Doxazosin review - prescribing fact sheet

Aim: **To ensure doxazosin prescribing is in line with the National Institute for Health and Care Excellence (NICE) guidance and to ensure the most cost-effective formulation of doxazosin is prescribed**

Key Points

1. NICE guidance recommends doxazosin is considered as an option at step 4 of the hypertension treatment algorithm and is used for the control of moderate to severe symptoms in men with benign prostatic hyperplasia (BPH) as detailed below
2. There are no significant clinical advantages to prescribing doxazosin modified release (MR) compared to doxazosin immediate release (IR)
3. Doxazosin MR is associated with a significantly higher acquisition cost and has been named as one of products being considered by the NHS England review of Low Value Prescribing

NICE Guidelines

- **Hypertension:** NICE recommends α-blockers, such as doxazosin, are considered at step 4 of the treatment algorithm for patients with resistant hypertension, where further diuretic therapy is not tolerated, or is contraindicated or ineffective
- **Benign prostatic hyperplasia:** NICE recommends α-blockers, such as doxazosin for the management of moderate to severe lower urinary tract symptoms in BPH in men, if conservative management options have been unsuccessful or are not appropriate. NICE suggest considering offering a combination of an alpha blocker and a 5-alpha reductase inhibitor to men with bothersome moderate to severe lower urinary tract symptoms (LUTS) and prostates estimated to be larger than 30 g or a prostate specific antigen (PSA) level greater than 1.4 ng/ml

Evidence Review doxazosin MR versus IR

Doxazosin is a long acting α-1 adrenergic blocker licensed for the treatment of hypertension and benign prostatic hyperplasia. It is available in MR and IR formulations:

- Both formulations of doxazosin are once daily preparations and provide effective blood pressure control. In terms of adverse effects, the MR version may be associated with less first dose hypotension, although this is still listed in the summary of product characteristics (SPC) as the most common side effect
- Doxazosin has a long half-life and both formulations are taken once daily, therefore there are no significant adherence issues expected as a result of switching from MR to IR preparations; although patients titrated to doxazosin IR doses of 8mg or more may have an increased number of tablets to take due to the different strengths available for this formulation

Dosing MR versus IR

- **It is essential to pay careful attention to the dosing regimens for doxazosin MR and doxazosin IR. While the MR preparation can be initiated at a 4mg dose, the SPC states that the IR formulation must be initiated at a dose of 1mg daily, increasing the dose gradually at weekly/fortnightly intervals as required to control the blood pressure or symptoms of BPH**
    - **<u>Hypertension</u>: The maximum licensed daily dose of doxazosin modified release is 8mg daily. The maximum licensed daily dose of doxazosin immediate release is 16mg daily**
    - **<u>BPH</u>: The maximum licensed daily dose of both doxazosin modified release and doxazosin immediate release is 8mg daily**

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South East London Area Prescribing Committee. A partnership between NHS organisations in South East London: Bexley/ Bromley/ Greenwich/ Lambeth/ Lewisham & Southwark Clinical Commissioning Groups (CCGs) & GSTFT/KCH/SLAM/Oxleas NHS Foundation Trusts & Lewisham & Greenwich NHS Trust

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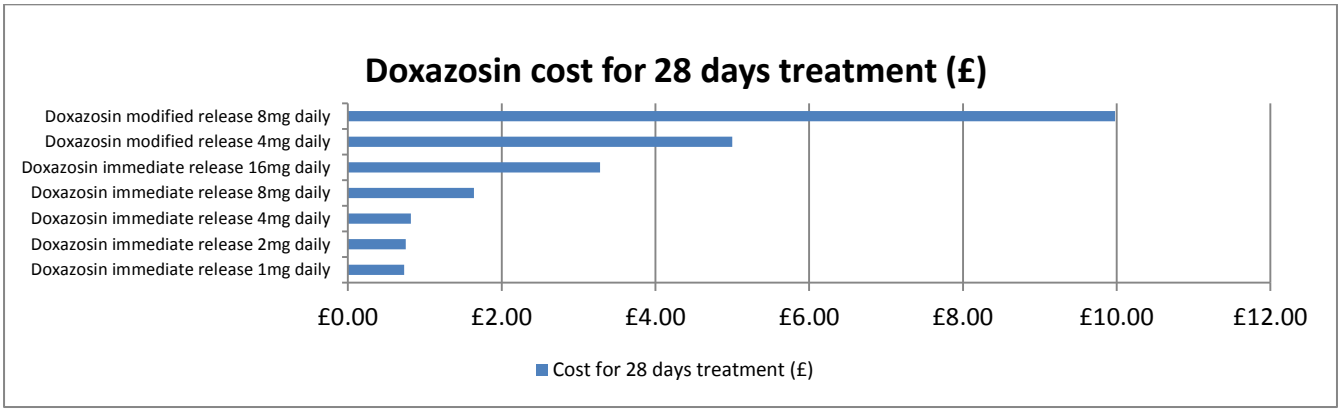
Costs

- The costs of doxazosin preparations vary significantly with the IR preparations having a significantly lower acquisition cost compared to the MR preparations (see graph)



- Doxazosin MR features in the PrescQIPP DROP-List (DRugs Of low Priority List) which are medicines regarded as low priority, poor value for money or medicines for which there are safer alternatives. The use of doxazosin MR has recently been highlighted for review by NHS England as one of 10 medicines which are ineffective, unnecessary, inappropriate for prescription on the NHS, or unsafe.

Recommendations

1. Identify all patients prescribed doxazosin on the practice register by running an EMIS/Vision search.
2. **Review clinical appropriateness**
   a) For patients prescribed doxazosin for the treatment of hypertension, ensure the NICE treatment algorithm has been followed and that doxazosin is being used appropriately at step 4 of the treatment algorithm, i.e. for patients with resistant hypertension, where further diuretic therapy is not tolerated, or is contraindicated or ineffective. If prescribing is not in line with NICE guidance – review therapy and prescribe in line with the NICE treatment algorithm where possible.
   b) For patients prescribed doxazosin for BPH in men – ensure it is being used in line the NICE guidance for the management of moderate to severe lower urinary tract symptoms

3. **Review doxazosin formulation and dose**

Where clinical appropriateness of doxazosin therapy is confirmed – identify patients prescribed doxazosin MR and consider changing to an IR formulation where clinically appropriate. There is no direct dose equivalence between doxazosin MR and IR. The relative *bioavailability* of doxazosin MR is roughly half that of the standard formulation, so a dose reduction is recommended when switching from doxazosin MR to IR doxazosin with subsequent dose titration if necessary. Two possible strategies to convert patients are:

a) Give half the dose of doxazosin MR as doxazosin IR e.g.:
   a. Change doxazosin MR 4mg once daily to doxazosin IR 2mg once daily
   b. Change doxazosin MR 8mg once daily to doxazosin IR 4mg once daily

Reducing the dose in this way will minimise the risk of patients experiencing orthostatic hypotension. Patients should be reviewed within 2 to 4 weeks with a view to increasing the prescribed dose if required to control the blood pressure or symptoms of BPH

b) Comply with the licensed dosing recommendations and initiate doxazosin IR therapy at 1mg daily, increasing at weekly/fortnightly intervals as required to control the blood pressure / symptoms of BPH.

Option a) may be preferable in patients with hypertension to protect against large fluctuations in blood pressure and option b) in BPH to ensure the lowest dose required to maintain control of symptoms is prescribed.

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