North of England
Commissioning Support Unit

Memo – shortage of supply

Re: Pioglitazone tablets, all strengths
Date: 26 November 2015

Description of product affected

Pioglitazone is licensed as a second or third line treatment of type 2 diabetes mellitus (T2DM). In its branded form (Actos®) it is licensed in adults (particularly those who are overweight) either as mono, dual or triple therapy:

- Monotherapy, in patients inadequately controlled by diet and exercise for whom metformin is contra-indicated or not tolerated
- Dual Therapy
    - In combination with metformin in patients with insufficient glycaemic control despite maximal tolerated dose of metformin.
    - In combination with a sulfonylurea in patients who are intolerant of metformin or in whom metformin is contra-indicated, and who have insufficient glycaemic control despite maximal tolerated dose of a sulfonylurea.
- Triple therapy
    - In combination with metformin and a sulfonylurea in patients with insufficient glycaemic control despite dual oral therapy.
- In combination with insulin in patients with insufficient glycaemic control, and for whom metformin is not tolerated or contra-indicated.

Various generic products are also available. There may be differences in licensed indications for each preparation.

Background

It is estimated that one in 16 people have diabetes, equating to 3.9 million people in the UK. 90% of those cases are T2DM. Current NICE guidance recommends pioglitazone as initial drug treatment for adults in whom metformin is contra-indicated or not tolerated, as well as a first and second intensification option in dual or triple therapy. It is estimated that there are 30- 40,000 prescriptions for each strength of pioglitazone per month in England.

Supply of all strengths of pioglitazone tablets are currently available and further deliveries are expected during December and January. However overall supply may be limited. In order to conserve supplies to ensure that patient management is not compromised it is recommended that prescription duration is limited to the amount the patient requires.

Alternative agents and management options

Limiting duration of prescription

As outlined above, there should be sufficient supplies available as long as everyone is aware that the supply chain may be fragile and modifies their ordering, stockholding and prescribing behaviour accordingly. It is suggested that prescriptions for pioglitazone are limited to a 28-day supplywhile supplies remain limited. This will avoid exacerbation of any shortages and may help to avoid any extra monitoring associated with switching medicines, particularly over the festive period.

If this measure is not sufficient then the following steps may need to be considered.

Medication Review
NICE guidance recommends discontinuing pioglitazone therapy if the patient does not have a beneficial metabolic response, defined as a reduction of at least 0.5 percentage points in HbA1C in 6 months. Discontinuation may therefore be an appropriate management strategy in such patients.

In some patients, it may be possible to increase the doses of concurrent hypoglycaemic agents in order to reduce the need for an alternative for the duration of the supply problems.

Switch to a Combination Product
Pioglitazone, alongside metformin, is available in a fixed-dose combination tablet (Competact®, Takeda UK Ltd). Each tablet contains 15mg of pioglitazone and 850mg metformin. The recommended dose is 1 tablet twice daily. This product may be an appropriate short-term option in patients who are stabilised on the separate components at the same dose. Supplies of Competact® are currently available, but it should be noted that stocks may be affected by the current shortage if many patients are switched. Competact® is significantly more expensive than prescribing the individual generic components (£35.89 vs £3.34 for 28 days treatment at a dose of 30 mg pioglitazone & 1700 mg metformin). Switching may therefore have cost implications. Reviewing and reverting to prescribing individual components once supplies are available is strongly advised.

Switch to an alternative treatment
In 2011, following the MHRA's recommendation to stop pioglitazone therapy in patients at risk of bladder cancer, the Association of British Clinical Diabetologists recommended insulin as the "fall-back position" for replacement of pioglitazone. This approach is unlikely to be practical in most patients, given that the current supply problems are expected to be short-term

Pioglitazone acts primarily by reducing insulin resistance. No other group of oral diabetes drugs acts in exactly the same way. Switching is therefore not an exact science, and patients should be more closely monitored during the shortage. Choice of agent should be on a patient by patient basis. The following table suggests alternatives based on NICE recommendations in existing guidance.

	NICE NG28 (2015)
Monotherapy in patients who are intolerant of metformin and whose diabetes is not adequately controlled.	Either a DPP-4 inhibitor, repaglinide, or a sulfonylurea
1st intensification (metformin)	Sulfonylurea or DPP-4 inhibitor
1st intensification (sulfonylurea)	DPP-4 inhibitor
2nd intensification (metformin & sulfonylurea	DPP-4 inhibitor
Combination therapy with insulin	No alternative suggested: refer to endocrinologist

DPP-IV inhibitors may be most useful in patients who are close to their glycaemic target, as they have a mild blood glucose lowering effect. Where renal impairment is an issue, saxagliptin should generally be the DPP-4 inhibitor of choice.

Exenatide, a GLP-1 analogue, may be particularly useful in patients who are significantly overweight.

References

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3. Summary of Product Characteristics- Competact (pioglitazone) 15mg/850 mg tablets. Takeda UK Ltd. Accessed via https://www.medicines.org.uk/emc/medicine/18719 on 26/11/2015 [date of revision of the text 23/07/2014
4. Pioglitazone replacement options. Association of British Clinical Diabetologists. 2011. Accessed via https://www.diabetologists.org.uk/Shared_Documents/position_papers/ABCD_pioglitazone_replacement_options.pdf on 26/11/2015
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7. Drug Tariff, Dec 2015. Accessed via http://www.drugtariff.nhsbsa.nhs.uk on 27/11/2015

Acknowledgements

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