac failure
<http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON105746>
5. Medsafe Prescriber Update, June 2008, Myocardial infarction with glitazones
http://www.medsafe.govt.nz/profs/PUArticles/PDF/PrescriberUpdate_Jun08.pdf
6. Medsafe Prescriber Update, November 2007, Glitazones: Fluid Retention, Cardiac Failure and Macular Oedema
<http://www.medsafe.govt.nz/profs/PUArticles/glits.htm>
7. Australian Prescriber, Medicines Safety Update, December 2013, Pioglitazone risk-benefit review
<http://www.australianprescriber.com/magazine/36/6/206/9>

For further prescribing information go to The New Zealand National Formulary www.nzf.org.nz