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 the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard Capsule (Capsule).
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

Paediatric population
The safety and efficacy of Tetralysal in children aged under 12 years of age have not been established. No data are available. For children over the age of 12 years, the adult dosage may be given. For children under the age of 8 years, see section 4.3.

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.

Method of administration
The capsules should be taken with a glass of water in order to reduce the risk of oesophageal irritation and ulceration (see section Special warnings and precautions for use).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Use in patients with hypersensitivity to tetracyclines.

Its use is contraindicated in children aged under 8 years due to the risk of permanent dental staining and enamel hypoplasia.

Concurrent treatment with oral retinoids (see section 4.5).

Use during pregnancy or lactation in women breast feeding infants. Use in patients with advanced renal insufficiency.

4.4 Special warnings and precautions for use

Oesophageal irritation and ulceration
Solid dosage forms of tetracyclines may cause oesophageal irritation and ulceration. To avoid oesophageal irritation and ulceration, adequate fluids (water) should be taken with this medicinal product (see Section 4.2).

Antibiotic resistance
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.

Paediatric population
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 as 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.

Hepatic impairment
Overdosage could result in hepatotoxicity.
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. Great care should be used with concurrent administration of other hepatotoxic drugs.

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

Myasthenia Gravis
Caution should be observed in the treatment of patients with myasthenia gravis who may be at risk of worsening of the condition

Intracranial pressure
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.

Systemic lupus erythematosus
Tetralysal can cause exacerbation of systemic lupus erythematosus.

Photosensitivity
Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. It is recommended to avoid exposure to direct sunlight or ultraviolet light during treatment with tetracycline drugs and treatment should be discontinued at the first evidence of skin erythema or skin discomfort.

4.5 Interaction with other medicinal products and other forms of interactions

Simultaneous administration of iron preparations and anti-acids, magnesium/aluminium and calcium hydroxides, oxides, salts and activated charcoal, cholestyramine, bismuth chelates and sucralfate may decrease cycline absorption.
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 preparations should not be taken within two hours before or after taking Tetralysal 300.
Some adverse effects have been reported with tetracycline therapy when used in combination with lithium; an interaction between lithium and the tetracycline class is a recognized interaction. Specifically, a combination of lymecycline with lithium may cause an increase in serum lithium levels.
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.
Concomitant use of oral retinoids is contraindicated due to risk of benign intracranial hypertension (see section 4.3). There is also a risk of intracranial hypertension with vitamin A (above 10,000 IU/day).
Bacteriostatic medicinal products including lymecycline may interfere with the bacteriocidal action of penicillin and beta-lactam antibiotics. It is advisable that tetracycline-class drugs and penicillin should not therefore be used in combination.
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 renal toxicity.
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).

Paediatric population
Interactions studies have only been performed in adults

4.6 Fertility, pregnancy and lactation

Pregnancy
Tetracyclines readily cross the placenta barrier. Therefore, Tetralysal 300 should not be administered to pregnant women (risk of enamel hypoplasia or dental dyschromia in the developing infant) (see section 4.3).

Breastfeeding
Tetracyclines are distributed into milk. Therefore, Tetralysal 300 should not be administered to breastfeeding women (risk of enamel hypoplasia or dental dyschromia in the infant) (see section 4.3).

Fertility
No data on the effect on fertility is available.

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

Tabulated list of adverse reactions
The list of undesirable effects shown below is presented by system organ class, MedDRA preferred term, and frequency. Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (≥1/10,000); Not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse Drug Reaction
Blood and lymphatic system disorders	Unknown	Neutropenia, thrombocytopenia
Eye disorders	Unknown	Visual disturbance*
Gastrointestinal disorders	Common Unknown	Nausea, abdominal pain, diarrhoea Glossitis, enterocolitis, vomiting, epigastralgia (gastrointestinal pain upper), oesophageal ulcer and oesophagitis.
General disorders and administration site conditions	Unknown	Pyrexia
Hepatobiliary disorders	Unknown	Jaundice, Hepatitis
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 Unknown	Headache Dizziness, intracranial hypertension
Skin and subcutaneous tissue disorders	Unknown	Erythematous rash, photosensitivity reactions, pruritus, Stevens Johnson Syndrome
Psychiatric disorders	Unknown	Depression Nightmare

Description of selected adverse reactions
Some adverse effects are reported with tetracycline therapy in general:

- Systemic Lupus Erythematosus
- Pancreatitis
- Dental dyschromia and /or enamel hypoplasia may occur if the product is administrated 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.
- *The manifestation of clinical symptoms, including vision disorders, or headache, must suggests the possibility of a cranial hypertension diagnosis. Treatment should cease if any evidence of raised intracranial pressure develops during treatment with Tetralysal.

Benign intracranial hypertension has been reported in association with tetracyclines with possible symptoms of headache, vomiting, vision disorders including blurred vision, scotoma, diplopia or permanent vision loss.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: http.hpra.ie.

4.9 Overdose

Acute overdose is rare with antibiotics and there is no specific treatment.

Management
Should overdose occur, gastric emptying should be considered. 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 then 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

Capsule Shells:
Gelatin
Titanium dioxide (E171)
Erythrosine (E127)
Quinoline Yellow (E104)
Indigotine (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Polypropylene Securitainers:	Unopened Shelf-life 2 years
Aluminium containers:	Unopened Shelf-life 2 years
Blister packs:	Unopened Shelf-life 3 years
Aluminium and Polyethylene Strips:	Unopened Shelf-life 3 years

6.4 Special precautions for storage

Containers/Strips:
Do not store above 25°C.
Store in the original container in order to protect from light and moisture.

Blisters:
Do not store above 25°C.
Keep container in the outer carton in order to protect from light and moisture.

6.5 Nature and contents of container

Polypropylene securitainers or aluminium containers of 20 or 100 capsules.
Aluminium/PVC/PVDC calendar blister strips of 14 capsules presented in a carton containing 28 capsules.
Aluminium and Polyethylene strips, carton containing 28 or 56 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

As with handling of any anti-infective, care should be taken to avoid contact with the substance.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Galderma International,Tour Europlaza,20, Avenue André Prothin,La Défense 4,92927 Paris,La Défense,CEDEX,France

8 MARKETING AUTHORISATION NUMBER

PA22743/016/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 February 1982
Date of last renewal: 26 February 2007

10 DATE OF REVISION OF THE TEXT

May 2022