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PrescQIPP Community Interest Company

Doxazosin modified release tablets

This bulletin focuses on modified release doxazosin and provides the rationale for patients to be switched to the immediate release formulation and for new patients not to be started on the modified release preparation. Information on the reasons for switching and potential savings are also provided. Further information and supporting materials are available on the PrescQIPP website www.prescqipp.info

Recommendations

- Ensure that prescribing of doxazosin for hypertension is in line with NICE Clinical Guideline 127.[1]
- Ensure that prescribing of doxazosin for benign prostatic hyperplasia (BPH) is in line with NICE Clinical Guideline 97.[2]
- Commence new patients requiring doxazosin on the immediate release tablet version of doxazosin.
- Review patients on doxazosin modified release for suitability for switching to immediate release doxazosin tablets.
- Switch patients to immediate release doxazosin tablets where it is clinically suitable to do so.

Background

The NHS England 'Items which should not routinely be prescribed in primary care guidance' lists products that are regarded as low priority for funding, poor value for money or for which there are safer alternatives (https://www.england.nhs.uk/wp-content/uploads/2017/11/items-which-should-not-be-routinely-precscribed-in-pc-ccg-guidance.pdf). Doxazosin modified release features on the list as an item that is poor value for money, as although it is clinically effective, more cost-effective products are available.

Doxazosin is licensed for the treatment of hypertension and benign prostatic hyperplasia (BPH) and is available in immediate release and modified release formulations.[3,4] The serum half-life of doxazosin is the same for both immediate and modified release preparations, allowing for once-daily administration for either formulation.[5] Doxazosin modified release (MR) was introduced to the market just as the Cardura® patent expired and generic versions of immediate release doxazosin became available.

Rationale for switching to immediate release tablets

Doxazosin has a long half-life of 22 hours making it suitable for once daily dosing for both immediate release and modified release formulations.[5] A modified release version of doxazosin therefore offers no advantage in terms of patient compliance.

There are no apparent differences in the type of adverse events reported in studies and in the Summary of Product Characteristics (SPC) of both immediate release and modified release products.[3,4] According to the manufacturer Pfizer, the modified release formulation, also referred to as GITS (gastrointestinal therapeutic system), was developed to enhance the pharmacokinetic profile, allowing more uniform plasma levels and eliminating at least two dose titration steps that may be needed with immediate release doxazosin, whilst reducing the likelihood of significant first dose hypotension.[6] The main advantage of the GITS formulation over the immediate formulation is a smoother plasma concentration

profile, with smaller peak concentrations and less variation over 24 hours. This may be associated with fewer side effects in some patients however trial data did not provide details about the types of serious side effects or the statistical significance of the difference between the standard and modified release formulations.[6]

The National Institute for Health and Care Excellence (NICE) in collaboration with the British Hypertension Society (BHS) has updated the guidance on hypertension in adults and recommends that alpha blockers, like doxazosin, should only be used as fourth line treatments for resistant hypertension when further fourth line diuretic therapy is not tolerated, contra-indicated or ineffective.[1] Before switching patients from modified release doxazosin, it would be beneficial to consider whether doxazosin prescribing is in line with NICE guidance in the first place.

NICE guidance on lower urinary tract symptoms in men (LUTS) (including BPH) states that drug treatment should only be offered to men with bothersome LUTS when conservative management options have been unsuccessful or are not appropriate. An alpha blocker should only be offered to men with moderate to severe LUTS.[2]

Switching options

Switching from modified-release to immediate release preparation

The initial dose of immediate release doxazosin is 1mg, to minimise the potential for postural hypotension and/or syncope. Dosage should then be increased to 2mg after one to two weeks and then 4mg if necessary, up to a maximum of 16mg daily for hypertension or 8mg daily for BPH.[3]

The following needs to be considered when switching a patient from the modified release to the immediate release preparation:

For hypertension:

- If used according to NICE/BHS guidelines, doxazosin therapy is additional to other antihypertensive medicines and only used as a fourth line add on treatment.[1]
- The patient will be taking a number of other hypertensive medicines as well as at least 4mg of doxazosin MR.
- Compliance with treatment should be assessed before a switch is undertaken as deprescribing may be more appropriate if compliance is an issue.
- If the patient is compliant with treatment, it is clinically reasonable to start immediate release doxazosin at a lower dose of 1mg in order to minimise potential postural hypotension and other unwanted effects. The dose should then be titrated up as appropriate.

For BPH:

- Consider compliance; if patient is not compliant with treatment then it may be more appropriate to deprescribe treatment.
- Ensure the treatment is being prescribed in line with NICE CG97

Where a switch is appropriate, there are three possible strategies to convert patients from modified release to immediate release doxazosin and all scenarios require follow up monitoring of blood pressure and patient tolerability:[5]

1. Give half the current dose of the modified-release doxazosin as immediate release doxazosin, i.e. 4mg XL switched to 2mg immediate release. There may be some patients who may require a higher dose and subsequent dose titration may be required.
2. Give the same dose as modified-release doxazosin but there may be some patients who suffer orthostatic hypotension and need a lower dose and subsequent dose titration may be required.
3. Discontinue modified release doxazosin and comply with the licensed dosing recommendations and initiate immediate release therapy at 1mg daily, increasing at weekly/fortnightly intervals.

Costs

There is a significant difference in cost between doxazosin modified release (priced at Cardura XL®) and immediate release doxazosin. Table 1 below illustrates the cost differences.

Table 1: Doxazosin product and price comparison – Drug Tariff December 2017[7]

Drug	Cost per 28 tablets (£)
Doxazosin 8mg MR tablets	9.98
Doxazosin 8mg MR tablets	5.00
Doxazosin 4mg tablets	0.73
Doxazosin 2mg tablets	0.68
Doxazosin 1mg tablets	0.67

Switch savings

In England and Wales almost £6.5 million is spent on Doxazosin MR tablets annually (ePACT July to September 2017).

Switching to an immediate release version of doxazosin **could save up to £5.4 million annually** across England and Wales (based on a milligram to milligram switch strategy). **This equates to £9,196 per 100,000 patients.**

Full data pack available here: https://pdata.uk/views/B195_DoxazosinMRupdateDROP-List/Bulletindata?%3Aiid=1&%3AisGuestRedirectFromVizportal=y&%3Aembed=y

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6. UKMI Medicines Q&As 22.6 What is the evidence comparing doxazosin XL with standard doxazosin. December 2015
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Additional PrescQIPP resources

Data pack

Available here: https://pdata.uk/#/views/B195_DoxazosinMRupdateDROP-List/FrontPage?:iid=1

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