

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Dutasteride

Benign prostatic hypertrophy (BPH) is the most common prostatic disorder, with an incidence rate that increases with age. Symptoms of urinary obstruction include hesitancy, dribbling after urination, nocturia, frequency and urgency and urinary retention. The gold standard for treatment is surgery. Where surgery is contraindicated or not desired, medications may be used to provide symptom relief by decreasing urinary outflow resistance.

Prostate size is the most important factor in influencing drug choice. Selective alpha blockers increase urinary flow by relaxing the bladder neck and prostatic smooth muscle. They are effective regardless of prostate size ($<40\text{cm}^3$) and have a fast onset of action (full effect in 4-6 weeks). The 5-alpha reductase inhibitors (5-ARI) reduce the prostate size but appears to be effective only if the prostate is significantly enlarged ($>40\text{cm}^3$) and full clinical response may take up to six months. Until recently, finasteride was the only 5-ARI available in Australia.

Dihydrotestosterone (DHT) is the principle androgen stimulating prostatic growth in men with BPH. Testosterone is converted to dihydrotestosterone (DHT) by the enzyme 5-alpha reductase (5-AR). The 5-AR inhibitors (5-ARI) achieve reductions in prostate volume through the inhibition of the nuclear bound steroid 5-AR isoenzymes which reduce testosterone to DHT. Dutasteride (Avodart[®]) is the first selective dual inhibitor of both type 1 and type 2 5-AR. In contrast, finasteride is a mono-inhibitor of type 2 5-AR.

Data from three randomised placebo controlled trials have demonstrated that treatment with 5-ARI dutasteride or finasteride results in reduced DHT and significant reductions in prostate volume with improvements in urinary symptoms and flow. Reductions in the risks of urinary retention and BPH related surgery have also been demonstrated but not as clearly as surrogate markers. Dutasteride is the first dual 5-ARI. Research has demonstrated that relative to placebo, dutasteride reduces both the risk and incidence of acute urinary retention by 57% (4.2% for placebo versus 1.8% for dutasteride) and the need for BPH related surgical intervention by 48% (4.1% for placebo versus 2.2% for dutasteride) over 24 months. In the PLESS study, finasteride reduced the risk of surgery by 55% (10.1% for placebo versus 4.6% for finasteride) and reduced the risk of acute urinary retention by 57% (6.6% for placebo versus 2.8% for finasteride) over four years. No studies have directly compared dutasteride with finasteride and assessed the clinical outcomes of reduced acute urinary retention and BPH related surgery.

Dutasteride is available in Australia via a private prescription only. It is not subsidised on the Pharmaceutical Benefits Scheme. The current cost of treatment with dutasteride is approximately \$50 per month (price may vary depending on pharmacy). In comparison, finasteride is available through the RPBS (\$5.40 per month). On a private prescription, the price of finasteride may range from \$60 to \$100 per month (depending on pharmacy).

The recommended dose of dutasteride is 500mcg (capsule) once a day orally. The product information does not highlight the need to adjust doses for renal or hepatic impairment. Dutasteride is mainly well tolerated in men with BPH. The most common adverse effects in clinical trials include impotence, decreased libido, ejaculation disorders and breast disorders including breast tenderness. Very rarely, allergic reactions, including rash, pruritus, urticaria, localised oedema and angioedema occurred.

Dutasteride is an alternative 5-ARI available for use in selected patients with symptomatic benign hypertrophy who are not fit for surgery. The full effects of dutasteride (reduction in prostate volume) may take up to 6 months, therefore symptomatic treatment with an alpha-blocker may be required on initiation.

This E-Bulletin is based on work by Winnie Tran, Senior Pharmacist, RGH

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