APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

CLAMELLE (Capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 262 mg azithromycin dehydrate equivalent to 250 mg azithromycin.

Contains sugar: Lactose anhydrous 141,60 mg.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Capsules.

White coloured powder filled in hard, gelatine opaque capsule size “0” with blue cap and white coloured body.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the treatment of:

Adults:

- Mild to moderate infections caused by susceptible organisms. In lower respiratory tract infections including bronchitis due to *Haemophilus influenza*, *Moraxella catarrhalis, Streptococcus pneumoniae* or *Staphylococcus aureau*

and pneumoniae due to *Streptococcus pneumoniae* or *Haemophilus influenza.*

- Uncomplicated skin and soft tissue infection.
- Sinusitis due to *Haemophilus influenza, Streptococcus pneumoniae* or *Staphylococcus aereus.*
- Uncomplicated genital infections due to *Chlamydia trachomatis* in men and women with sexually transmitted diseases.

Children (5 years of age and over):

- Acute otitis media and pharyngitis/tonsillitis caused by susceptible organisms in children.

4.2. Posology and method of administration

Posology

Take the recommended dose at least 1 hour before, or 2 hours after a meal.

For sexually transmitted diseases caused by *Chlamydia trachomatis*:

- A single dose of 1 g azithromycin.

Other infections:

- Adults and children, 16 years and over: A total dose of 1,5 g which should be given as 500 mg daily for 3 days or alternatively an initial single oral dose of 500 mg on day 1, then 250 mg as a single daily dose for 4 days.

Special populations

Elderly persons: The normal adult dosage is recommended.

Paediatric population

Children, 45 kg and over: Dose as for adults.

Method of administration

For oral administration.

4.3. Contraindications

- Hypersensitivity to azithromycin, erythromycin, or any of the macrolide antibiotics.
- Co-administration with ergot alkaloids.
- Hepatic impairment - since biliary excretion is the major route of elimination.
- Pregnancy and lactation: the safety in pregnancy and lactation has not been established (see section 4.6).

4.4. Special warnings and precautions for use

- Serious allergic reactions such as anaphylaxis angioedema, fever, eosinophilia, and skin eruptions have rarely been reported. Despite discontinuation of CLAMELLE and successful symptomatic treatment of the allergic reactions, allergic symptoms have recurred in some patients when the symptomatic therapy was discontinued. These patients may require prolonged periods of observation and symptomatic treatment.
- Pseudomembranous colitis has been reported and may range in severity from mild to life threatening. It is important to consider the possibility of pseudomembranous colitis in patients that develop diarrhoea subsequent to the administration of azithromycin.
- Signs of super-infection of non-susceptible organisms should be observed.
- Caution should be used when CLAMELLE is prescribed for patients with

renal impairment, as no data regarding the use of azithromycin in these patients is available.

- Ergotism is theoretically possible therefore CLAMELLE should not be administered with ergot derivates.
- CLAMELLE contains lactose (as lactose anhydrous). Patients with the rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take CLAMELLE.

4.5. Interaction with other medicines and other forms of interaction

Antacids:

As the concurrent use of aluminium and magnesium-containing antacids decrease the peak serum concentration of azithromycin, it is advisable that azithromycin be administered at least 1 hour before or 2 hours after taking the antacids.

Cimetidine:

No effect on the pharmacokinetics of azithromycin was observed after the administration of a single dose of cimetidine two hours prior to the administration of CLAMELLE capsules.

Methylprednisolone:

No significant evidence of any interaction was observed, when administered with azithromycin.

Zidovudine:

No significant effects on the pharmacokinetic parameters of zidovudine and its glucuronide metabolite were found in the preliminary studies of HIV-positive patients. A shortening in the time to reach maximal concentration when the first and the last

day levels were compared, was found in the pharmacokinetics of azithromycin.

Ergot alkaloids:

Ergot alkaloids has been associated with acute ergot toxicity characterised by severe peripheral vasospasm and dysesthesia. Co-administration of CLAMELLE and ergot alkaloids is not recommended (see section 4.3).

General:

Azithromycin may potentiate the effects of astemizole, carbamazepine, corticosteroids, cyclosporine, digoxin (may increase serum digoxin concentrations, therefore monitoring of digoxin serum concentrations is recommended), terfenadine (may increase serum concentration of terfenadine, therefore monitoring of serum levels of terfenadine is recommended), theophylline (the area under the plasma concentration–time curve may be increased, therefore monitoring of theophylline serum concentrations is recommended), triazolam, valproate and warfarin (prothrombin time should be monitored) by the possible interference with cytochrome P450-mediated metabolism of these medicines.

4.6. Fertility, pregnancy and lactation

Pregnancy and lactation: the safety in pregnancy and lactation has not been established. CLAMELLE is contra-indicated during pregnancy and breastfeeding (see section 4.3).

Fertility: No data on fertility is available.

4.7. Effects on ability to drive and use machines

No data are available regarding the influence of CLAMELLE on a patient's ability to drive or operate machinery. However, the possibility of undesirable effects like

dizziness, somnolence, fatigue, and convulsions should be considered when performing these activities (see section 4.8).

Patients are therefore advised not to drive or use machinery or engage in other activities requiring mental alertness and coordination until they have established how CLAMELLE affects them.

4.8. Undesirable effects

a. Summary of the safety profile

Use of CLAMELLE may cause an overgrowth of non-susceptible organisms. Appropriate measures should be taken to prevent or treat such superinfection.

b. Tabulated summary of adverse reactions

The adverse reactions are listed below according to system organ class.

MedDRA system organ class	**Frequency**	**Adverse reactions**
Infections and infestations	Frequency unknown	Vaginitis.
Blood and lymphatic system disorders	Frequent	Neutropoenia.
Immune system disorders	Less frequent	[1]Anaphylaxis and angioedema.
Nervous system disorders	Frequent	Headache, dizziness, tinnitus, hearing loss, convulsions, somnolence, vertigo, fatigue, asthenia, paraesthesia.
Ear and labyrinth disorders	Frequency unknown	[2]Transient auditory impairment.

Cardiac disorders	Less Frequent	Palpitations, arrhythmias including ventricular tachycardia, chest pain.
Gastrointestinal disorders	Frequent	Nausea, anorexia, vomiting, abdominal pain, flatulence, diarrhoea, loose stools, constipation, dyspepsia, melaena, taste changes.
	Less frequent	Pseudomembranous colitis (abdominal cramps or pain, tenderness, severe, watery diarrhoea which may also be bloody, fever).
Skin and subcutaneous tissue disorders	Less frequent	Erythema multiforme, Steven's-Johnson syndrome, toxic epidermal necrolysis.
	Frequency unknown	Photosensitivity.
Hepatobiliary disorders	Less frequent	Cholestatic jaundice, hepatitis, transient elevations in liver enzymes (elevated liver transaminases and bilirubin values).
Renal and urinary disorders	Less frequent	Acute interstitial nephritis: fever, skin rash and painful joints.

c. Description of selected adverse reaction

[1]Serious allergic reactions such as anaphylaxis and angioedema have rarely been

reported. These patients may require prolonged periods of observation and symptomatic treatment.

[2]Transient auditory impairment is a potential complication when higher doses of azithromycin are used for prolonged periods of time.

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. Health care 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

There is no data on overdosage with azithromycin.

Typical symptoms may include nausea, vomiting and diarrhoea. Transient hearing loss may occur. Gastric lavage is indicated. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacological classification: A 20.1.1 Broad and medium spectrum antibiotics.

Pharmacotherapeutic group: Antibacterials for systemic use; macrolides; azithromycin, ATC code: J01FA10

Mechanism of action:

Azithromycin is a macrolide antibiotic with bactericidal activity. These agents inhibit protein synthesis by binding reversibly to 50 S ribosomal subunits of sensitive micro-

organisms.

Azithromycin demonstrates activity *in vitro* against a wide range of gram-negative and gram-positive organisms such as: *H. influenza, M. catarrhalis, Chlamydia spp., Mycoplasma pneumoniae, B. Burgdoferi, Campylobacter spp., Pasteurella multocisa, L. pneumophila* and *Fusobacterium* spp.

Azithromycin is also active against the protozoan *Toxoplasma gondii,* enterobacteriaceae such as *Escherichia coli, Salmonella and Shigella* spp and *Staphylococcus aureus, Chlamydia tragomatis* and *S. epidermis. Haemophilis ducreyi, Streptococcus pneumoniae, Streptococcus pyogenes* and other species, also *Treponema pallidum.*

In vitro activity does not necessarily imply *in vivo* efficacy.

5.2. Pharmacokinetic properties

Absorption:

Absorbed rapidly and distributed throughout the body, except the cerebrospinal fluid. Peak plasma concentration is achieved 2 – 3 hours after the initial dose. The bioavailability of azithromycin is significantly reduced by food (by up to 43 %).

Elimination:

Only 6 % is excreted unchanged in the urine.

The major route of elimination is through biliary excretion.

The elimination half-life may be up to 68 hours because of the extensive tissue distribution.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Capsule content:

Colloidal Silicon Dioxide.

Lactose anhydrous.

Magnesium stearate.

Maize Starch.

Sodium Lauryl Sulphate.

Capsule shell:

Gelatine (Cap & Body).

Blue Cap: Brilliant Blue (C. I. No. 42090); Titanium Dioxide (C.I. No. 77891); Methyl Paraben; and Propyl Paraben.

White Body: Titanium Dioxide (C.I. No. 77891); Methyl Paraben; and Propyl Paraben.

6.2. Incompatibilities

None known.

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store below 25 °C in well-closed container.

6.5. Nature and contents of container

Blister strips of 4 or 6 capsules.

7. HOLDER OF CERTIFICATE OF REGISTRATION

STRIDES PHARMA (SA) (Pty) LTD

106 16th Road

Building 2

Midrand

South Africa

8. REGISTRATION NUMBER(S)

33/20.1.1/0269

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28 August 2001

10. DATE OF REVISION OF THE TEXT

21 April 2023