

Applicant/PHCR: Galderma Laboratories South Africa (Pty) Ltd

Product proprietary name: Tetralysal® 300 mg

Registration no: E/20.1.1/67

Dosage form and strength: Each capsule contains Lymecycline equivalent to 300 mg Tetracycline Base

PACKAGE INSERT

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE

TETRALYSAL® 150 mg Capsules

TETRALYSAL® 300 mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TETRALYSAL® 150 mg: Each capsule contains Lymecycline equivalent to 150 mg Tetracycline Base.

TETRALYSAL® 300 mg: Each capsule contains Lymecycline equivalent to 300 mg Tetracycline base.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule

TETRALYSAL® 150 mg: Hard gelatin capsule, orange cap yellow body containing a granular yellow powder.

TETRALYSAL® 300 mg: Hard gelatin capsule, red cap yellow body containing a granular yellow powder.

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4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

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.

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4.2 Posology and method of administration

Adults:

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

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

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

Elderly

As for other tetracyclines, no specific dose adjustment is required.

Paediatric population:

The safety and efficacy of **TETRALYSAL®** in children aged under 12 years of age have not been established.

Methods of administration:

The 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 as this may result in local corrosive irritation and ulceration.

4.3 Contraindications

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Hypersensitivity to lymecycline or any other tetracyclines or to any of the excipients listed in section 6.1.

In patients with impaired renal function.

Should not be given to children younger than 12 years of age as permanent discolouration of the child's teeth and enamel hypoplasia may occur.

Should not be given to patients with systemic lupus erythematosus.

Concurrent treatment with oral retinoids (see Interaction with other Medications).

Pregnancy and breastfeeding

4.4 Special warnings and precautions for use

Use with care in patients with renal or liver function impairment.

Oesophageal irritation and ulceration

Solid dosage forms of the tetracyclines may cause oesophageal irritation and ulceration. To avoid oesophageal irritation and ulceration, adequate fluids (water) should be taken with **TETRALYSAL®** (see 'Posology and method of administration').

Hepatotoxicity

Overdosage could result in hepatotoxicity.

Frail or elderly patients are susceptible to hepatotoxic medicines and antianabolic effects of tetracyclines.

Do not use concomitantly with hepatotoxic medicines.

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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.

Phototoxicity

Photosensitivity may occur (see section 4.8 “Undesirable Effects”). Due to the risks of photosensitivity, it is recommended to avoid exposure to direct sunlight and ultraviolet light during the treatment which should be discontinued if erythematous cutaneous manifestations occur.

Expired medication

The use of expired tetracyclines 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, readily reversible when treatment is discontinued altogether.

Systemic lupus erythematosus

May cause exacerbations of systemic lupus erythematosus (see Section 4.3)

Myasthenia Gravis

Symptoms of Myasthenia gravis may be aggravated

Paediatric population

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Use in children under the age of 12 years is contraindicated 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 Vitamin A or other retinoids are given concomitantly.

4.5 Interaction with other medicinal products and other forms of interaction

Preparations containing sodium bicarbonate and iron, magnesium/aluminium and calcium hydroxides, oxides, salts, cholestyramine, bismuth chelate, sucralfate and quinapril may decrease the absorption of lymecycline. Patients should therefore not receive antacid therapy or milk concomitantly. Enzyme inducers such as barbiturates, carbamazepine, 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 after taking **TETRALYSAL®**.

Concomitant use of oral retinoids and vitamin A (above 10 000 IU/day) should be avoided as this may increase the risk of benign intracranial hypertension.

Doses of anticoagulants may need to be reduced if given concomitantly.

Concomitant use of diuretics should be avoided.

Penicillin and beta-lactam antibiotics should not be given concomitantly with tetracyclines as antagonism may occur.

Tetracyclines may diminish the effectiveness of oral contraceptives.

Fatal renal toxicity may follow the concomitant use with methoxyflurane

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Concomitant use of lithium may cause an increase in serum lithium levels

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

TETRALYSAL® should not be used by pregnant or breastfeeding women.

Pregnancy

Lymecycline crosses the placenta and is deposited in foetal bones and teeth.

Pregnant women are particularly susceptible to severe tetracycline-induced liver damage.

Breastfeeding

Lymecycline is readily excreted into breast milk.

Fertility

No data on the effect on fertility is available.

4.7 Effects on ability to drive and use machines

TETRALYSAL® is not known to affect the ability to drive or use machines

4.8 Undesirable effects

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Tabulated list of adverse reactions

The most frequently reported adverse events with **TETRALYSAL®** are gastrointestinal disorders of nausea, abdominal pain, diarrhoea and nervous system disorder of headache. The most serious adverse events reported with **TETRALYSAL®** are Stevens Johnson syndrome, anaphylactic reaction, angioneurotic oedema and intracranial hypertension.

System Organ Class	Frequency	Adverse Reaction
Blood and lymphatic system disorders	Unknown	Haemolytic anaemia Eosinophilia Neutropenia Thrombocytopenia
Eye disorders	Unknown	Visual disturbance
Gastrointestinal disorders	Common (≥1/100 and <1/10)	Nausea Abdominal pain Diarrhoea
	Unknown	Epigastralgia (gastrointestinal pain upper) Glossitis Vomiting Enterocolitis
General disorders and administration site conditions	Unknown	Pyrexia
Hepatobiliary disorders	Unknown	Jaundice Hepatitis

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Immune system disorder	Unknown	Anaphylactic reaction Hypersensitivity Urticaria Angioneurotic oedema
Investigations	Unknown	Transaminases increased Blood alkaline phosphatase increased Blood bilirubin increased
Nervous system disorders	Common ($\geq 1/100$ and $< 1/10$)	Headache
	Unknown	Dizziness Intracranial hypertension
Skin and subcutaneous tissues disorders	Unknown	Erythematous rash Photosensitivity Pruritus Stevens Johnson syndrome
Psychiatric disorders	Unknown	Depression Nightmare

Description of selected adverse reactions

Symptoms resulting from the overgrowth of non-susceptible organisms:

Overgrowth of *Candida albicans* in the mouth causes soreness, redness and thrush which may extend into the trachea and bronchi; overgrowth of *C. albicans* in the bowel results in pruritis ani and vulvovaginitis and there may be overgrowth of resistant coliform organisms, such as

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Pseudomonas spp. and *Proteus* spp., 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 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).

Photosensitivity of the skin and nails; onycholysis and nail discolouration may occur.

Increased severity of uraemia and hepatotoxicity in patients with renal disease given high doses.

Vitamin deficiencies may result during prolonged administration.

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

In the elderly a negative nitrogen balance may be induced.

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 professionals are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications:

<http://www.sahpra.org.za/Publications/Index/8>

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4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity. (See Section 4.8 “Undesirable effects”.)

If adverse reactions or idiosyncrasy occurs, discontinue medication.

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Tetracyclines

ATC code: J01AA04

Mode of action

Lymecycline is a bacteriostatic antibiotic which inhibits bacterial growth by binding to 30S ribosomal subunit with consequent misreading of information for protein synthesis. It is effective *in-vitro* against the following gram-positive and gram-negative organisms (*in-vitro* activity does not necessarily imply *in-vivo* efficacy):

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

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Lyme cycline is also effective against the following organisms in-vitro:

Haemophilus ducreyi, Actinomyces israelii, Francisella tularensis, Treponema pertenu.

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, Streptococcus.*

5.2 Pharmacokinetic properties

Lyme cycline is incompletely absorbed from the intestinal tract. Effective blood levels are reached in about two to four hours after oral administration and are maintained with the recommended dosages.

Lyme cycline is distributed into pleural and peritoneal fluid, saliva, semen and prostatic fluid. It passes the placental barrier readily (amniotic fluid) and is also present in milk of lactating patients. It is concentrated by the liver and excreted into the bile. Enterohepatic circulation is an important step in the metabolic pathway. Excretion in the urine is by glomerular filtration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

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TETRALYSAL® 150 mg: Magnesium stearate, colloidal hydrated silica, maize starch, lactose monohydrate.

Gelatin capsule is composed of gelatin, erythrosin colour (E127), quinoline yellow (E104) and titanium dioxide (E171).

TETRALYSAL® 300 mg: Magnesium stearate, colloidal hydrated silica.

Gelatin capsule is composed of gelatin, erythrosin colour (E127), indigo carmine colour (E132), quinoline yellow (E104) and titanium dioxide (E171).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in a cool dry place at or below 25 °C.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container:

TETRALYSAL® 150 mg and 300 mg: Blister packs containing 28 capsules, packed in a carton.

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7. HOLDER OF THE CERTIFICATE OF REGISTRATION:

Galderma Laboratories South Africa (Pty) Ltd

Nicol Main Office Park,

Block C First Floor,

FutureSpace,

2 Bruton Road,

Bryanston,

2191

8. REGISTRATION NUMBER

TETRALYSAL® 150 mg: A549 (Act 101/1965)

TETRALYSAL® 300 mg: E/20.1.1/67

9. DATE OF FIRST AUTHORISATION

TETRALYSAL® 150 mg and 300 mg: March 1995

10. DATE OF REVISION OF THE TEXT

21 September 2022