DORSET MEDICINES ADVISORY GROUP

COMMISSIONING STATEMENT ON ALPROSTADIL CREAM 3mg/G (VITAROS®) FOR THE TREATMENT OF ERECTILED DYSFUNCTION IN MEN 18 YEARS AND ABOVE WITH ERECTILE DYSFUNCTION

SUMMARY

NHS Dorset Clinical Commissioning Group does not recommend the use of Vitaros® (alprostadil cream 3mg/g) for the treatment of men 18 years of age or older with erectile dysfunction (ED).

BACKGROUND	Alprostadil causes vasodilatation of blood vessels in the erectile tissues of the corpora cavernosa and increases cavernosal artery blood flow, causing penile rigidity. Vitaros is a white to off-white cream supplied in AccuDose, a single dose container. AccuDose is a container consisting of a plunger, barrel, and protective cap provided in a protective sachet. Vitaros is applied to the tip of the penis. It is available in two dosage strengths of 200 and 300 mcg alprostadil in 100 mg of cream. Vitaros should be used as needed to achieve an erection. The onset of effect is within 5 to 30 minutes after administration. The duration of effect is approximately 1 to 2 hours, although the actual duration will vary from patient to patient. Each patient should be instructed on proper technique for administration of Vitaros prior to self-administration. The maximum frequency of use no more than 2-3 times per week and only once per 24-hour period.
RELEVANT NICE GUIDANCE	Vitaros® has not been considered by NICE and is not on the timetable
FORMULARY STATUS	Not Recommended
PbR STATUS	Included within PbR tariff arrangements
COMMISSIONING IMPLICATIONS	Sildenafil is the first line treatment for ED in Dorset, with alprostadil injection or tadalafil as alternatives. For patients with severe distress the treatment options are alprostadil injection, sildenafil or tadalafil, (all for hospital use only), and erectile dysfunction appliances, which should be initiated in hospital.
RELEVANT CLINICAL COMMISSIONING PROGRAMME	General Medical and Surgical Maternity, reproductive and family health

PATIENT PATHWAY IMPLICATIONS	Current European guidance states that three potent selective PDE5I's have been approved by the European Medicines Agency (EMA) for the treatment of ED. If PDE5I's are not clinically appropriate, intracavernous pharmacotherapy is considered a second-line treatment. Patients not responding to oral drugs may be offered intracavernous injections with a high success rate of 85%. Dorset CCG has advised that of the PDE5I's, sildenafil is the first line choice, and tadalafil is an alternative. Dorset CCG recommends the use of alprostadil intracavernous injection as 2nd line choice. Patients with severe distress can be prescribed erectile dysfunction appliances following hospital initiation. Vitaros® should be used no more than 2-3 times per week and only once per 24-hour period.
SUMMARY OF EVIDENCE TO SUPPORT FORMULARY STATUS	Independent guidance on the safety and efficacy of Vitaros® is lacking, and full-text reports on published trials are not available. Because of concerns on the safety of topical alprostadil cream (a transgenic mouse carcinogenicity study), it is not licensed in the US. **Efficacy** Vitaros® has been studied in over 3300 patients and demonstrated statistically significant and clinically meaningful improvements in erectile function from baseline, versus placebo at 12 weeks. 73% of men rolled over from the 12 week phase III studies opted to continue with alprostadil for 6 months in an open label extended safety study, providing an intermittent exposure to alprostadil of 3385 patient months (282 patient years) over 9 months. Clinically relevant effects have also been demonstrated in high risk populations with medical histories that included stable cardiac disease, hypertension, diabetes and prostatectomy (all excluded from PDE5 inhibitor treatment. **Safety** Vitaros® is contraindicated • For use by men having intercourse with women with child-bearing potential unless the couple uses a condom barrier. • In men with orthostatic hypotension, myocardial infarction, syncope and those for whom sexual activity is inadvisable e.g. in men with unstable cardiovascular or unstable cerebrovascular conditions. • In men with conditions that might predispose them to priapism • In men with abnormal penile anatomy such as severe hypospadias, or with anatomical deformation of the penis, or in men with urethritis and balanitis The vast majority of adverse events reported (>97%) were mild or moderate in intensity and of short duration (60 mins or less). Approximately, 2% of all adverse events reported were partner related. The majority of partner related adverse events were mild vaginal burning of short duration (less than

<table>
<tr><td></td><td>60 minutes post intercourse). There were 3 reports of hypotension reported in patients treated with alprostadil 300µg.</td></tr>
<tr><td>ASSESSMENT OF COST IMPLICATIONS</td><td>
<table>
<tr><th>Preparation</th><th>Strength and cost</th><th>Cost/week at max use</th></tr>
<tr><td>Alprostadil cavenosal injection (Caverject®)
Max 3 x weekly</td><td>10mcg = £7.35
20mcg = £9.50</td><td>£22.05
£28.50</td></tr>
<tr><td>Alprostadil cavenosal injection (Viridal Duo®)
Max 3 x weekly</td><td>10mcg = £16.55
20mcg =£21.39
40mcg =£27.22</td><td>£49.65
£64.17
£81.66</td></tr>
<tr><td>Alprostadil urethral application (MUSE®)
Max 7 x week</td><td>250mcg = £11.30
500mcg = £11.30
1mg = £11.56</td><td>£79.10
£79.10
£80.92</td></tr>
<tr><td>Alprostadil cream (Vitaros®)
Max 3 x week</td><td>£40 for 4 doses</td><td>£30</td></tr>
</table>
(Prices from BNF August 2014)
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<tr><td>REFERENCES</td><td>

Summary of Product Characteristics. Vitaros 3mg/g cream. Takeda UK Ltd. Accessed on 16th May 2014 www.medicines.org.uk/emc

Personal communication, Takeda UK Ltd. June 2014

UKMi New Drugs online

European Association of Urology. K. Hatzimouratidis (chair), I. Eardley, F. Giuliano, D. Hatzichristou, I. Moncada, A. Salonia, Y. Vardi, E. Wespes. Guidelines on Male Sexual Dysfunction: Erectile dysfunction and premature ejaculation. Update March 2013

Hackett G, Dean J, Kell P, Price D, Ralph D, Speakman M, Wylie K for the British Society for Sexual Medicine. British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction. 2007. Accessed via on 29th August 2014

Decisions from adjacent CCGs

Somerset CCG – not listed

West Hampshire CCG (Basingstoke, Southampton and Winchester District Prescribing Committee (DPC) – not listed

Bath Clinical Area Partnership (BCAP) – not listed

North and East Devon Formulary and referral – not listed

The Plymouth Area Joint Formulary – not listed
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Date	August 2014
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