SCHEDULING STATUS
S2

1. NAME OF THE MEDICINE
FLUOMIZIN®, 10 mg vaginal tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each vaginal tablet contains 10 mg dequalinium chloride.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Vaginal tablets

FLUOMIZIN vaginal tablets are white or almost white, oval, biconvex tablets.
The tablet has the following dimensions: length of 19,1 mm; width of 12,2 mm; height of 6,4 mm.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
FLUOMIZIN is indicated for the treatment of bacterial vaginosis in adult patients (see section 4.4).
Consideration should be given to official guidance on the appropriate use of antibacterial medicines.

4.2 Posology and method of administration
Posology
Adults (18 - 55 years):
One vaginal tablet daily for six days.
The vaginal tablets should be inserted deeply into the vagina in the evenings before retiring. This is best performed in a reclining position with the legs slightly bent.

The treatment should be interrupted during menstruation and resumed afterwards.

Although relief of discharge and inflammation generally occurs within 24 to 72 hours, the treatment should be continued even when there is no subjective discomfort (itching, discharge, smell) anymore. A treatment less than six days could result in a relapse.

FLUOMIZIN contains excipients which do not dissolve completely, such that remains of the tablet are occasionally found on underwear. This will not affect the efficacy of FLUOMIZIN.

In rare cases of a very dry vagina, it is possible that the vaginal tablet does not dissolve and is discharged by the vagina as intact tablet. As consequence, the treatment is not optimal. For prevention, the vaginal tablet can be moistened with a drop of clean water before insertion into a very dry vagina.

Patients should use a sanitary towel or panty liner. The tablet will not discolour the underwear.

Women over the age of 55 years and the elderly
There is a lack of data on the efficacy and safety of FLUOMIZIN in women above 55 years of age.

Paediatric population
There is a lack of data on the efficacy and safety of FLUOMIZIN in children below 18 years of age.

Method of administration
For vaginal use.

4.3 Contraindications
- Hypersensitivity to dequalinium chloride or to any of the excipients listed in section 6.1.
- Ulceration of the vaginal epithelium and the vaginal portion of the cervix.
- Young girls who have not yet had their first menstruation, and thus did not reach sexual maturity must not use FLUOMIZIN.

4.4 Special warnings and precautions for use
To minimise exposure of the newborn to dequalinium chloride, FLUOMIZIN vaginal tablets should not be used within 12 hours before birth.

There are no efficacy and safety data available on the re-treatment of patients who did not respond to or relapsed immediately after initial therapy with FLUOMIZIN. Patients should be advised to consult their medical practitioner if the symptoms persist at the end of the treatment or in case of recurrence.

Using a higher daily dose or increasing the recommended treatment duration might increase the risk of vaginal ulcerations.

No efficacy and safety data on the treatment of bacterial vaginosis in women aged less than 18 years or more than 55 years are available.

4.5 Interaction with other medicines and other forms of interaction
Anionic substances such as soaps, detergents and surfactants can reduce the antimicrobial activity of dequalinium chloride. Thus, concomitant intravaginal use of soaps, spermicides or vaginal douches (vaginal washes) are not recommended.

FLUOMIZIN vaginal tablets do not impair the functionality of latex condoms. There are no data on the interaction with non-latex condoms and other intravaginal devices such as diaphragms. Thus, concomitant use of non-latex condoms and other intravaginal devices is not recommended for at least 12 hours following the treatment.

4.6 Fertility, pregnancy and lactation
Pregnancy
Limited data from four clinical studies in 181 pregnant patients did not suggest adverse effects on the pregnancy or on the foetus / neonate.

No reproductive toxicity studies have been conducted in animals because of the expected low systemic exposure to dequalinium chloride after vaginal administration.

FLUOMIZIN should only be used in pregnancy if clearly necessary.

Breastfeeding
Systemic exposure of the breastfeeding women to FLUOMIZIN is negligible. Therefore, no harmful effects on the breastfed newborn/infant are anticipated.
FLUOMIZIN can be used during lactation if clinically needed.

To minimise exposure of the newborn to dequalinium chloride, vaginal tablets should not be used within 12 hours before birth.

Fertility
No studies on effects on fertility have been conducted in animals.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects
The following undesirable effects possibly or probably related to dequalinum chloride (e.g. FLUOMIZIN) have been reported.
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Tabulated list of adverse reactions

System Organ Class	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1,000 to <1/100)**	**Not known (cannot be estimated from the available data)**
Infections and infestations	vaginal candidiasis	bacterial vaginitis, fungal skin infection, vulvitis, vulvovaginitis	cystitis
Nervous system disorders		headache	
Gastrointestinal disorders		nausea	
Reproductive system and breast disorders	vaginal discharge, vulvovaginal pruritus, vulvovaginal burning sensation	vaginal haemorrhage, vaginal pain	ulceration and maceration of vaginal epithelium, uterine bleeding, redness, vaginal dryness
General disorders and administration site conditions			allergic reactions with symptoms like urticaria, erythema, exanthema, swelling, rash or pruritus, fever

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/publications/index/8.

4.9 Overdose
No case of overdose has been reported. However, use of a higher daily dose might result in vaginal ulcerations. In case of overdose with adverse events, a vaginal lavage can be performed.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Gynaecological anti-infective and antiseptic, Quinoline derivatives. ATC code: G01A C05
A. 18.6 Vaginal preparations

Dequalinum chloride is an anti-infective and antiseptic medicine belonging to the class of quaternary ammonium compounds.

Mechanism of Action
Dequalinium chloride is a surface-active substance. The primary mechanism of action is an increase in bacterial cell permeability and the subsequent loss of enzyme activity, finally resulting in cell death.

Dequalinium chloride exhibits a rapid bactericidal activity.

Dequalinium chloride in vaginal tablets exerts its action locally within the vagina. Marked relief of discharge and inflammation generally occurs within 24 to 72 hours.

Pharmacokinetic/pharmacodynamics relationship
No major PK/PD determinant of efficacy has been established for dequlinium chloride. As the bactericidal effect of dequalinium chloride occurs within 30 to 60 minutes, the maximum local concentration within the first hour after application is considered crucial for the efficacy.

Mechanism(s) of resistance
The mechanisms resulting in the inherent resistance of some pathogens are not known. No mechanisms of acquired resistance have been observed thus far.

Breakpoints
No Breakpoints for dequalinium chloride are available by any recommending body and no relationship between minimal inhibitory concentrations and the clinical efficacy has been established. Thus, the information on susceptibility in the table below is descriptive and is based on the concentrations achievable in the vagina (see section 5.2) and respective MIC data of the pathogens.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the medicine in at least some types of infection is questionable.

Commonly susceptible species
Aerobic Gram-positive bacteria
Enterococcus faecalis
Lactobacillus spp.
Staphylococcus aureus
Streptococcus agalactiae (Group B streptococci)
Streptococcus pyogenes (Group A streptococci)

Aerobic Gram-negative bacteria
Enterobacter spp.
Escherichia coli
Klebsiella spp.
Pseudomonas spp.
Serratia spp.
Anaerobic bacteria
Atopobium vaginae
Bacteroides spp.
Fusobacteria
Gardnerella vaginalis
Prevotella spp.
Peptostreptococci
Poryphyromonas spp
Species for which acquired resistance may be a problem
None known
Inherently resistant organisms
Gram-negative bacteria
Proteus sp.
Chlamydia trachomatis
Other micro-organisms
Trichomonas vaginalis

5.2 Pharmacokinetic properties
After dissolution of a FLUOMIZIN vaginal tablet (10 mg dequalinium chloride) in an estimated 2,5 to 5 mL of vaginal fluid, the dequalinium chloride concentration in the vaginal fluid is 2 000 – 4 000 mg/L.

Preclinical data indicate that dequalinium chloride is absorbed only to a very small amount after vaginal application.

Therefore, systemic exposure to FLUOMIZIN is negligible and no further pharmacokinetic data are available.

5.3 Preclinical safety data
Systemic toxic effects of FLUOMIZIN are unlikely on the basis of the negligible systemic exposure of dequalinium chloride administered intravaginally.

In vivo and *in vitro* studies with dequalinium chloride did not yield any indication of a potential to cause mutagenicity.

No reproduction toxicity studies have been conducted with dequalinium chloride.

A study in rabbits showed good vaginal tolerance of FLUOMIZIN.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Microcrystalline cellulose
Lactose monohydrate
Magnesium stearate

6.2 Incompatibilities
FLUOMIZIN is incompatible with soaps and other anionic surfactants.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store at or below 30 °C.
Store in the original packaging.
Do not remove the blister from the carton until required for use.

6.5 Nature and contents of container
FLUOMIZIN vaginal tablets are packed in blisters which consists of a polymer film (PVC/PE/PVdC) with an aluminium push through foil.
FLUOMIZIN vaginal tablets are packed in units of 6 vaginal tablets per blister.
One blister of FLUOMIZIN vaginal tablets is packed into a carton box.

6.6 Special precautions for disposal and other handling
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Adcock Ingram Limited
1 New Road,
Erand Gardens,
Midrand, 1685
Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER(S)
55/18.6/0091

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
22 February 2022

10. DATE OF REVISION OF THE TEXT