EARLY RELEASE

New drugs

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Avanafil

Approved indication: erectile dysfunction

Spedra (A Menarini)
50 mg, 100 mg and 200 mg tablets
Australian Medicines Handbook section 13.3, Drugs for sexual dysfunction

Avanafil is another phosphodiesterase 5 inhibitor. It will compete with sildenafil, tadalafil and vardenafil as a treatment for erectile dysfunction.

By inhibiting phosphodiesterase 5, these drugs stop the breakdown of cyclic guanosine monophosphate. This molecule is responsible for the smooth muscle relaxation in the corpus cavernosum which enables the inflow of blood that results in erection.

The tablets are rapidly absorbed. Maximum plasma concentrations are reached in 30–45 minutes and in some men, erection occurs 20 minutes after a 200 mg dose of avanafil. Absorption is delayed by food. So the tablets may take longer to work if taken after a meal.

Avanafil is mainly metabolised with most of its metabolites being excreted in the faeces. It should not be used by people with severe liver disease. The half-life is 6–17 hours. As the metabolism involves cytochrome P450 (CYP) 3A4, there is the potential for many drug interactions. Avanafil is contraindicated in patients taking strong inhibitors of CYP3A4, such as itraconazole, clarithromycin and ritonavir. The dose should be limited in patients taking moderate inhibitors, such as erythromycin, and there may be reduced clearance in people taking drugs such as fluoxetine.

Avanafil also has pharmacodynamic interactions. Nitrates, such as glyceryl trinitrate, increase concentrations of guanosine monophosphate, so their action can be potentiated by phosphodiesterase inhibitors. This can cause severe hypotension. Avanafil is therefore contraindicated in patients taking nitrates. Its vasodilatory action may also have an additive effect with alcohol and antihypertensive drugs, particularly alpha blockers.

The main clinical studies of avanafil have been the subject of a meta-analysis. In these five double-blind trials, 1379 men took avanafil and 605 took placebo. The odds ratio, compared with placebo, for successful intercourse was 2.51 with avanafil 100 mg and 2.87 with 200 mg.[1]

One of the trials in the meta-analysis involved 298 men who had a nerve-sparing radical prostatectomy. The men took avanafil 100 mg, 200 mg or a placebo 30 minutes before sexual activity. Compared with baseline, over a 12-week period only 7.3% of the placebo group were able to insert their penis into their partner's vagina. The corresponding figures for avanafil 100 mg and 200 mg were 30.9% and 38.5%.[2]

A total of 712 patients who had completed two of the efficacy studies of avanafil continued in a 52–week open-label extension study. Most of the patients asked to use avanafil 200 mg. The average treatment duration was 35 weeks with only 153 men using the drug for 52 weeks. They were required to attempt sex at least four times a month. Approximately 80% were able to penetrate their partners and for 65% intercourse was successful.[3]

In the meta-analysis the main adverse effects of avanafil were headache, flushing and nasal congestion. Compared to placebo, there was not a significant difference in the number of patients stopping treatment because of adverse effects.[1]

There are some adverse effects which have occurred with other phosphodiesterase inhibitors that are an indication for stopping avanafil. These include loss of vision or hearing. In the open-label extension study one patient developed cyanopsia.[3] All phosphodiesterase inhibitors can cause priapism.

Physical causes of erectile dysfunction include cardiovascular disease, but these patients may not be suitable for treatment with avanafil. It is contraindicated in men with hypertension (>170/100 mmHg), unstable angina and congestive heart failure.

Not all patients will respond to avanafil and in those that do the erection may not last long enough for successful intercourse. It is therefore similar to other phosphodiesterase 5 inhibitors. Although the patients in the extension study favoured the 200 mg dose to the 100 mg dose, the difference in efficacy may be limited.[3]

A meta-analysis of 82 trials involving over 47,000 patients helps to suggest the place of avanafil in therapy. Although the confidence intervals overlap, avanafil appears to have lower efficacy relative to sildenafil. However, avanafil has a lower frequency of adverse effects, depending on the dose. Avanafil 100 mg had an adverse event rate similar to that of sildenafil 50 mg, but its efficacy was less.[4]

T manufacturer provided the product information

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

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The Transparency Score (T) 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 European Medicines Agency and the Therapeutic Goods Administration.