

# NEW DRUG EVALUATION

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## DUTASTERIDE

Dutasteride is a 5-alpha reductase inhibitor licensed for the treatment of benign prostatic hyperplasia. In clinical trials, dutasteride produced a significant improvement in symptoms and reduced the incidence of acute urinary retention compared with placebo. The most common adverse effects associated with dutasteride are sexual dysfunction and gynaecomastia. No published trials have directly compared dutasteride with finasteride, or the alpha blockers. At present, the 5-alpha reductase inhibitors are recommended only for men with larger prostates, or in men who do not respond to, or who are unable to tolerate the alpha blockers.

### *What is it?*

Dutasteride (Avodart®, GlaxoSmithKline) is a 5-alpha reductase inhibitor licensed for the treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH), and to reduce the risk of acute urinary retention and surgery.

The recommended dose is 0.5 mg daily. It may take up to 6 months before a clinically meaningful response to the drug is observed.<sup>1</sup>

### *How effective is it?*

The efficacy of dutasteride has been investigated in a pooled analysis of three, randomised, double-blind, placebo-controlled, clinical trials (n=4325).<sup>2</sup> Men of ≥ 50 years with moderate to severe symptoms of BPH were randomised to receive dutasteride 0.5 mg or placebo daily for 2 years. The primary endpoints were changes in the American Urological Association-Symptom Index (AUA-SI), and the risk of acute urinary retention (AUR). Secondary endpoints included risk of BPH-related surgical intervention.

Significantly more patients in the placebo group withdrew due to lack of efficacy compared to the active treatment group (10% vs 6%, p<0.001).

Dutasteride produced a significant improvement in symptoms of BPH compared to placebo from 6 months onwards. The average baseline AUA-SI of 17 points was reduced by 3.2 points vs 2.5 points at 6 months and by 4.5 points vs 2.3 points at 24 months for dutasteride and placebo respectively (p<0.001). By 24 months, there had been 90 episodes of AUR (incidence of 4.2%) and 39 episodes (incidence of 1.8%) in the placebo and

active treatment groups respectively (p<0.001). Dutasteride also reduced the risk of BPH-related surgical intervention compared to placebo (2.2% vs. 4.1%, p<0.001).<sup>2</sup>

Unpublished data from 2 year open-label extensions of these 3 clinical trials showed that dutasteride continued to improve BPH-related symptoms.<sup>3</sup>

There are no published trials that have directly compared dutasteride with finasteride. An unpublished, 1 year, randomised double-blind trial (n=1630) found no statistically significant difference in the effects of dutasteride or finasteride on prostate volume, symptoms or urinary flow rates.<sup>4</sup>

Dutasteride has not been directly compared with the selective alpha-1 adrenoceptor antagonists (alpha blockers).

### *How safe is it?*

In clinical trials, the withdrawal rate due to drug-related adverse events was 4% and 3% for the active treatment and placebo groups respectively.<sup>5</sup> Drug-related adverse events occurred in 14% of placebo-treated and 19% of dutasteride-treated patients.<sup>2</sup> Over 24 months, adverse events that occurred significantly more frequently with dutasteride compared to placebo included impotence (7.3% vs 4%), reduced libido (4.2% vs 2.1%), ejaculation disorders (2.2% vs 0.8%) and gynaecomastia (2.3% vs 0.7%).<sup>2</sup>

In the unpublished, comparative trial with finasteride, there was no significant difference in the incidence of drug-related sexual events between either treatment group.<sup>4</sup>

### What other options are there?

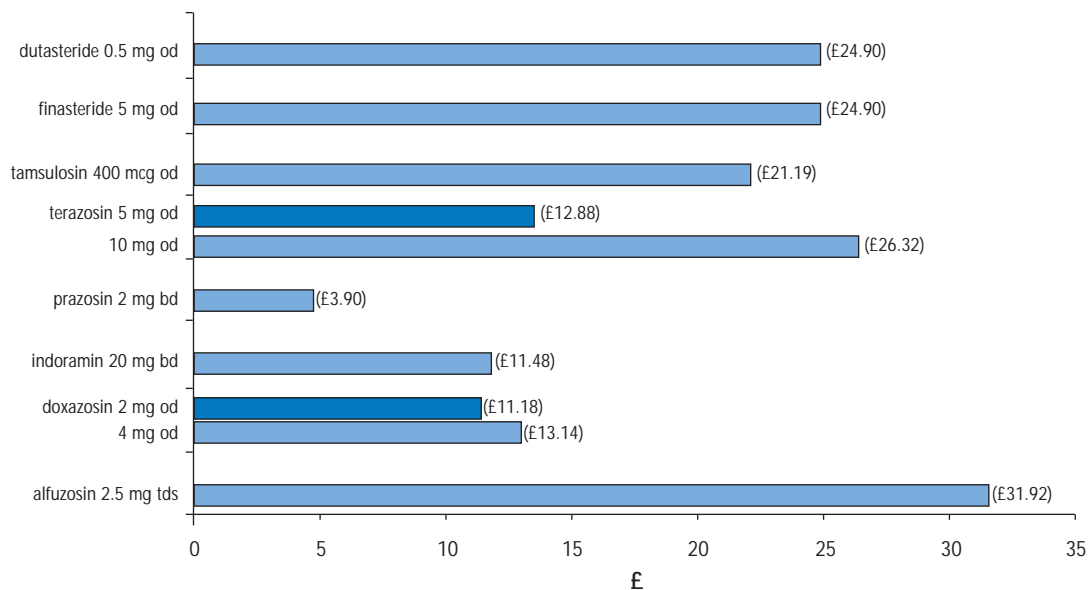
Self-management techniques are appropriate for men with BPH, who have mild to moderate symptoms.<sup>6</sup> The alpha blockers are currently considered the drugs of first choice for the symptomatic treatment of BPH.<sup>6,7</sup> They relieve symptoms within a few days by reducing the tone of smooth muscle in the prostate and bladder neck.<sup>6</sup> Finasteride, the only other 5-alpha reductase inhibitor available, reduces prostate size but it may take 6 months for the maximum effect of the drug to develop.<sup>6</sup> Therefore, a 5-alpha reductase inhibitor has been suggested as an alternative for men with larger prostates (>40 g or >40 ml), or in men who do not respond to, or who are unable to tolerate alpha blockers.<sup>6,7</sup>

### When should it be used?

At the recommended dose of 0.5 mg daily, dutasteride costs the same as finasteride 5 mg daily. There are no published trials that have directly compared dutasteride with finasteride, or the alpha blockers. The manufacturer claims that dutasteride is the only 'dual' inhibitor of 5-alpha reductase because it inhibits both the type 1 and type 2 isoenzymes.<sup>1</sup> However, there is no evidence that it offers any specific advantages over finasteride, a selective inhibitor of the type 2 isoenzyme. At present, the 5-alpha reductase inhibitors are considered second-line to the alpha blockers in the treatment of BPH.<sup>6</sup>

### How much does it cost?

Cost for 28 days treatment (prices from MIMS/Drug Tariff May 2003)



NB Doses shown are for general comparison only and do not imply therapeutic equivalence.

### REFERENCES

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- 3 Roehrborn CG et al. The 98th Annual Meeting of the American Urological Association. 2003.(U)
- 4 GlaxoSmithKline. Data on File. Letter March 2003.(U)
- 5 Roehrborn CG et al. Long-term effect of dutasteride on symptoms, BPH-specific health status and urinary flow rate. *BJU Int* 2002;90(suppl.2):12-18.(A)
- 6 Anon. Managing lower urinary tract symptoms in men. *Drug Ther Bull.* 2003;41:18-21.(R)
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KEY RCT - randomised controlled trial, CT-controlled trial, O-open study, MA-meta analysis, R-review, U-unpublished, A- abstract, E-editorial

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