Avanafil (Spedra): increasing the choice of PDE-5 inhibitors

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Avanafil is a new PDE-5 inhibitor for treating erectile dysfunction. In our New products review, Steve Chaplin presents the data relating to its efficacy and adverse effects.

The introduction of avanafil (Spedra) brings to four the number of PDE-5 inhibitors for the treatment of erectile dysfunction (ED); the others are sildenafil – now available generically – tadalafil (Cialis) and vardenafil (Levitra).

The recommended dose is 100mg 30 minutes before sexual activity, which may be increased to a maximum dose of 200mg or decreased to 50mg according to tolerability and response. Avanafil should not be taken more than once per day.

Dose adjustment is not required in men over 65 years old (though there is little clinical experience in the over-70s) or in patients with mild to moderate renal impairment. Treatment should begin with the minimum effective dose in patients with mild to moderate hepatic impairment.

Avanafil is contraindicated in men with severe renal or hepatic impairment and with concurrent treatment with potent inhibitors of CYP3A4 (eg clarithromycin, some protease inhibitors). With concurrent therapy with a moderate CYP3A4 inhibitor (eg erythromycin, diltiazem, verapamil), the maximum dose should not exceed 100mg and the interval between doses should be at least 48 hours.

Other contraindications and prescribing cautions are similar to those for other PDE-5 inhibitors.

Clinical trials

Avanafil has been evaluated in three phase 3 trials of 12 weeks’ treatment in men with ED (mean age 57), including two in men with diabetes or after nervesparing prostatectomy. It has not been directly compared with other PDE-5 inhibitors.

These trials randomised 1334 men with mild to severe ED (defined as the inability to achieve vaginal penetration on at least half of attempts at sexual intercourse without medication) of at least six months’ duration.

The trials shared three primary endpoints. At baseline, the proportion of attempts resulting in successful intercourse ranged from 4 to 14 per cent. After placebo, the mean increase was about 14 per cent, significantly less than with avanafil 50mg (28 per cent), 100mg (28–43 per cent) or 200mg (29–44 per cent).

The percentage of attempts with successful vaginal penetration was 20–48 per cent at baseline, increasing by 7–8 per cent after placebo and by 18, 22–27 and 26–30 per cent after avanafil 50, 100 or 200mg. Avanafil also significantly improved ED function scores. There was
no significant difference between the 100mg and 200mg doses.

As with other PDE-5 inhibitors, treatment with avanafil was less effective in men with diabetes or after prostatectomy, who also had worse ED at baseline, than in the overall population.

A total of 536 men were recruited to a 52-week nonblinded extension study, beginning at a dose of 100mg per day. Of these, 75 per cent voluntarily increased their dose to 200mg daily and 0.4 per cent reduced their dose. During the treatment period, the mean increase in the proportion of attempts resulting in successful intercourse was 55 per cent.

### Adverse effects

The adverse events reported during clinical trials were similar to those of other PDE-5 inhibitors, the most frequent being headache, flushing, nasal congestion and dyspepsia. The rate of discontinuation due to adverse events was about 2 per cent with avanafil and 1 per cent with placebo.

### Conclusion

Avanafil widens the choice of treatment for ED. It appears to be a typical PDE-5 inhibitor but its efficacy and tolerability compared with other agents in this class is not known. It is much more expensive than generic sildenafil.

### Reference


### Declaration of interests

None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics

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**Table 1. Summary of trial results for the primary efficacy end-points**

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<th>change LS mean</th>
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<th>treatment mean</th>
<th>change LS mean</th>
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*statistically significant p-value for the treatment comparison between avanafil and placebo