Silodosin

Aust Prescr 2018;41:129–30
https://doi.org/10.18773/austprescr.2018.030
First published 12 June 2018

Approved indication: benign prostatic hypertrophy

Urorec (Mayne)
4 mg and 8 mg capsules
Australian Medicines Handbook section 13.2.1

Benign prostatic hyperplasia can cause lower urinary tract symptoms such as slow urine flow, nocturia and incomplete emptying of the bladder. If these symptoms are sufficiently bothersome as to require treatment, selective alpha-blockers such as alfuzosin and tamsulosin are one option. These drugs block $alpha_1$ adrenoreceptors in the smooth muscle of the prostate and bladder to reduce resistance and so improve urinary flow. Silodosin is another selective alpha-blocker. It has much greater affinity for the $alpha_{1A}$ receptor than the $alpha_{1B}$ receptor found in vascular smooth muscle.

Silodosin is taken once a day with food. The dose is halved if the patient has moderate kidney impairment (creatinine clearance 30–59 mL/min) and silodosin is not recommended for those with severe impairment (creatinine clearance <30 mL/min). Most of the dose is metabolised, but no data are available on the effect of severe hepatic impairment. The terminal half-life of silodosin is about 11 hours. As the metabolism of silodosin involves cytochrome P450 3A4, it should not be used with strong inhibitors of this enzyme system, such as ketoconazole and ritonavir. Silodosin is also a substrate of P-glycoprotein so using it with strong inhibitors (amiodarone, verapamil) of this transporter is not recommended.

The Australian approval of silodosin is mainly based on three randomised trials. Two of them compared silodosin with placebo in a total of 923 men.[1] These patients had an average baseline score of 21.3 on the 35-point International-Prostate Symptom Score (I-PSS). After 12 weeks of treatment this had reduced by 6.4 points in the 466 men who took silodosin 8 mg daily and by 3.5 points in the 457 who took placebo. There was also a significant difference in urine flow rate. Patient satisfaction was higher with silodosin, with 32% of the men who took it being 'delighted, pleased or mostly satisfied' compared with 22.5% of the placebo group.[1]

The third trial compared silodosin with tamsulosin, as well as placebo.[2] In this trial the baseline I-PSS was 19.1. After 12 weeks of treatment it had reduced by a mean of 7.0 points in the 371 men taking silodosin 8 mg daily and by 6.7 points in the 376 taking tamsulosin 0.4 mg. The average reduction for the 185 taking placebo was 4.7 points. The proportions of patients who had an improvement of at least 25% in the I-PSS were 66.8% with silodosin and 65.4% with tamsulosin. These results were significantly better than the 50.8% response rate to placebo. While 44–45% of the men were 'delighted, pleased or mostly satisfied' with the active treatments, only 34% of the placebo group agreed.[2]

Silodosin was generally well tolerated, but caused more adverse effects than placebo. In the placebo-controlled trials, 6.4% of the silodosin group withdrew because of adverse events compared with 2.2% of the placebo group. Problems that were more frequent with silodosin included dizziness, orthostatic hypotension, diarrhoea and headache. A major difference between silodosin and placebo was the adverse effect of retrograde ejaculation (28.1% vs 0.9%).[1] This abnormal ejaculation is thought to be a consequence of the selective blockade of the $alpha_{1A}$ receptors. This specificity should reduce cardiovascular adverse effects, but in the comparative study silodosin did not have significantly different effects from tamsulosin on pulse and blood pressure.[2] Alpha-blockers may cause floppy iris syndrome so the patient's ophthalmologist should be informed when cataract surgery is being planned.

There can be a high placebo response when treating symptoms associated with benign prostatic hyperplasia. The trials controlled for this by only randomising patients who had not responded during a placebo run-in phase. Despite this the differences between silodosin and placebo were small. Although it is statistically significant, a difference of 2–3 points in the I-PSS is only a slight advantage. The mean difference in maximum urine flow rates was 1 mL/second.[1] Such a small advantage over placebo is of questionable value.[3] The overall efficacy of silodosin is non-inferior to tamsulosin, but silodosin is more likely to cause retrograde ejaculation (14.2% vs 2.1%).[2]

[X] manufacturer did not respond to request for data

REFERENCES

1. Marks LS, Gittelman MC, Hill LA, Volinn W, Hoel G. Rapid efficacy of the highly selective $alpha_{1A}$-adrenoceptor antagonist silodosin in men with signs and symptoms of benign prostatic hyperplasia: pooled results of 2 phase 3 studies. J Urol 2009;181:2634-40. https://doi.org/10.1016/j.juro.2009.02.034
2. Chapple CR, Montorsi F, Tammela TL, Wirth M, Koldewijn E, Fernández Fernández E; European Silodosin Study Group. Silodosin therapy for lower urinary tract symptoms in men with suspected benign prostatic hyperplasia: results of an international, randomized, double-blind, placebo- and active-controlled clinical trial performed in Europe. Eur Urol 2011;59:342-52. https://doi.org/10.1016/j.eururo.2010.10.046
3. Dawson A. The price of urine. Aust Prescr 1995;18:26-7. https://doi.org/10.18773/austprescr.1995.031

NEW DRUGS

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.