Indian Health Service
Alpha$_1$ Adrenergic Antagonists
IHS National Pharmacy and Therapeutics Committee
Last Reviewed: March 2011

Background:

In March 2011, the IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed the agents used for the treatment of benign prostatic hyperplasia (BPH). The NPTC voted to maintain terazosin and doxazosin on the IHS National Core Formulary (NCF). In addition, they voted to add the selective alpha$_1$ adrenergic antagonist, tamsulosin, to the NCF.

Clinical Review:

Alpha blockers reduce urethral sphincter tone and facilitate voiding by blocking alpha$_1$ receptors in the prostate and base of the bladder. There are two classes of alpha blockers: the non-selective agents (doxazosin, prazosin, and terazosin) and the selective agents (alfuzosin, silodosin, and tamsulosin). The selective agents have less affinity for alpha-1B receptors which are more prevalent in the smooth muscle of vascular walls, leading to a reduction in orthostatic side effects.

Efficacy: A meta-analysis published in 1999 looked at placebo-controlled trials involving 6333 patients and direct comparative studies involving 507 patients treated with alfuzosin, doxazosin, tamsulosin, and terazosin. This analysis showed comparable reductions in lower urinary tract symptoms (LUTS) and urinary flow among these agents. Scores utilizing the American Urological Association (AUA) Urinary Symptom Score decreased by 30-40% overall and maximal urinary flow rates increased by 16-25%. The selective agents were shown to have an improved tolerability, with tamsulosin showing less effect on blood pressure compared to alfuzosin.[1] Clinical trials of combined treatment with an alpha$_1$ adrenergic antagonist and a 5-alpha reductase inhibitor have shown greater reductions in risk for clinical progression, acute urinary retention, symptom scores, and improved quality of life measures in those treated with combination therapy versus monotherapy with either class of agent when used in men with clinically enlarged prostate glands with moderate to severe LUTS.[2-4]

Side Effects:

Orthostatic hypotension can be seen with all agents within the alpha$_1$ adrenergic antagonists class, though this is much more common for the non-selective agents. The non-selective agents should be started at a lower dose, preferably given at bedtime, and titrated up for effect. Caution should be used when utilizing these agents in conjunction with phosphodiesterase-5 inhibitors (i.e. sildenafil, vardenafil, tadalafil) as the risk of hypotension is increased. This risk can be decreased by separating the dosing of these agents by at least 4 hours, particularly when using the non-selective agents.

Ejaculatory problems have been seen with the use of tamsulosin (reduced ejaculate in 90% of patients, no ejaculate in 35%) and silodosin (retrograde ejaculation in 28% of patients). Alfuzosin has not been observed to cause these effects.

Intraoperative Floppy Iris Syndrome (IFIS), first described in 2005, is a triad of progressive intraoperative miosis despite preoperative dilation, billowing of a flaccid iris, and iris prolapse toward the incision site during phacoemulsification for cataracts. It can lead to posterior capsule rupture with vitreous loss or postoperative intraocular pressure spikes. It has been associated with alpha$_1$ adrenergic antagonist use, particularly tamsulosin. There is no current evidence to support a reduction in this risk by stopping the alpha blocker pre-operatively. The AUA recommends avoidance of the use of alpha blockers in patients who may be candidates for cataract surgery.

If you have any questions regarding this document, please contact the NPTC at nptc1@ihs.gov.

References:

1. Djavana B, Marberger M. A meta-analysis of the efficacy and tolerability of alpha1-adrenorecptor antagonists in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction. *Eur Urol* 1999; 36(1): 1-13.
2. McConnel JD, et.al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *NEJM* December, 2003; 349(25): 2387-2398.
3. Roehrborn CG, et.al. The effects of combination therapy with dutasteride and tamsulosin on clinical outcomes in men with symptomatic benign prostatic hyperplasia: 4-year results from the CombAT study. *Eur Urol*, 2010;574(1): 123-131.
4. Montorsi F, et.al. Effect of dutasteride, tamsulosin, and the combination on patient-reported quality of life and treatment satisfaction in men with moderate-to-severe benign prostatic hyperplasia: 4-year data from the CombAT study. *Int J Clin Pract*, 2010; 64(8): 1042-1051.