

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tetralysal 300mg Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 408 mg lymecycline equivalent to 300 mg of tetracycline base.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard Capsule (Capsule)

Product imported from the UK

Hard gelatin capsule, red cap and yellow body.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Tetralysal 300 is for the treatment of acne.

As Tetralysal 300 contains a broad spectrum antibiotic, it is also recommended for the treatment of infections due to micro-organisms sensitive to tetracyclines.

4.2 Posology and method of administration

Adults and children over 12 years of age or 50kg.bw :

Acne:

The usual dosage for the chronic treatment of acne is 1 capsule daily: treatment should be continued for at least 8 weeks.

Tetracycline sensitive infections:

The usual daily dosage is two capsules in divided doses (1 capsule, twice daily). This may be increased to four capsules daily if required.

Elderly: As with other tetracyclines, no specific dose adjustment is required.

4.3 Contraindications

Use in patients hypersensitive to Lymecycline or any other component of the preparation.

Use in patients with hypersensitivity to tetracyclines.

Use during pregnancy or lactation in women breast feeding infants.

Use in patients with advanced renal insufficiency.

Use in children under the age of 8 years due to the risk of dental dyschromia and/or enamel hypoplasia.

Concurrent treatment with oral retinoids (see Interaction with other medicinal products and other forms of interactions).

4.4 Special warnings and precautions for use

Prolonged use of an anti-infective may result in the development of infection due to micro-organisms resistant to the anti-infective.

Cross-resistance between tetracyclines may develop in micro-organisms, and cross sensitisation in patients.

Tetracyclines are absorbed to some extent by developing bones and teeth and may produce staining and enamel hypoplasia. In children up to the age of 8 years, tetracyclines should only be administered if considered essential by the physician, and for a short a treatment period as feasible. Repeated courses should be avoided. The effect appears to be related to total dosage given, and not only the duration of treatment.

Tetracyclines should only be used with caution in patients with hepatic dysfunction, lest accumulation occurs with increased toxicity. Careful monitoring of dosage by serum levels is necessary. High dosage of tetracyclines may be hepatotoxic and great care should be used with concurrent administration of other hepatotoxic drugs.

Tetracyclines should only be administered with great caution in patients with renal insufficiency lest accumulation occurs with increased toxicity. Dosage may require reduction. High dosage of tetracyclines may be nephrotoxic.

Bulging fontanelles in infants and benign intracranial hypertension in adults has been reported during treatment with tetracyclines. Therefore treatment should cease if evidence of raised intracranial pressure develops during treatment with Tetralysal.

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with tetracycline drugs, be warned to avoid direct exposure to natural and artificial sunlight and that treatment should be discontinued at the first evidence of skin erythema or skin discomfort.

The use of expired tetracyclines can lead to renal tubular acidosis (Pseudo-Fanconi syndrome) readily reversible when treatment is discontinued altogether.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of tetracyclines may be affected by the simultaneous administration of antacids and/or iron preparations. These preparations should not be taken within two hours before or after taking Tetralysal 300.

Unlike earlier tetracyclines, absorption of Tetralysal 300 is not significantly impaired by moderate amounts (e.g. a glass) of milk.

Tetracyclines may prolong the action of coumarin anticoagulants, and per se delay coagulation.

Concurrent use of barbiturates, phenytoin or carbamazepine may decrease plasma levels of tetracyclines.

Concomitant use of oral retinoids should be avoided as this may increase the risk of benign intracranial hypertension.

Absorption of drug has been reported to be decreased by administration of drugs inhibiting secretion of gastric acid.

Concurrent use with the anaesthetic methoxyflurane increases the risk of kidney failure and has been reported to result in fatal kidney failure.

Lymecycline could cause false-positive urine glucose determinations. It could also interfere with fluorometric determinations of urine catecholamines resulting in falsely increased values (Hingerty's method).

4.6 Fertility, pregnancy and lactation

Tetracyclines readily cross the placenta barrier and are distributed into milk. Therefore, Tetralysal 300 should not be administered to pregnant or breast-feeding women (risk of enamel hypoplasia or dental dyschromia in the infant).

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

Body System (MeDRA)	Frequency	Adverse Drug Reaction
Blood and lymphatic system disorders	Unknown	Neutropenia, thrombocytopenia
Eye disorders	Unknown	Visual disturbance
Gastrointestinal disorders	Common ($\geq 1/100$ to $< 1/10$)	Nausea, abdominal pain, diarrhoea
	Unknown	Glossitis, enterocolitis, vomiting, epigastralgia (gastrointestinal pain upper)
General disorders and administration site conditions	Unknown	Pyrexia
Hepatobiliary disorders	Unknown	Jaundice
Immune system disorder	Unknown	Hypersensitivity, urticaria, angioneurotic oedema, anaphylactic reaction
Investigations	Unknown	Transaminases increased, blood alkaline phosphatase increased, blood bilirubin increased
Nervous system disorders	Common ($\geq 1/100$ to $< 1/10$)	Headache
	Unknown	Dizziness, intracranial hypertension
Skin and subcutaneous tissue disorders	Unknown	Erythematous rash, photosensitivity reactions, pruritus, Stevens Johnson Syndrome

Some adverse effects are reported with tetracycline therapy in general:

- Dental dyschromia and /or enamel hypoplasia may occur if the product is administered in children younger than 8 years of age.
- Haemolytic anaemia, eosinophilia and other hematologic disorders have been reported with tetracycline therapy.
- Extra-renal hyperazotemia linked to an anti-anabolic effect which may be intensified by the association with diuretics has been reported with tetracycline therapy.
- Treatment should cease if any evidence of raised intracranial pressure develops during treatment with Tetralysal.

4.9 Overdose

There is no specific treatment, but gastric lavage should be performed as soon as possible. Supportive measures should be instituted as required and a high fluid intake maintained.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Tetracycline Antibiotics ATC code: J01AA04

Lymecycline is a broad-spectrum anti-infective. It has antimicrobial activity and uses similar to those of tetracycline hydrochloride. It acts by interfering with bacterial protein synthesis and is active against a large number of Gram-positive and Gram-negative pathogenic bacteria including some which are resistant to penicillin.

5.2 Pharmacokinetic properties

After oral dosing it is absorbed readily with or without the presence of food and is excreted slowly in urine with a half-life of about 7 to 12 hours. The drug is lipid soluble.

Lymecycline is more readily absorbed from the gastro-intestinal tract than tetracycline with a peak serum concentration of approximately 2mg/l after 3 hours following a 300mg dose. In addition, similar blood concentrations are achieved with smaller doses.

When the dose is doubled an almost correspondingly higher blood concentration has been reported to occur.

5.3 Preclinical safety data

Lymecycline has been used over a number of years and has shown a good toxicological profile in man. In the mouse toxicity studies have shown an LD50 of 181mg/kg and by an unreported route 253mg/kg in an unnamed mammal.

The active part of lymecycline is tetracycline and the toxicity of this has been studied in a number of animals. Acute oral toxicity in the guinea pig is 1875mg/kg, in the mouse 678mg/kg, in the rat 807mg/kg. One result has been reported in women at a dose of 600mg/kg and the effects were observed as somnolence, constipation and a reduction in urine output.

Reproductive studies have been carried out in the mouse and an oral dose of 700mg/kg resulted in developmental abnormalities of the skin in the new-born. Two results have been reported in women with effects on the new-born observed at 80mg/kg and 200mg/kg.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate
Colloidal hydrated silica
Gelatin
Titanium dioxide (E171)
Erythrosine (E127)
Quinoline yellow (E104)
Indigotine (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product shall be the date shown on the container and outer packaging of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C.

Store in the original container in order to protect from light and moisture.

6.5 Nature and contents of container

Polyethylene/foil blister strips of 4 capsules each, in a cardboard carton containing 28 capsules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

As with handling of any anti-infective, care should be taken to avoid contact with the substance.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

Clear Pharma Limited
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Belfast BT12 5QA
United Kingdom

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1823/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th September 2013

10 DATE OF REVISION OF THE TEXT