PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

LYMECYCLINE ACTIVO hard capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each LYMECYCLINE ACTIVO hard capsule contains 408 mg lymecycline equivalent to 300 mg tetracycline base.

LYMECYCLINE ACTIVO is sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsules.

A size 0 capsule with a blue cap and a white body.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LYMECYCLINE ACTIVO is indicated for the treatment of infections caused by susceptible strains of pathogens:

Upper and lower respiratory tract infections:

Sinusitis, pharyngitis, Mycoplasma pneumoniae, psittacosis and chronic bronchitis.

Genito-urinary tract infections:

Non-specific urethritis (only if the strain is sensitive), lymphogranuloma venereum, chancroid and granuloma inguinale, gonococcal salpingitis, epididymitis, acute epididymo-orchitis, endocervical infections, syphilis and gonorrhoea (in cases of penicillin allergy).

Soft tissue infections:

Acne.

Ophthalmic infections:

Trachoma and inclusion conjunctivitis.

Intestinal infections:

Cholera, Whipple's disease and tropical sprue.

Miscellaneous infections:

Rickettsial infections, brucellosis, tularemia, actinomycosis, Lyme disease, yaws, relapsing fever, leptospirosis during the early infective phase.

It is effective *in-vitro* against gram-positive and gram-negative organisms (*in-vitro* activity does not necessarily imply *in-vivo* efficacy), including:

Vibrio cholerae, Ureaplasma urealyticum, Mycoplasma pneumoniae, Chlamydia trachomatis, Chlamydia psittaci, Borrelia recurrentis, Calyminatobacterium granulomatis, Borrelia burgdorferi, penicillin sensitive Neisseria gonorrhoea and *Rickettsiae*.

Lymecycline is also effective against the following organisms *in-vitro*:
Haemophilus ducreyi, Actinomyces israelii, Francisella tularensis and *Treponema pertenue*.

4.2 Posology and method of administration

Posology

Adults:

The recommended dose for acne is 300 mg/day with a usual treatment duration of 12 weeks.

The usual dose for indications other than acne is 300 mg every 12 hours (depending on the severity of infection).

The maximum dose of LYMECYCLINE ACTIVO should not exceed 3 g daily for adults and 50 mg/kg body mass per day for children.

Special populations

Elderly

No specific dose adjustment is required.

Paediatric population

The safety and efficacy in children younger than 12 years of age have not been established.

Method of administration

Capsules should be taken either one hour before meals or two hours after meals with adequate liquid to avoid lodging of capsules in the distal oesophagus resulting in local corrosive irritation and ulceration.

4.3 Contraindications

LYMECYCLINE ACTIVO is contraindicated in:

- patients with hypersensitivity to lymecycline, any other tetracyclines or any of the other excipients listed is section 6.1.
- patients with impaired renal function.
- children under the age of 12 years due to the risk of permanent discolouration of teeth and enamel hypoplasia.
- patients with systemic lupus erythematosus.
- patients on concurrent treatment with oral retinoids (see sections 4.5).
- pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

Prescribers must abide by the principles of antibiotic stewardship.

Impaired renal or liver function

LYMECYCLINE ACTIVO is contraindicated for use in patients with impaired renal function (see section 4.3). Increased severity of uraemia and hepatotoxicity have been found in patients with renal disease given high doses.

Caution should be exercised if LYMECYCLINE ACTIVO is administered to patients with liver-function impairment.

Oesophageal irritation and ulceration

Solid dosage forms of tetracyclines, as contained in LYMECYCLINE ACTIVO, may cause oesophageal irritation and ulceration. To avoid oesophageal irritation and ulceration, LYMECYCLINE ACTIVO should be taken with adequate fluids (water) (see section 4.2).

Hepatotoxicity

Overdosage could result in hepatotoxicity.

Frail or elderly patients are susceptible to hepatotoxic medicines and the anti-anabolic effects of tetracyclines.

Do not use LYMECYCLINE ACTIVO in combination with hepatotoxic medicines.

Antibiotic resistance

Prescribers must adhere to the principles of antibiotic stewardship.

Prolonged use of broad spectrum antibiotics may result in the appearance of resistant organisms and superinfection (see section 4.8).

Phototoxicity

Photosensitivity of the skin and nails may occur (see section 4.8). Due to the risks of photosensitivity, it is recommended to avoid exposure to direct sunlight and ultraviolet light for the duration of treatment. Treatment should be discontinued if erythematous cutaneous manifestations occur.

Expired medication

The use of expired tetracyclines, like LYMECYCLINE ACTIVO, may lead to a Fanconi-type syndrome renal tubular acidosis (Pseudo-Fanconi syndrome) which is characterised by polyuria and polydipsia with nausea, vomiting, proteinuria, glucosuria, acidosis, aminoaciduria, hypophosphatemia and hypocalcaemia. This is readily reversible upon treatment discontinuation.

Systemic lupus erythematosus

Treatment with LYMECYCLINE ACTIVO may cause exacerbations of systemic lupus erythematosus (see section 4.3).

Myasthenia Gravis

LYMECYCLINE ACTIVO should be used with caution in Myasthenia Gravis, as it can cause weak neuromuscular blockade, which may aggravate the symptoms associated with this condition.

Jarisch-Herxheimer-like reaction

A Jarisch-Herxheimer-like reaction has been reported in patients with relapsing fever treated with tetracyclines.

Vitamin deficiencies

Vitamin deficiencies may occur with prolonged use of LYMECYCLINE ACTIVO.

Special Population

Elderly

A negative nitrogen balance may be induced with lymecycline, as contained in LYMECYCLINE ACTIVO, in elderly patients.

Paediatric population

Use in children under the age of 12 years is not recommended due to the risk of permanent dental staining and enamel hypoplasia (see section 4.3).

Raised intracranial pressure may occur, particularly in infants, and especially if LYMECYCLINE ACTIVO is used concurrently with Vitamin A or other retinoids (see sections 4.3 and 4.5).

4.5 Interaction with other medicines and other forms of interaction

The risk of benign intracranial hypertension may be increased by the concurrent use of LYMECYCLINE ACTIVO with oral retinoids and Vitamin A (above 10 000 IU/day). This combination must be avoided (see section 4.3).

Simultaneous administration of iron preparations or preparations containing magnesium, aluminium and calcium hydroxides, sodium bicarbonate, oxides, salts, cholestyramine, bismuth chelates, sucralfate and quinapril may decrease the absorption of lymecycline, as contained in LYMECYCLINE ACTIVO. Patients should therefore not

receive antacid therapy or milk concomitantly. Enzyme inducers such as barbiturates, carbamazepine and phenytoin may accelerate the decomposition of tetracycline due to enzyme induction in the liver thereby decreasing its half-life. These products should not be taken within two hours before or two hours after taking LYMECYCLINE ACTIVO.

An increase in the effects of anticoagulants may occur with concurrent tetracycline use, resulting in an increased risk of haemorrhage. Doses of anticoagulants may need to be reduced if used simultaneously.

Concurrent use with diuretics should be avoided.

Medicines containing penicillin and beta-lactams should not be used concurrently with tetracyclines, as contained in LYMECYCLINE ACTIVO, as an antagonistic effect may occur.

The interaction between lithium and the tetracycline class is a recognised one and adverse effects have been reported with tetracycline therapy in general when used simultaneously with lithium. The concurrent use of lymecycline, as contained in LYMECYCLINE ACTIVO, with lithium may cause an increase in serum lithium levels.

LYMECYCLINE ACTIVO may decrease the effectiveness of oral contraceptives.

Serious nephrotoxicity may occur with concurrent use of LYMECYCLINE ACTIVO with methoxyflurane.

Paediatric population

There are no data available from interaction studies in this population group.

4.6 Fertility, pregnancy and lactation

Pregnancy

Lymecycline crosses the placental barrier and is deposited in foetal bones and teeth. Pregnant women are at an increased risk of developing severe tetracycline-induced liver damage. LYMECYCLINE ACTIVO should not be used by pregnant women (see section 4.3).

Breastfeeding

Lymecycline is readily excreted into breast milk. LYMECYCLINE ACTIVO should not be administered to breastfeeding women (due to the risk of enamel hypoplasia or dental dyschromia in the infant) (see section 4.3).

Fertility

No data on the effect on fertility are available.

4.7 Effects on ability to drive and use machines

The effect of lymecycline, as contained in LYMECYCLINE ACTIVO, on the ability to drive and use machines is determined by the adverse effects such as visual disturbances and dizziness (see section 4.8). Patients should establish the effect of adverse effects before they drive or use machines.

4.8 Undesirable effects

Summary of safety profile

The most frequently reported adverse events are gastrointestinal disorders of nausea, abdominal pain, diarrhoea and nervous system disorder of headache. The most serious adverse events reported are Stevens-Johnson syndrome, anaphylactic reaction, angioedema and intracranial hypertension.

List of adverse reactions

Blood and lymphatic system disorders

Frequency unknown: haemolyic anaemia, eosinophilia, neutropenia and thrombocytopenia.

Immune system disorders

Frequency unknown: anaphylactic reaction, hypersensitivity, urticaria and angioedema.

Psychiatric disorders

Frequency unknown: depression and nightmare.

Nervous system disorders

Frequent: headache.*

Frequency unknown: dizziness and intracranial hypertension.

Eye disorders

Frequency unknown: visual disturbance.*

Gastrointestinal disorders

Frequent: nausea, abdominal pain and diarrhoea.

Frequency unknown: epigastralgia (gastrointestinal pain upper), glossitis, vomiting and enterocolitis.

Hepato-biliary disorders

Frequency unknown: jaundice and hepatitis.

Skin and subcutaneous tissues disorders

Frequency unknown: erythematous rash, photosensitivity of the skin and nails, pruritus, Stevens-Johnson syndrome, nail discolouration and oncholysis.

General disorders and administration site conditions

Frequency unknown: pyrexia.

Investigations

Frequency unknown: transaminases increased, blood alkaline phosphatase increased and blood bilirubin increased.

Description of selected adverse reactions

* *Increased intracranial pressure*

The manifestation of clinical symptoms, including vision disorders, or headache, may be indicative of the possibility of a cranial hypertension diagnosis. If increased intracranial pressure is suspected during treatment with LYMECYCLINE ACTIVO, treatment should be discontinued.

Benign intracranial hypertension and bulging fontanelles in infants have been reported with tetracyclines, as contained in LYMECYCLINE ACTIVO, with possible symptoms of headaches, vomiting, visual disturbances including blurring of vision, scotomata, diplopia or permanent visual loss.

Symptoms resulting from the overgrowth of non-susceptible organisms

Overgrowth of non-susceptible organisms may cause candidiasis, pseudomembranous colitis (*Clostridium difficile* overgrowth), glossitis, stomatitis, vaginitis or staphylococcal enterocolitis. Overgrowth of *Candida albicans* in the mouth causes soreness, redness and thrush, which may extend into the bronchi and trachea; overgrowth of *C. albicans* in the bowel results in pruritis ani and vulvovaginitis and there may be overgrowth of resistant coliform organisms, such as *Pseudomonas* species and *Proteus* species, causing diarrhoea. Colitis due to *Clostridium difficile* may occur. Super-infection due to resistant *staphylococci* may cause fulminating enteritis.

Allergic (hypersensitivity) reactions

Allergic reactions to lymecycline, as contained in LYMECYCLINE ACTIVO, and its analogues have been reported.

Cross-sensitisation is common. Symptoms include maculopapular rashes, exfoliative dermatitis, exacerbation of systemic lupus erythematosus, pericarditis and Henoch-Schönlein purpura (anaphylactoid purpura).

Tetracyclines class adverse effects

The following adverse effects were reported with tetracyclines in general and may occur with LYMECYCLINE ACTIVO: dysphagia, oesophagitis, oesophageal ulceration,

systemic lupus erythematosus, pancreatitis, teeth discolouration, hepatitis and hepatic failure. Dental dyschromia and/or enamel hypoplasia may occur if administered to children younger than 12 years of age.

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

If idiosyncrasy or adverse reactions occur, discontinue the use of LYMECYCLINE ACTIVO.

There is no specific treatment for overdosage. Treatment should be supportive and symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological Classification: A 20.1.1 – Broad and medium spectrum antibiotics.

Pharmacotherapeutic group: Tetracyclines.

ATC code: J01AA04.

Mechanism of action

Lymecycline is a bacteriostatic antibiotic which acts by inhibiting bacterial growth by binding to 30S ribosomal sub unit with consequent misreading of information for protein synthesis.

Resistant pathogens:

Many of the following strains are resistant*: Staphylococci, Enterococci, Proteus vulgaris,* Fungi and Yeasts *(except Actinomyces), Pseudomonas aeruginosa* (all strains), *E. coli, Shigella* and *Streptococcus*.

5.2 Pharmacokinetic properties

Absorption

The absorption of lymecycline from the gastrointestinal tract is incomplete, however it is more readily absorbed compared to tetracycline. Effective blood levels are achieved within 2 – 4 hours following oral administration and are maintained with the recommended dosages.

Distribution

Lymecycline is distributed into pleural and peritoneal fluid, prostatic fluid, saliva and semen. It passes through the placental barrier (amniotic fluid) and is present in the milk of lactating women.

Biotransformation and elimination

Lymecycline is concentrated by the liver and excreted into the bile via entero-hepatic circulation. Enterohepatic circulation is an important step in the metabolic pathway.

Excretion in the urine is via glomerular filtration. The plasma half-life of lymecycline is approximately 10 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate.

Colloidal hydrated silica.

The gelatine capsules are composed of: black iron oxide (E172), gelatine, indigo carmine FD&C blue (E132), titanium dioxide (E171) and yellow iron oxide (E172).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

15 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Store in original packaging.

6.5 Nature and contents of container

Aluminium (Al/OPA/PVC) / Aluminium blister strips containing 7, 14 or 28 hard capsules packed in an outer unit carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Activo Health (Pty) Ltd

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272 West Avenue

Centurion

0157

South Africa

8. REGISTRATION NUMBER(S)

57/20.1.1/0408

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24 June 2025

10. DATE OF REVISION OF THE TEXT