

Alpha-blockers in the treatment of benign prostatic hypertrophy

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KEY POINTS

- there are currently six alpha-blockers indicated for use in the treatment of benign prostatic hyperplasia
- alfuzosin, doxazosin, tamsulosin and terazosin are recommended by NICE for men with moderate to severe symptoms
- tamsulosin is also available in combination with dutasteride
- by relaxing smooth muscle they increase urine flow and reduce symptoms due to obstruction
- they lower blood pressure and should be avoided in patients with a history of postural hypotension; patients should be warned that the first dose may cause markedly reduced blood pressure, and those taking antihypertensives may need lower doses
- cardiovascular side-effects are generally less troublesome with tamsulosin and alfuzosin
- other side-effects include tiredness, dizziness and nasal stuffiness

Steve Chaplin and Professor Roger Kirby provide an overview of the properties of alpha-blockers and how they compare in the management of benign prostatic hypertrophy.

Six alpha-blockers are licensed for use in the treatment of benign prostatic hyperplasia (BPH, see Table 1). In its 2010 clinical guideline, NICE recommends four – alfuzosin, doxazosin, tamsulosin and terazosin – for men with moderate to severe lower urinary tract symptoms. Prazosin (Hypovase) and indoramin were excluded because they are now little used for this indication and they are not discussed further.

Tamsulosin is available in combination with the 5-alpha-reductase inhibitor dutasteride as Combodart; NICE recommends this for men with bothersome moderate to severe symptoms who also have a large prostate (>30g) or a prostate specific antigen (PSA) level >1.4ng per ml.

Tamsulosin is also available from pharmacies without prescription under the brand Flomax Relief

MR for symptomatic relief in men aged 45–75 for up to six weeks pending a clinical medical assessment.

Mechanism of action

Alpha-blockers have a common mechanism of action and adverse reaction profile. By relaxing smooth muscle they increase urine flow rate and reduce symptoms due to obstruction.

They lower blood pressure and should be avoided in patients with a history of postural hypotension and micturition syncope. Patients taking antihypertensive drugs may need lower doses and specialist supervision.

Alpha-blockers should be prescribed cautiously in elderly patients and, due to the risk of floppy iris syndrome, in those undergoing cataract surgery.

Adverse effects

Adverse effects involve the cardiovascular system (hypotension, syncope, dizziness, tachycardia, palpitations, oedema), the gastrointestinal system (dry mouth, gastrointestinal disturbances) and the CNS (drowsiness, depression, headache, blurred vision) and also include erectile dysfunction and rhinitis.

Treatment with doxazosin and terazosin should be introduced at a low dose, which should be increased at intervals of one to two weeks according to the response. Alfuzosin should be initiated at a low dose in elderly patients. No dose adjustment is recommended for tamsulosin.

Patients should be warned that the first dose may cause a marked reduction in blood pressure and they should lie down if this occurs.

Alpha-blocker	Dose				Cost per 28 days (maintenance)
	maintenance	maximum	elderly	modified release	
<i>Alfuzosin</i>	2.5mg tds	10mg/day	initially 2.5mg twice daily	10mg once daily	IR £9.88 MR £11.68
<i>Doxazosin</i>	initially 1mg/day, maintenance 2–4mg/day	8mg/day	no dose change	4–8mg once daily	IR 78p–£1.13 MR £5.00–£9.98
<i>Tamsulosin</i>	400µg/day				IR £4.15 MR £3.99
<i>Tamsulosin plus dutasteride</i>	400/500µg daily (MR only)				MR £18.48
<i>Terazosin</i>	initially 1mg at bedtime, usual maintenance 5–10mg/day	10mg/day	no dose change	-	£2.39–£7.51
Not recommended by NICE					
<i>Indoramin</i>	initially 20mg twice daily	100mg/day in divided doses	20mg at night	-	£11.71 (20mg twice daily)
<i>Prazosin</i>	500µg twice daily for 3–7 days, usual maintenance 2mg twice daily	2mg twice daily	initiate at lowest possible dose	-	£2.51
IR = immediate release, MR = modified release ^a Tabphyn MR					

Table 1. Dosages and cost of currently available alpha-blockers

They should also be warned that alpha-blockers may affect driving and other skilled tasks.

The *BNF* recommends caution when prescribing alfuzosin or doxazosin (but not other alpha-blockers) in patients with heart failure. Additional caution is needed with alfuzosin if angina worsens and in patients with a history of prolonged QT interval or taking concurrent treatment that may prolong the QT interval.

Doxazosin should be prescribed cautiously in patients with hepatic impairment; it – and tamsulosin – should be avoided

in patients with severe hepatic impairment.

Alfuzosin should be avoided in patients with severe renal impairment (eGFR <30ml per min per 1.73m²) and tamsulosin should be prescribed with caution in patients with very severely impaired renal function (eGFR <10ml per min per 1.73m²).

Drug interactions

The *BNF* lists many drug interactions with alpha-blockers. Classes of drugs associated with potentially clinically significant interactions include MAOIs, antiviral

agents, beta-blockers, calcium-channel blockers, diuretics, moxislyte (Opilon) and H₂-antagonists.

Concurrent sildenafil (Viagra) and other PDE5 inhibitors increase the risk of hypotension and they should be used only when alpha-blocker therapy has been stabilised.

The doses of sildenafil and vardenafil (Levitra) should be separated from those of alpha-blockers by four and six hours respectively; tadalafil (Cialis) should be avoided by patients taking an alpha-blocker.

Declaration of interests

Steve Chaplin has undertaken paid writing work for several pharmaceutical companies.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics

Place in therapy

BPH affects more than two million men in the UK. Men afflicted by this condition suffer lower urinary tract symptoms that may negatively affect quality of life.

The nonselective alpha-blocker phenoxybenzamine was derived from nitrogen mustard and binds irreversibly to both α_1 and α_2 adrenoceptors. This was the first agent in this class to be used to treat BPH. Subsequent studies revealed that it was both carcinogenic and mutagenic in mice and it was withdrawn from clinical usage.

Subsequently the alpha-1 selective alpha-blockers prazosin and doxazosin were introduced, but both required careful dose titration and were associated with postural hypotension in a significant number of patients.

More recently tamsulosin and alfuzosin have become available as first-line therapy for men with LUTS associated with BPH. The cardiovascular side-effects of tamsulosin and alfuzosin are generally less of a problem than those seen with other alpha-blockers.

The main symptoms that trouble men with this very prevalent condition are reduced urinary flow and frequency of urination. The need to get out of bed at night (nocturia), as well as the feeling of incomplete bladder emptying, are especially troublesome.

These agents provide rapid relief of these symptoms but at the expense of side-effects including tiredness, dizziness and nasal stuffiness, and occasionally syncope. Patients with a past history of recurrent fainting attacks should therefore not be treated with these drugs.

Tamsulosin usage is often associated with reduced ejaculation and patients should be informed about this reversible side-effect. Alfuzosin is less troublesome in this respect.

Declaration of interests

Professor Kirby has worked on publications on BPH in conjunction with GlaxoSmithKline.

Professor Kirby is director of The Prostate Centre, London