

# Dapoxetine: licensed treatment for premature ejaculation

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**Dapoxetine (Priligy) is a new treatment for premature ejaculation licensed for as-required use. In our New products review, Steve Chaplin presents the data relating to its efficacy and adverse events, and Dr Penny Mostyn discusses its place in therapy.**



## KEY POINTS

- dapoxetine is an SSRI licensed for as-required treatment of premature ejaculation
- available as 30 and 60mg tablets; 30mg: 3=£14.71, 6=£26.48, 60mg: 3=£19.12, 6=£34.42
- dosage initially 30mg 1–3 hours before sexual activity, increasing to 60mg if poor response and no adverse reaction or symptoms of syncope
- to be eligible for treatment, men must meet 5 diagnostic criteria
- In clinical trials over 12–24 weeks, dapoxetine significantly increased time to ejaculation from about 1 minute to about 3 (vs 2 minutes with placebo)
- this was associated with improvement in other measures of sexual satisfaction in the man and female partner
- responder rates were about 30 per cent at a dose of 30mg and 40 per cent at 60mg, compared with 18 per cent with placebo
- dapoxetine has a relatively large number of contraindications, prescribing cautions and clinically significant drug interactions
- adverse effects include nausea, dizziness and headache; there is a risk of orthostatic hypotension and syncope
- dapoxetine has a limited role in the management of premature ejaculation, although some prescribers will welcome the choice of a licensed treatment

**P**remature ejaculation has been defined as a sexual disorder in men who have vaginal intercourse as: ejaculation that always or nearly always occurs prior to or within about one minute of vaginal penetration, and the inability to delay ejaculation on all or nearly all vaginal penetrations, associated with negative personal consequences such as distress, bother, frustration and/or the avoidance of sexual intimacy.<sup>1</sup>

Evidence-based guidelines suggest that drug treatment is the basis of management, supported by behavioural therapy. Options include topical local anaesthetics used as required, daily administration of an SSRI (unlicensed indication) and as-required dapoxetine (Priligy; Menarini),<sup>2</sup>

## Dapoxetine

Dapoxetine is an SSRI licensed for the treatment of premature ejaculation in men

aged 18–64 who meet five diagnostic criteria (see Table 1).

The recommended dose is 30mg taken one to three hours before anticipated sexual activity. If this dose is well tolerated but insufficient, it may be increased to 60mg.

Although taken on demand, dapoxetine does not have a short half-life (19 hours). It should not be taken more than once daily and is not intended for daily use. Treatment should be evaluated after four weeks or at least six doses and reviewed every six months.

Patients with a history of orthostatic hypotension should not take dapoxetine and an orthostatic test should be performed before starting treatment. Dapoxetine has not been evaluated in men aged over 65. It should be used with caution in men with mild or moderate renal

All criteria must be met:

- intravaginal ejaculatory latency time (IELT) of <2 minutes
- persistent or recurrent ejaculation with minimal sexual stimulation before, on or shortly after penetration and before the patient wishes
- marked personal distress or interpersonal difficulty as a consequence of premature ejaculation
- poor control over ejaculation
- a history of premature ejaculation in the majority of intercourse attempts during the previous 6 months

**Table 1.** Treatment criteria for dapoxetine

impairment and is contraindicated in those with severe renal impairment or moderate or severe hepatic impairment.

Other contraindications include heart failure, valvular disease, cardiac disease, conduction abnormalities and a history of syncope, mania or severe depression.

It should not be taken within 14 days of other drugs affecting serotonin function (including MAOIs and tricyclic antidepressants) or with potent inhibitors of CYP3A4 (eg some protease inhibitors).

It has other clinically significant interactions with drugs affecting CYP2D6 or CYP3A4 enzymes (details in the SPC).

## Clinical trials

Dapoxetine has been evaluated in five phase 3 trials<sup>3</sup> which have been pooled for analysis.<sup>4</sup> These double-blind trials included a total of 6081 heterosexual men in stable relationships (mean age 41) who were randomised to receive placebo or dapoxetine at the licensed doses.

One trial included men treated with 60mg daily and this group was excluded from the efficacy analysis; this trial did not require intravaginal ejaculatory latency time (IELT) of less than two minutes.

The main end-points were change in IELT, control over ejaculation and patient-reported clinical global impression of change.

About 30 per cent of men discontinued trials, evenly divided between dapoxetine and placebo recipients. The proportions withdrawing due to adverse events were 1.0 per cent with placebo and

3.5 and 8.8 per cent with dapoxetine 30 and 60mg.

Mean baseline IELT was 0.9 minutes. After 12 weeks, dapoxetine 30 and 60mg significantly increased mean IELT to 3.1 minutes and 3.5 minutes respectively compared with 1.9 minutes with placebo. These increases were maintained at 24 weeks (see Figure 1).

Significantly more men reported their premature ejaculation was at least better at week 12 (31 and 38 per cent with dapoxetine vs 14 per cent with placebo) with a similar proportion reporting it was slightly better.

The proportion of men reporting control over ejaculation increased from a mean of 1 per cent at baseline to 26 and 32 per cent with dapoxetine at week 12, significantly more than with placebo (11 per cent).

These changes were associated with significant improvements in personal distress/interpersonal difficulty and satisfaction with intercourse compared with placebo, and were independent of baseline IELT. Women partners reported increased satisfaction with intercourse.

Defining response as improved control over ejaculation and reduced distress, the responder rates were 31 per cent with dapoxetine 30mg and 40 per cent at a dose of 60mg, compared with 18 per cent with placebo.<sup>3</sup>

## Adverse effects

Adverse effects are dose related (see Table 2); other common adverse effects

	30mg	60mg
nausea	11%	22%
dizziness	6%	11%
headache	6%	9%
diarrhoea	4%	7%
insomnia	2%	4%
fatigue	2%	4%

**Table 2.** Adverse effects reported most frequently in phase 3 trials<sup>5</sup>

include psychiatric and gastrointestinal disorders.<sup>5</sup>

Orthostatic hypotension and syncope may occur and patients should be warned of the risk and able to take appropriate measures if they have prodromal symptoms.

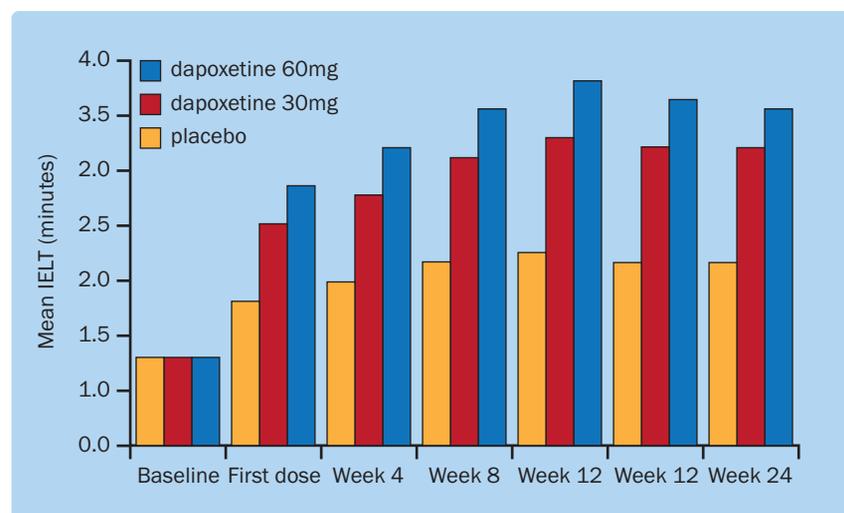
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## Declaration of interests

None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics



**Figure 1.** Effect of dapoxetine on intravaginal ejaculatory latency time (IELT)

## Place in therapy

A new and licensed treatment for premature ejaculation is needed. However, as the aetiology of this common problem is not known,<sup>1</sup> any new treatment simply increases the range of suboptimum options available.

Current unlicensed treatments include local anaesthetics and daily or on-demand SSRIs and phosphodiesterase type 5 (PDE5) inhibitors alone or in combination with behavioural exercises.<sup>1</sup>

Behavioural exercises can improve ejaculatory control, although more research is needed.<sup>2</sup>

The efficacy of dapoxetine is unremarkable if comparing its threefold improvement in IELT<sup>3</sup> to an eightfold improvement in IELT with off-label daily paroxetine<sup>2</sup> or a sixfold improvement for an initial daily dosing regimen followed by on-demand paroxetine three to four hours prior to sexual activity.<sup>4</sup>

Better data for dapoxetine are shown in a 30 per cent increase in ejaculatory control,<sup>3</sup> and perceived control has been

shown to be a more important outcome variable than IELT alone.<sup>2</sup>

Apart from the 0.2 per cent risk of syncope<sup>3</sup> the side-effects of dapoxetine are consistent with other SSRIs. My clinical experience parallels that of the results of a clinical trial where men often decline 'antidepressant' medication due to perceived side-effects and discontinue due to actual side-effects and/or disappointing results.<sup>5</sup>

Patient preference is frequently for a trial of behavioural exercises alone or in combination with on-demand medication; when there are concomitant erectile difficulties this would be a PDE5 inhibitor.

In my opinion there is a place for dapoxetine in the management of premature ejaculation but it is limited. It could be used in combination with behavioural exercises in the short term, or as a second- or third-line treatment option in the long term.

Some prescribers will prefer to use a licensed drug although cost is a factor, as treatment for premature ejaculation

may not be an NHS priority. Off-label SSRIs and PDE5 inhibitors, especially sildenafil that is now off patent, are cheaper for what might be a lifelong prescription.

## References

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## Declaration of interests

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