**IRISH MEDICINES BOARD ACT 1995**

**MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998**

**(S.I. No.142 of 1998)**

**PA0590/012/001**
Case No: 2032800

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

**Galderma (UK) Ltd**

**Meridien House**, **69-71 Clarendon Road**, **Watford**, **Herts WD17 1DS**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

**Tetralysal 150mg Capsules**

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **20/04/2007**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

# Part II

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Tetralysal 150mg Capsules

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 204 mg Lymecycline equivalent to 150 mg of Tetracycline base.

For excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Hard capsules
White, opaque capsule containing a yellow powder.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

In the treatment of infections due to micro- organisms sensitive to tetracycline.

### 4.2 Posology and method of administration

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

*Tetracycline sensitive infections:*

The usual daily dosage is 4 capsules in divided doses (2 capsules, twice daily).

This may be increased to 8 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.

### 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 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.

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 ot 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.

## 4.5 Interaction with other medicinal products and other forms of interaction

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

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.

## 4.6 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 emanel hypoplasia or dental dyschromia in the infant).

## 4.7 Effects on ability to drive and use machines

None known.

## 4.8 Undesirable effects

| Body system (MeDRA) | Frequency | Adverse Drug Reaction |
|---|---|---|
| Eye disorders | Unknown | Visual disturbance |
| Gastrointestinal disorders | Common (1/100 to <1/10)<br><br>Unknown | Nausea, abdominal pain, diarrhoea<br>Glossitis, enterocolitis |
| Immune system disorders | Unknown | Hypersensitivity, urticaria angioneurotic oedema |
| Investigations | Unknown | Transaminases increased, blood alkaline phosphatase Increased, blood bilirubin increased |
| Nervous system disorders | Common (1/100 to <1/10)<br>Unknown | Headache<br>Dizziness |
| Skin and subcutaneous tissue disorders | Unknown | Erythematous rash, photosensitivity reactions, pruritus |

## 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

Lymecycline is a broad-spectrum and 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 per 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 newborn. Two cases have been reported in women with effects on the newborn observed at 80mg/kg and 200mg/kg.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Colloidal Hydrated Silica
Magnesium Stearate

Capsule shell:
Gelatin

Sealing agent:
Gelatin
Glyceryl mono-oleate

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf Life

2 years.

## 6.4 Special precautions for storage

Do not store above 25°C.
Keep container in the outer carton.

## 6.5 Nature and contents of container

Polypropylene securitainers with polypropylene caps or aluminium containers with aluminium caps of 20 or 100 capsules packed in outer cartons.

## 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-infectives, care should be taken to avoid contact with the substance.

## 7 MARKETING AUTHORISATION HOLDER

Galderma (UK) Limited
Meridien House
69-71 Clarendon Road
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UK

## 8 MARKETING AUTHORISATION NUMBER

PA 590/12/1

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1977

Date of last renewal: 26 February 2007

## 10 DATE OF REVISION OF THE TEXT

April 2007