Vitaros: topical alprostadil for erectile dysfunction

Steve Chaplin BPharm, MSc and Michael Cummings MD, FRCP

Vitaros, a topical cream formulation of alprostadil, is licensed for the treatment of erectile dysfunction in adults. In our New products review, Steve Chaplin presents the clinical data relating to its efficacy and adverse events and Professor Michael Cummings discusses its place in therapy.

Steve Chaplin

Options for the pharmacological treatment of erectile dysfunction include an oral PDE-5 inhibitor or alprostadil, a vasodilator prostaglandin. Alprostadil has the advantage of local rather than systemic administration but until now has only been available for intracavernosal injection (Caverject, Viridal Duo) or transurethral insertion (MUSE), for which training is required.

Alprostadil cream

Vitaros is a cream formulation containing alprostadil for the treatment of erectile dysfunction in adults. It is supplied in single-use containers of 100g containing 200 or 300µg alprostadil. The cream is applied externally to the meatus, producing an erection within 5–30 minutes that persists for one to two hours. It should be used no more than once per 24 hours and up to three times per week. Prescribing at NHS expense is limited to the same patients who are eligible for other treatments for erectile dysfunction.

The initial dose in men with serious erectile dysfunction, co-morbidity or after failure of PDE-5 inhibitor is 300µg, adjusted to 200µg according to tolerability. Patients should be given instruction on administration technique, advised about possible adverse effects and warned to avoid operating machinery until their tolerance is known. Vitaros is contraindicated in men who are susceptible to priapism and in men with unstable cerebrovascular or cardiovascular disease, or underlying orthostatic hypotension, myocardial infarction or syncope. Alprostadil is associated with reproductive toxicity in animals; men who have intercourse with a woman of childbearing age should wear a condom.

No studies of interactions with other drugs used to treat sexual dysfunction have been carried out.

Clinical trials

A pooled analysis of two placebo-controlled trials involved a total of 1732 men randomised to receive up to 24 doses of
100, 200 and 300µg; outcomes for the lowest dose are not detailed here. The primary end-points were the differences from baseline in erectile dysfunction score and sexual encounter profile score (assessing the success of vaginal penetration and maintenance of erection to ejaculation).

After 12 weeks, erectile dysfunction score worsened slightly with placebo but improved significantly and to a similar extent with alprostadil 200 or 300µg. Scores of vaginal penetration and maintenance of erection also increased significantly (see Table 1). Assessment of patient satisfaction showed corresponding improvements, with 47 and 52 per cent of men reporting improved erections during 12 weeks compared with 20 per cent with placebo.

The discontinuation rate in men randomised to the 300µg dose was 30 per cent compared with 20 per cent at 200µg. Trial participants were offered enrolment in a nonblinded extension trial (n=1161, including 163 previously untreated men). The dose was adjusted over two 30-day periods of eight doses each, after which patients who were not ‘normoresponsive’ were excluded. After one month using a dose of 200µg, 73 per cent opted for the 300µg dose. The main reasons for discontinuation were patient or partner withdrawal (16 per cent) and hyper- or hyporesponsiveness (12 per cent).

Severity of erectile dysfunction improved from moderate-to-severe to mild-to-moderate in most patients. After dose titration, the proportion of men reporting vaginal penetration was about 75–85 per cent, with about 65 per cent reporting maintenance of erection.

Post-hoc analysis showed that alprostadil cream was superior to placebo in improving sexual function in men for whom oral sildenafil was unsatisfactory, largely in those with severe erectile dysfunction.

Adverse effects
Common adverse effects include local pain and erythema, rash and urethral pain. In clinical trials, dizziness, hypotension and syncope were reported in 0.4–0.5 per cent of men and priapism in 0.1–0.4 per cent. In the extension trial, 4 per cent of men discontinued treatment due to adverse effects. One to two per cent of partners reported vulvovaginal burning or itching and 5–6 per cent of men inserted the applicator device into the penis.

References

Declaration of interests
Steve Chaplin has none to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics

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### Table 1. Mean change from baseline in erectile dysfunction, vaginal penetration and maintenance of erection scores for Vitaros versus placebo; after reference 1

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Vitaros 200µg</th>
<th>300µg</th>
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<tbody>
<tr>
<td>patients (n)</td>
<td>411</td>
<td>410</td>
<td>410</td>
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<tr>
<td><strong>International Index of Erectile Function domain scores</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>baseline</td>
<td>14.0</td>
<td>13.6</td>
<td>13.6</td>
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<tr>
<td>end-point</td>
<td>13.3</td>
<td>16.1</td>
<td>16.1</td>
</tr>
<tr>
<td>mean change</td>
<td>-0.7</td>
<td>2.5</td>
<td>2.5</td>
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<tr>
<td>LS mean change ± SE p value</td>
<td>-0.7 ± 0.34</td>
<td>2.5 ± 0.34 &lt;0.001</td>
<td>2.4 ± 0.34 &lt;0.001</td>
</tr>
<tr>
<td><strong>Vaginal penetration/attempt rates</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>baseline</td>
<td>55.9</td>
<td>52.9</td>
<td>49.9</td>
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<tr>
<td>end-point</td>
<td>51.2</td>
<td>58.2</td>
<td>57.5</td>
</tr>
<tr>
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<td>-4.7</td>
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<tr>
<td>LS mean change ± SE p value</td>
<td>-4.5 ± 1.65</td>
<td>5.1 ± 1.65 &lt;0.001</td>
<td>7.2 ± 1.65 &lt;0.001</td>
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<td><strong>Intercourse completion to ejaculation</strong></td>
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<td></td>
</tr>
<tr>
<td>baseline</td>
<td>29.4</td>
<td>27.6</td>
<td>28.7</td>
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<tr>
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<tr>
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<td>0.4 ± 1.64</td>
<td>13.8 ± 1.63 &lt;0.001</td>
<td>9.1 ± 1.63 &lt;0.001</td>
</tr>
</tbody>
</table>

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**NEW PRODUCTS**

**Vitaros**

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Place in therapy

Michael Cummings

At first sight, Vitaros, which is applied locally as a cream to promote tumescence, represents just a different administration route for alprostadil. Indeed, this observation is correct. However, there are additional practical considerations to consider. The other versions of alprostadil (transurethral alprostadil or intracavernosal alprostadil) have been typically considered the domain of specialist care management once oral PDE-5 inhibitors (usual first-line therapy prescribed in primary care) have failed to be effective or tolerated, or are contraindicated (e.g., patients on nitrate therapy).

The rationale for specialist care involvement with traditional routes of alprostadil administration is usually based upon lack of experience in primary care of managing more invasive erectile dysfunction therapy. Alternatively, it may be due to the limited availability of time to train patients, which needs to incorporate advice on technique, dose titration or side-effects such as priapism.

Vitaros offers the opportunity to extend the options for treating erectile dysfunction within primary care. The available evidence suggests that there will be a group of patients who will respond to Vitaros that are oral PDE-5 nonresponders in addition to responders who are erectile dysfunction treatment naive. Vitaros probably represents the next least invasive pharmacological approach after oral therapy and intuitively is likely to be the preferred option chosen by many patients considering alprostadil therapy.

Given the ease of administration and simplicity of teaching patients to apply the cream, I believe that Vitaros will be an option that could be prescribed and managed within primary care. Apart from the ease of application, advantages for patients also include the removal of waiting time to see a specialist. For GPs this removes the cost associated with specialist care referral.

The effectiveness of Vitaros is reasonable but falls below that seen with transurethral or intracavernosal injection therapy. However, for those patients in whom this application is successful, it offers perhaps a less invasive and quicker therapeutic option for the treatment of erectile dysfunction.

References

Declaration of interests

Professor Cummings has previously received educational grants and honours from Takeda; however, none were related to Vitaros.

Professor Cummings is consultant physician and honorary professor, diabetes and endocrinology, Academic Department of Diabetes and Endocrinology, Queen Alexandra Hospital, Portsmouth