

New drugs

Dapoxetine

Priligy (A Menarini)

30 mg tablets

Approved indication: premature ejaculation

Australian Medicines Handbook section 13.3.2

Delayed ejaculation is an adverse effect of selective serotonin reuptake inhibitors (SSRIs) in men.

Dapoxetine, a short-acting SSRI, is the first drug to be marketed for premature ejaculation.

After oral administration, peak plasma concentrations of dapoxetine are reached after an hour. Elimination is relatively rapid and the terminal half-life is approximately 19 hours.

There have been several randomised controlled trials of dapoxetine for premature ejaculation.¹⁻⁶

The primary outcome for most of the trials was 'intravaginal ejaculatory latency time' measured by the partner using a stopwatch.

An analysis of two trials,¹ in which 2614 men (aged 18–77 years) were randomised to dapoxetine (30 mg or 60 mg) or placebo (all taken 1–3 hours before intercourse), found that dapoxetine increased intravaginal ejaculatory latency time significantly more than placebo. At baseline, men were required to have an intravaginal ejaculatory latency time of 2 minutes or less at least 75% of the time. After 12 weeks, 29% of men taking the 30 mg dose and 34% taking the 60 mg dose had a latency time of 3 minutes or more. This was compared to only 14% of men taking placebo. Men taking dapoxetine perceived that they had better control of ejaculation and were more satisfied with their sexual performance than those taking placebo.

In another trial, dapoxetine (60 mg) was compared to paroxetine (20 mg), another SSRI, in 340 men (aged 22–48 years) with premature ejaculation. Treatments were taken each day divided into two doses. After 12 weeks, intravaginal ejaculatory latency times had increased from 38 to 179 seconds for dapoxetine, from 31 seconds to 370 seconds for paroxetine, and from 34 to 55 seconds for placebo. More men reported sexual satisfaction with dapoxetine and paroxetine than with placebo (66% vs 78% vs 16%). A similar trend in sexual satisfaction was seen with partners who were interviewed independently of their husband. Eleven men dropped out because of lack of efficacy – 3/104 with dapoxetine, 2/105

with paroxetine and 6/100 with placebo. The timing of dosing in relation to sexual intercourse was not described in this trial.⁶

During the trials, nausea (11%), headache (5.6%), diarrhoea (3.5%), somnolence (3.1%) and dizziness (5.8%) were more commonly reported with dapoxetine 30 mg than with placebo. These events were dose-related – all of them were more frequent with the 60 mg dapoxetine dose. Nausea and dizziness were the most common reasons for discontinuation with dapoxetine 30 mg. Because of the increased risk of adverse events, patients should be warned to take no more than one tablet in a 24-hour period.

Sexual adverse effects including erectile dysfunction, abnormal ejaculation and decreased libido were more common with dapoxetine than placebo. These occurred in 2.9% of patients taking dapoxetine 30 mg and 3.8% taking dapoxetine 60 mg versus 1.5% of patients taking placebo.¹

Postural hypotension occurred in some patients and caution is urged with concomitant use of vasodilators such as alpha blockers, nitrates and phosphodiesterase 5 inhibitors. Syncope has been reported with dapoxetine and appeared to be dose-related (0.05% with placebo, 0.06% with 30 mg and 0.23% with 60 mg dose). Possible prodromal symptoms such as nausea, dizziness and light-headedness were also more common with dapoxetine than with placebo. Patients should be warned about this risk and advised to maintain adequate hydration and avoid alcohol.

Dapoxetine is metabolised by enzymes in the liver and kidneys, in particular cytochrome P450 (CYP) 2D6 and 3A4. It also moderately inhibits CYP 2D6 and weakly induces CYP 3A4 so numerous interactions are expected. Poor CYP 2D6 metabolisers may be at increased risk of adverse events. Concomitant treatment with potent CYP 3A4 inhibitors such as ketoconazole and ritonavir is contraindicated. Dapoxetine is also contraindicated with antidepressants including monoamine oxidase inhibitors, serotonin reuptake inhibitors, tricyclics and other drugs with serotonergic effects (tramadol, St John's wort and lithium).

Dapoxetine should not be taken in combination with recreational drugs such as ketamine, methylenedioxymethamphetamine (MDMA) and lysergic acid diethylamide (LSD) because of the



Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data 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. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

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potential risk of serious adverse events including arrhythmia, hyperthermia and serotonin syndrome. Concomitant sedatives can increase the risk of somnolence and dizziness.

Dapoxetine is contraindicated in patients with heart problems such as heart failure, conduction abnormalities or significant ischaemic or valvular disease. It is also contraindicated in moderate and severe hepatic impairment. Dapoxetine is not recommended in patients with severe renal impairment or with psychiatric disorders.

Although dapoxetine prolongs intravaginal latency time before ejaculation, improvements seem modest and a placebo effect was apparent in most of the studies. In an analysis of two trials, mean latency time increased from an average of 0.9 minutes at baseline to 1.75 minutes with placebo and 2.78 minutes with dapoxetine (30 mg taken on-demand).¹ In a comparative trial, paroxetine was more effective than dapoxetine, although it was unclear when treatment was taken in relation to sexual intercourse. This may have affected efficacy.⁶ The benefits and adverse effects of dapoxetine treatment should be reviewed after four weeks (or six doses).

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First published online 2 October 2013