

### Commissioning guidance:

Commissioners may wish to bear the following in mind when considering the commissioning of dequalinium chloride:

- For the treatment of bacterial vaginosis, the recommended first line options are 400 mg twice daily oral metronidazole for 5 to 7 days, 0.75% metronidazole vaginal gel for 5 days or 2% clindamycin vaginal cream for 7 days.
- Dequalinium may be a suitable alternative treatment if:
  - Women cannot tolerate metronidazole or clindamycin, or in other circumstances where those treatments are not suitable e.g. women with inflammatory bowel disease, or antibiotic-associated colitis where clindamycin is contraindicated.
  - In situations where fewer treatments are available due to interactions or allergies, e.g. in pregnancy
  - Where it would be beneficial to avoid use of an antibiotic (according to local specialist opinion, metronidazole resistance and clindamycin resistance is an increasing but under-recognised problem largely because women with BV are not tested for resistance.)

### Strength of the evidence for efficacy

The evidence for efficacy for dequalinium chloride was supplied by one phase 3, non-inferiority trial that compared dequalinium with topical clindamycin 2% vaginal cream for the treatment of bacterial vaginosis. The trial found that dequalinium was non-inferior to clindamycin with similar cure rates achieved at follow-up visits.

*MTRAC considered dequalinium as a product that may be used in primary care.*

### Description of technology

Dequalinium chloride (Fluomizin<sup>®</sup>) is a quaternary ammonium compound that acts as a surface antiseptic agent. In 2015, a vaginal tablet formulation was licensed for the treatment of bacterial vaginosis. Dequalinium acts on bacterial cells to increase cell permeability and decrease bacterial enzyme activity leading to cell death.<sup>1,2</sup>

The recommended dose and course of treatment is one vaginal tablet daily for six days. Tablets should be inserted deep within the vagina in the evenings before retiring.<sup>1,2</sup>

### Background

Bacterial vaginosis (BV) is a common condition in women that can lead to an abnormal vaginal discharge. It is caused by an infection in the vagina where the normal bacterial flora are disrupted, there is an overgrowth of anaerobic bacteria and the pH rises to a level in the range 4.5 to 6, whereas normal values are lower than 4.5.<sup>3</sup>

About half of women will experience no symptoms with the infection, others may experience a fishy-smelling discharge.<sup>4</sup> BV is not regarded as a sexually transmitted infection (STI), but is associated with sexual activity; women with BV are at increased risk of acquiring STIs<sup>5</sup>. In pregnancy, bacterial vaginosis is associated with late miscarriage, pre-term labour,

pre-term birth, pre-term premature rupture of membranes, low birth weight and postpartum endometritis.<sup>6</sup>

For the treatment of bacterial vaginosis, guidelines<sup>4,5</sup> are consistent in advising that the recommended options are: 400 mg twice daily oral metronidazole for 5 to 7 days, 0.75% metronidazole vaginal gel for 5 days or 2% clindamycin vaginal cream for 7 days.

Alternative options are<sup>5</sup>:

- metronidazole 2g as a single oral dose
- tinidazole 2g as a single oral dose,
- tinidazole 1 g orally for 5 days
- clindamycin 300 mg orally twice daily for 7 days
- dequalinium chloride 10mg vaginal tablet one daily for 6 days.

The Scottish Medicines Consortium and the All Wales Medicines Strategy Group advise that dequalinium chloride is recommended for use as second-line treatment after initial treatment for bacterial vaginosis has been ineffective or not tolerated.<sup>7,8</sup>

### Clinical evidence for efficacy and safety

The evidence for the efficacy of dequalinium chloride for the treatment of bacterial vaginosis comes from one phase 3, single-blind, non-inferiority trial that compared dequalinium chloride 10 mg vaginal tablets with clindamycin 2% vaginal cream.<sup>9</sup>

The trial enrolled 321 premenopausal women aged 18 to 55 years (one was aged 16 years) with bacterial vaginosis diagnosed by the presence of all four Amsel criteria<sup>4</sup>: a grey, homogeneous, malodorous discharge, pH > 4.5, positive potassium hydroxide test for amines, and clue cells constituting  $\geq 20\%$  of epithelial cells on a wet mount. Exclusion criteria included pregnancy, acute genital infection, suspicion of or clinically manifest STI, ulcerative colitis or medical history of antibiotic-induced colitis.

Women were randomised to treatment with either a dequalinium chloride 10 mg vaginal tablet once daily for 6 days (n = 164), or clindamycin 2% vaginal cream once daily for 7 days (n = 157). Follow-up visits occurred 7 days, and 25 days after the end of treatment; outcome assessors were blind to treatment assignment. The incidence of previous episodes of bacterial vaginosis was comparable between treatment groups (69.3% in the dequalinium chloride group and 71.7% in the clindamycin group), but details of previous treatments were not recorded.

The primary outcome was clinical cure at the first follow-up visit, defined as the absence of clue cells and a negative result for at least two other Amsel criteria. Secondary outcomes included clinical cure at second follow-up visit, clinical improvement at first and second follow-up visits (two or more Amsel criteria negative), rate of treatment failures at second follow-up visit, and incidence of post-treatment vulvovaginal candidosis.

Results of the trial showed that similar cure rates were achieved at both follow up visits for women treated with dequalinium chloride or clindamycin 2% cream. In the per protocol population after seven days' treatment, 81.5% of women receiving dequalinium chloride and 78.4% of clindamycin-treated women were considered to be cured; there was no significant difference between the cure rates. The two-sided confidence interval for the difference between treatments was within the pre-specified margin of  $\pm 15\%$ , demonstrating the non-inferiority of dequalinium to 2% clindamycin. Similar rates of cure were seen at the second follow up visit, 25 days after treatment.

### Adverse events

No serious adverse events were reported in the trial<sup>9</sup>. At the first and second follow-up visits, the overall tolerability of the treatment was considered to be very good or good by 90% of the women treated, and the study investigators.

There were no statistically significant differences between the numbers of women with treatment-related adverse events reported in the dequalinium chloride (n = 29; 17.8%) and clindamycin (n = 31; 20.3%) treatment groups. The two most frequently reported adverse drug reactions were vaginal discharge, occurring in 9.2% of dequalinium chloride-treated women and 4.6% of clindamycin-treated women; and vulvovaginal pruritus, occurring in 4.9% of dequalinium chloride-treated women and 8.5% of clindamycin-treated women.

### Considerations for cost impact

The list below shows prices of the available treatment options for a single course of treatment lasting up to seven days (Source [MIMs November 2018](#); excluding VAT):

Metronidazole (generic 400mg tab)	£ 5.18
Metronidazole Zidova® 0.75% gel	£ 4.31
Metronidazole Flagyl® 400mg tab	£ 6.34
Dequalinium Chloride Fluomizin® 10mg vag tab	£ 6.95
Clindamycin Phosphate Dalacin® 2% cream	£10.86

### References

1. Dequalinium chloride (Fluomizin®) 10 mg vaginal tablets. All Wales Therapeutics and Toxicology Centre AWMSG Secretariat Assessment Report 2016 <http://www.awmsg.org/awmsgonline/app/appraisalinfo/2775>
2. Fluomizin 10 mg vaginal tablets. EMC 2017 [www.medicines.org.uk/emc/product/1997](http://www.medicines.org.uk/emc/product/1997)
3. Dequalinium for bacterial vaginosis. *Drug Ther Bull* 2017; 55(5):54-57.
4. UK National Guideline for the management of Bacterial Vaginosis 2012. BASHH [www.bashhguidelines.org/media/1041/bv-2012.pdf](http://www.bashhguidelines.org/media/1041/bv-2012.pdf)
5. 2018 European (IUSTI/WHO) Guideline on the Management of Vaginal Discharge. NICE CKS 2018 [www.iusti.org/regions/europe/pdf/2018/IUSTIvaginalDiscargeGuidelines2018.pdf](http://www.iusti.org/regions/europe/pdf/2018/IUSTIvaginalDiscargeGuidelines2018.pdf)
6. Bacterial vaginosis. NICE 2018 <https://cks.nice.org.uk/bacterial-vaginosis>
7. Dequalinium (Fluomizin). Scottish Medicines Consortium 2016 [www.scottishmedicines.org.uk/medicines-advice/dequalinium-fluomizin-fullsubmission-119416/](http://www.scottishmedicines.org.uk/medicines-advice/dequalinium-fluomizin-fullsubmission-119416/)
8. Dequalinium chloride (Fluomizin®). All Wales Medicines Strategy Group 2016 <http://www.awmsg.org/awmsgonline/app/appraisalinfo/2775>
9. Weissenbacher ER *et al.* A comparison of dequalinium chloride vaginal tablets (Fluomizin(R)) and clindamycin vaginal cream in the treatment of bacterial vaginosis: a single-blind, randomized clinical trial of efficacy and safety. *Gynecol Obstet Invest* 2012; 73(1):8-15.

Launch date: April 2016

Manufacturer: Kora Healthcare

WARNING: This sheet should be read in conjunction with the Summary of Product Characteristics

This guidance is based upon the published information available in English at the time the drug was considered. It remains open to review in the event of significant new evidence emerging.



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