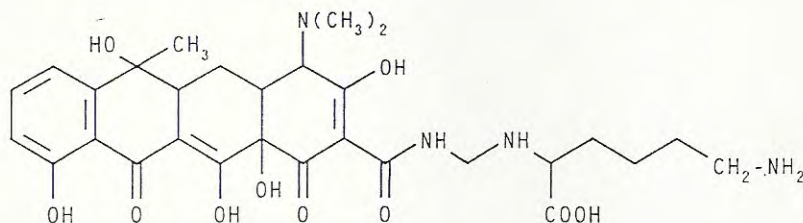


1. GENERAL DESCRIPTION

Tetralysal 150 is available as orange and yellow hard gelatine capsules (size 1) containing a quantity of lymecycline equivalent to 150 mg of tetracycline base as the active ingredient in a mixture of magnesium stearate (lubricant), levilite (lubricant), maize starch (disintegrating agent) and lactose (diluant). Lymecycline whose structural formula is reproduced below, is a water-soluble combination of tetracycline, lysine and formaldehyde.



2. PROPERTIES

2.1 Pharmacological Properties

Lymecycline is an antibiotic belonging to the tetracycline family (group of the semi-synthetic cyclines).

Antibacterial activity: the natural antibacterial spectrum of lymecycline is that of cyclines:

- Sensitive species: *Brucella*, *Pasteurella*, *Chlamydiae*, *Propionibacterium acnes*, *Gonococci*, *Haemophilus*, *Leptospira*, *Mycoplasma pneumoniae*, *Ureaplasma urealyticum*, *Rickettsiae*, *Treponema pallidum*, *Vibrio cholerae*.
- Species with variable sensitivity (10 to 40% resistant strains): Anaerobic organisms (*Clostridium*, *Bacteroides*, *Fusobacterium*), *Escherichia coli*, *Klebsiella*, *Legionella pneumophila*, *Pneumococci*, *Proteus morgani*, *Shigella*, *Staphylococci*, *Streptococci* groups A, C and G.
- Resistant species (MIC \geq 16 mg/L): *Enterobacter*, *Mycobacterium tuberculosis*, *Proteus rettgeri*, *Providencia*, *Pseudomonas*, *Serratia*, *Streptococci* groups B and D.

Effects on acne: The exact mechanisms by which tetracyclines reduce lesions of *acne vulgaris* have not been fully elucidated; however, the effect appears to result in part from the antibacterial activity of the drugs. Following oral administration, the drugs inhibit the growth of susceptible organisms (mainly *Propionibacterium acnes*) on the surface of the skin and reduce the concentration of free fatty acids in sebum. The reduction in free fatty acids in sebum may be an indirect result of the inhibition of lipase-producing organisms which convert triglycerides into free fatty acids or may be a direct result of interference with lipase production in these organisms. Free fatty acids are comedogenic and are believed to be a possible cause of the inflammatory lesions, e.g. papules, pustules, nodules, cysts, of acne. However, other mechanisms also appear to be involved because clinical improvement of *acne vulgaris* with oral tetracycline therapy does not necessarily correspond with a reduction in the bacterial flora of the skin or a decrease in the free fatty acid content of sebum.

2.2 Pharmacokinetic Properties

Absorption: Absorption is rapid, effective plasma levels are reached within the first hour following drug intake. The peak plasma level is reached within 3 to 4 hours after oral administration. Concurrent food intake, milk in particular, does not significantly modify the absorption of lymecycline.

Distribution: Oral administration of 300 mg, in the adult, gives rise to:

- a peak plasma level of 1.6 to 4 µg/mL,
- a highly variable residual concentration (0.29 to 2.19 µg/mL),
- a plasma half-life of approximately 10 hours.

Repeated administration results in a steady mean plasma concentration between 2.3 and 5.8 µg/mL.

Wide intra- and extra-cellular diffusion, under normal dosage conditions, results in effective concentrations in most body tissues and fluids, and notably in the lungs, bones, muscles, liver, bladder, prostate, bile and urine.

Excretion/elimination: The product is principally excreted in urine and secondarily in the bile. About 65% of the administered dose are eliminated within 48 hours.

3. THERAPEUTIC INDICATIONS

The therapeutic indications of **Tetralysal 150** are derived from the antibacterial and pharmacokinetic properties of lymecycline. They take into account the place of this antibiotic within all antimicrobial agents available as well as the current knowledge of lymecycline-resistant organisms. The product should be reserved for the treatment of *Brucella* infection, *Pasteurellae* infection, pulmonary, genito-urinary and ophthalmologic infections to *Chlamydiae*, pulmonary and genito-urinary infections to *Mycoplasmae*, *Rickettsiae* infection, *Coxella burnetti* (Q fever), *Gonococci* infection, respiratory, broncho-pulmonary infections to *Haemophilus influenzae*, particularly when there is an acute exacerbation of chronic bronchitis, *Treponema* (tetracyclines are indicated in syphilis only when the patient is allergic to β lactamines), *Spirochetes* (Lyme disease, leptospirosis), cholera, acne (cutaneous manifestations in relation with *Propionibacterium acnes*).

4. CONTRAINDICATIONS

- Patients hypersensitive to tetracyclines.
- The use of this product is to be avoided in children under 8 years of age due to the risk of permanent dental staining and enamel hypoplasia.
- Concurrent treatment with retinoides (see *Interaction with other Medications*).

Pregnancy and Lactation: Tetracyclines readily cross the placental barrier and are distributed into milk. Therefore, **Tetralysal 150** should not be administered to pregnant or breast-feeding women (risk of enamel hypoplasia or dental staining in the infant).

5. PRECAUTIONS

- Caution should be exercised if the product is administered to patients with impaired renal or hepatic functions.
- Overdosage could result in hepatotoxicity.
- 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.
- The use of expired tetracyclines can lead to renal tubular acidosis readily reversible when treatment is discontinued altogether.

6 INTERACTION WITH OTHER MEDICATIONS AND OTHER FORMS OF INTERACTION

- Retinoids: risk of intracranial hypertension.
- Simultaneous administration of iron preparations and antacids such as aluminium hydroxide may decrease cycline absorption. Consequently, a minimum 2-hour gap is necessary between the two treatments.

Laboratory test interferences: Lymecycline could cause false-positive urine glucose determinations (Benedict's reagent, Clinitest®). It could also interfere with fluorometric determinations of urine catecholamines resulting in falsely increased values (Hingerty's method).

7. ADVERSE REACTIONS

- Discoloration of the permanent teeth and/or enamel hypoplasia may occur if the product is administered in children younger than 8 years of age.
- Gastro-intestinal disturbances (nausea, epigastric burning and distress, diarrhoea, glossitis, enterocolitis).
- Hypersensitivity reactions (urticaria, erythematous rash, pruritus, Quincke's oedema).
- Photosensitivity reactions.
- Hemolytic anaemia, thrombocytopenia, neutropenia eosinophilia and other hematologic disorders have been reported with tetracycline therapy.
- Extra-renal hypernatremia linked to an antibiotic effect which may be intensified by the association with diuretics has been reported with tetracycline therapy.

8. OVERDOSAGE

Acute overdosage is rare with antibiotics and there is no specific treatment. Should this happen gastric emptying should be considered. Supportive measures should be instituted as required and a high fluid intake maintained.

9. DOSAGE AND ADMINISTRATION

The usual recommended dose for indications other than acne in the adult is 600 mg/day (4 capsules). The recommended dose for acne is 300 mg/day for 15 days (2 capsules), then 150 mg/day (1 capsule) or 300 mg every other day (2 capsules) for maintenance therapy.

10. PRODUCT PRESENTATION

The product is supplied in carton boxes containing two blister strips of 8 capsules (16 capsules).

11. STORAGE

Tetralysal 150 should be stored in a cool dry place.