The Dorset Medicines Advisory Group does not recommend the use of dapoxetine for premature ejaculation. The cost of dapoxetine is significantly greater than that of other SSRIs used off-label, the evidence for its use is limited and long-term safety outcomes are not available.

**BACKGROUND**

Dapoxetine is an oral treatment for premature ejaculation (PE). It is a short-acting SSRI which can be taken when required up to 1-3 hours prior to anticipated sexual intercourse, no more than once a day. It is not intended for continuous daily dosing and should only be used by men who meet specific criteria.

Use of dapoxetine is contra-indicated in a number of medical conditions (such as cardiovascular) and with certain medications (such as those affecting serotonin release or CYP3A4 enzyme inhibitors).

**RELEVANT NICE GUIDANCE**

Dapoxetine has not been considered by NICE

**FORMULARY STATUS**

Not recommended

**PBR STATUS**

Included within PbR tariff arrangements

**COMMISSIONING IMPLICATIONS**

Currently oral SSRIs (paroxetine, sertraline and fluoxetine, which must be taken on a daily basis) are used off-label; dapoxetine offers a licenced therapeutic option that could be initiated in primary care. PE must be distinguished from erectile dysfunction (ED) and if ED exists, it should be treated before or at the same time as PE.

**RELEVANT CLINICAL COMMISSIONING PROGRAMME**

General Medical and Surgical
Maternity, reproductive and family health

**PATIENT PATHWAY IMPLICATIONS**

Dapoxetine is the first oral treatment for PE to be licensed in the UK and unlike other SSRIs, which are used off-label and must be taken daily, dapoxetine is short-acting and taken as required (maximum once a day). Dapoxetine should only be used in men aged 18-64 years who meet certain criteria.

The cost of dapoxetine is significantly greater than that of other SSRIs used off-label. Treatment with dapoxetine costs more than 10 times the cost of paroxetine or fluoxetine.

**SUMMARY OF**

There are five randomised, double-blind, placebo-controlled phase 3 studies evaluating dapoxetine 30mg and 60mg over 9-24 weeks. In all studies, men had to meet the diagnostic criteria for PE as specified in the Diagnostic and Statistical Manual of Mental Disorders 4th edition (DSM-IV-TR); onset of orgasm and ejaculation with minimal sexual stimulation before, on, or shortly after.
penetration and before the person wished, in most intercourse episodes in the 6 months before enrolment, and marked distress or interpersonal difficulty due to PE. Men were enrolled if they had been in a stable monogamous, heterosexual relationship for ≥6 months and had an intravaginal ejaculatory latency time (IELT) of ≤2 minutes in at least 75% of intercourse episodes at baseline in four of the studies. Exclusion criteria included erectile dysfunction, concomitant use of SSRIs or tricyclic antidepressants, major psychiatric disorders, history of medical illness, uncontrolled hypertensions or other forms of sexual dysfunction.

There are a number of limitations to the studies:
• Even though the majority of results with dapoxetine were significantly better than those with placebo (and proportionately greater), there were still some placebo effects in terms of the subjective secondary endpoints. A quarter of men taking placebo in the integrated analysis still perceived that they had slight better/better/much better improvements in PE. In one study, over half of those treated with placebo achieved ≥1 category increase in satisfaction with sexual intercourse, or decrease in personal distress related to ejaculation at endpoint.
• The study populations were restricted to those with IELT consistently ≤2 minutes and with PE described as moderate to severe. These results cannot be generalised to milder forms of PE, but do reflect the criteria for dapoxetine use stated in the Summary of Product Characteristics (SPC).
• The effects of dapoxetine on PE associated with erectile dysfunction or PE due to other causes has not been assessed.
• Only three of the studies stated how often men were to try to attempt sexual intercourse; the other two did not and some men may have been more active than others, potentially influencing the results.
• In three studies the majority of men were Caucasian (84-87%) and in one the majority were Asian (92%), and most were ≤49 years of age; robust conclusions of the efficacy of dapoxetine in other ethnic groups and older men could not be made.
• Only men in stable, monogamous, heterosexual relationships were included in the studies.
• No active comparators were used, which may reflect the fact that no other oral therapies are licensed to treat PE.
• Just over half of those enrolled completed study NCT00229073, with 21% in each of the dapoxetine groups and 31% of the placebo group discontinuing by choice.
• Factors contributing to discontinuation included the long trial duration and the burden of evaluation (stopwatch-measured IELT and more than five monthly questionnaires). Analysis using subjects with both baseline and post-baseline IELT measurements showed that the discontinuation rate did not affect the treatment outcomes. Protocol deviations occurred in a large number of patients with treatment deviations in approximately 60% (including subjects taking >1 dose in a 24 hour period or receiving the wrong dose/medication): the investigators did not explain if these affected the treatment results or not.
<table>
<thead>
<tr>
<th>Drug and dose</th>
<th>Cost per pack</th>
<th>Cost per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine, 20-60mg/day</td>
<td>30 x 20mg capsules = £1.02</td>
<td>£12.14 - £36.72 (20-60mg capsules/day)</td>
</tr>
<tr>
<td>[off-label indication]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine, 20-40mg/day</td>
<td>30 x 20mg tablets = £1.63</td>
<td>£19.56 - £39.12</td>
</tr>
<tr>
<td>[off-label indication]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sertraline, 25-200mg/day</td>
<td>28 x 50mg tablets = £6.35</td>
<td>£82.55 – £200.46</td>
</tr>
<tr>
<td>[off-label indication]</td>
<td>28 x 100mg tablets = £7.71</td>
<td></td>
</tr>
<tr>
<td>Dapoxetine, 30-60mg prn</td>
<td>3 x 30mg = £14.71</td>
<td>Based on six attempts a month (as per study requirements): £317.76 (30mg prn) to ~£400 (60mg, but initiating with 30mg).</td>
</tr>
<tr>
<td></td>
<td>6 x 30mg = £26.48</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 x 60mg = £19.12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 x 60mg = £34.42</td>
<td></td>
</tr>
</tbody>
</table>

London New Drugs Group has estimated budgetary impact based on a population of 100,000. They estimate that of this group, 1,151 men will have severe PE, 25% of whom will seek treatment. 70% of those (202) are likely to be given dapoxetine and take 3 tablets/month. Assuming all treatments are prescribed in general practice, and there is 100% uptake in 5 years, the likely cost will be £22,257.

REFERENCES

London New Drugs Group/London Medicines Network evaluation review: Dapoxetine (Priligy®) for premature ejaculation. November 2013


DATE OF APPROVAL AND REVIEW

Approved: December 2013
For review: December 2014 or earlier in the light of new information