SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ledermycin Capsules 150mg
Demeclocycline Hydrochloride 150mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

LEDERMYCIN capsules each contain 150mg of demeclocycline hydrochloride.

3. PHARMACEUTICAL FORM

capsule, hard

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

For the treatment of infections caused by tetracycline-sensitive organisms. For example, LEDERMYCIN is highly effective in the treatment of infections caused by *Borrelia recurrentis* (relapsing fever), *Calymmatobacterium granulinatis* (granuloma inguinale), *Chlamydia* species (psittacosis, lymphogranuloma vereneum, trachoma, inclusion conjunctivitis), *Francisella tularensis* (tularaemia), *Haemophilus ducreyi* (chancroid), *Leptospira* (meningitis, jaundice), *Mycoplasma pneumoniae* (non-gonococcal urethritis), *Pseumomonas mallei* and *pseudomallei* (glanders and melioidosis), *Rickettsiae* (typhus fever, Q fever, rocky mountain spotted fever), *Vibrio* species (cholera). It is also highly effective, alone or in combination with streptomycin, in the treatment of infections due to *Brucella* species (brucellosis) and *Yersinia pestis* (bubonic plague). Severe acne vulgaris.

Other sensitive organisms include: *Actinomyces israelii*, *Bacillus anthracis* (pneumonia), *Clostridium* species (gas gangrene, tetanus), *Entamoeba histolytica* (dysentery), *Neisseria gonorrhoeae* and anaerobic species, *Treponema pallidum* and *pertenue* (syphilis and yaws).

For the treatment of chronic hyponatraemia associated with the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) secondary to malignant disease, where water restriction is ineffective and the patient does not have concomitant cirrhosis.

4.2. Posology and Method of Administration

Posology

For Antibiotic Use

Adults
*(Capsules***)** - 600mg daily in 2 or 4 divided doses. For primary atypical pneumonia, the average daily dose is 900mg in 3 divided doses for 6 days.

Elderly
Use with caution in elderly patients. (See Section 4.3 Contra-indications and Section 4.4 Special warnings and special precautions for use)

Paediatric population
Not recommended for children under 12 years of age.

For the treatment of Chronic Hyponatraemia due to SIADH

Adults only

Initially: 900mg-l200mg daily in divided doses

Maintenance dose: 600-900mg daily in divided doses

LEDERMYCIN should be swallowed whole with plenty of fluid while sitting or standing. Doses should be taken an hour before or 2 hours after meals as absorption of LEDERMYCIN is impaired by milk and food. Antibiotic therapy should be continued for one to three days after characteristic symptoms of fever have subsided. The incidence of rheumatic fever or glomerulonephritis following streptococcal infections suggests that therapy of a streptococcal infection should be continued for 8 full days even though symptoms have subsided.

LEDERMYCIN therapy in the treatment of chronic hyponatraemia due to SIADH should not be withdrawn without commencing other methods of control.

Method of administration
Oral administration.

4.3 Contraindications

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

The use of LEDERMYCIN is contraindicated in patients with acute porphyria, patients who are pregnant or breast-feeding, children under 12 years of age, patients with a history of hypersensitivity to tetracyclines and patients with renal impairment.

4.4 Special warnings and precautions for use

LEDERMYCIN should be used with caution in patients with renal or hepatic dysfunction, or in conjunction with other potentially hepatotoxic or nephrotoxic drugs. Concurrent use with the anaesthetic methoxyflurane increases the risk of kidney failure. The anti-anabolic action of the tetracyclines may cause an increase in BUN. The treatment of chronic hyponatraemia may necessitate the administration of high doses of LEDERMYCIN for prolonged periods, so increasing the potential for nephrotoxicity (manifested by rises in plasma urea and creatinine) and photoallergic reactions. Cross-resistance between tetracyclines may develop in micro-organisms and cross sensitisation in patients. LEDERMYCIN should be discontinued if there are signs/symptoms of overgrowth of resistant organisms including candida, enteritis, glossitis, stomatitis, vaginitis, pruritis ani or staphylococcal enterocolitis.

Lower doses are indicated in cases of renal impairment to avoid excessive systemic accumulation and if therapy is prolonged, serum level determinations are advisable. Patients who have known liver disease should not receive more than 1g daily. In long term therapy, periodic laboratory evaluation of organ systems, including haematopoietic, renal and hepatic studies should be performed.

LEDERMYCIN has the greatest potential of the tetracycline analogues for causing photo-allergic reactions in hypersensitive persons. Such patients should be warned to avoid direct exposure to natural or artificial sunlight and to discontinue therapy at the first sign of skin discomfort. Exacerbation of pre-existing SLE has been reported with tetracyclines.

LEDERMYCIN may increase muscle weakness in patients with myasthenia gravis.

4.5 Interactions with other medicinal products and other forms of interaction

LEDERMYCIN should not be used with penicillins.

Tetracyclines depress plasma prothrombin activity and reduced doses of concomitant anti-coagulants such as Coumarins and phenindione may be required.

Absorption of LEDERMYCIN is impaired by the concomitant administration of milk and dairy products, food, iron, calcium, zinc, magnesium and particularly aluminium salts commonly used as antacids.

Absorption of tetracyclines is possibly reduced by kaolin, quinapril tablets (quinapril tablets contain magnesium carbonate), strontium ranelate, sucralfate, tripotassium dicitratobismuthate.

There is a possible increased risk of benign intracranial hypertension with concomitant use of tetracyclines and retinoids, e.g. acitretin, isotretinoin, tretinoin. There is increased risk of ergotism when tetracyclines given with ergotamine and methysergide.

Typhoid Vaccine (oral): Antibacterials inactivate oral typhoid vaccine and therefore Ledermycin should be avoided for 3 days before and after oral typhoid vaccine.

4.6. Pregnancy and Lactation

LEDERMYCIN is contra-indicated during pregnancy and lactation.

Pregnancy
Results of animal studies indicate that tetracyclines cross the placenta, are found in foetal tissues and can have toxic effects on the developing foetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.

The use of tetracyclines during tooth development (last half of pregnancy and children to the age of 12 years) may cause permanent discoloration of the teeth (yellow-grey-brown). This adverse reaction is more common during long term use of the drugs but has been observed following repeated short term courses. Enamel hypoplasia has also been reported.

Breast-feeding
Tetracyclines have been found in the milk of lactating women who are taking a drug in this class. Permanent tooth discoloration may occur in the developing infant and enamel hypoplasia has been reported. Therefore, LEDERMYCIN should not be administered to lactating women.

4.7. Effects on Ability to Drive and Use Machines

Headache, dizziness, visual disturbances and rarely impaired hearing have been reported with tetracyclines and patients should be warned about the possible hazards of driving or operating machinery during treatment.

4.8 Undesirable effects

The following undesirable effects have been reported for Demeclocycline hydrochloride.

The undesirable effects are listed according to their frequency:
Not known (cannot be estimated from the available data)

System organ class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Not Known	Haemolytic anaemia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and eosinophilia[a]

Immune system disorders	Not Known	Hypersensitivity reactions including urticaria, Stevens-Johnson syndrome, angioneurotic oedema, anaphylaxis, anaphylactoid purpura, pericarditis and exacerbation of systemic lupus erythematosus
Nervous system disorders	Not Known	Headache, dizziness, bulging fontanelles (in infants), benign intracranial hypertension (in juveniles and adults), raised intracranial pressure (such as severe or persistent headache or blurred vision) [b], myasthenia
Eye disorders	Not Known	Visual disturbances
Ear and labyrinth disorders	Not Known	Impaired hearing
Gastrointestinal disorders	Not Known	Nausea, vomiting, diarrhoea, dysphagia, oesophagitis, oesphageal ulceration,[c] candidiasis, pseudomembranous colitis (Clostridium difficile overgrowth) glossitis, stomatitis, vaginitis, or staphylococcal enterocolitis, pancreatitis
Skin and subcutaneous tissue disorders	Not Known	Photosensitivity, erythematous, maculo-papular rashes, pruritus, bullous dermatoses, exfoliative dermatitis, skin discolouration, serious skin reactions
Renal and urinary disorders	Not Known	Renal dysfunction, especially in patients with pre-existing renal impairment, acute renal failure or nephritis, reversible nephrogenic diabetes insipidus (prolonged and/or at high dosages)
Hepatobiliary disorders	Not Known	Hepatitis, jaundice, hepatic failure
Investigations	Not Known	Transient increases in liver function test values

a. When given over prolonged periods, tetracyclines have been reported to produce brown-black discoloration of the thyroid gland. No abnormalities of thyroid function are known to occur.
b. While the condition and related symptoms usually resolve soon after discontinuation of the tetracycline, the possibility of permanent sequelae exists.

c. In patients taking oral tetracyclines in solid dose form, usually where medication was taken immediately before retiring or with inadequate fluids.

Reporting of Adverse reactions

Reporting suspected adverse reactions after authorization 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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

Management
No specific antidote. Gastric lavage plus oral administration of milk or antacids. Maintain fluid and electrolyte balance.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Antibacterial for systemic use, Tetracyclines.
ATC code: J01AA01

Mechanism of action
Tetracyclines have **a** broad spectrum of anti-microbial activity and act by interfering with bacterial protein synthesis. They are active against a large number of gram positive and gram negative pathogenic bacteria, including some which are resistant to penicillin.

5.2 Pharmacokinetic properties

Absorption
Tetracyclines are incompletely and irregularly absorbed from the gastrointestinal tract. Absorption is affected by the soluble salts of divalent and trivalent metals, milk and food.
Distribution
Plasma concentrations of up to 2.4mg per ml have been reported 3 to 4 hours after an oral dose of 300mg, only falling to about 1mg per ml after 24 hours. 41-90% of circulating demeclocycline is bound to plasma proteins. Tetracyclines are widely distributed throughout the body tissue and fluids, and are retained at sites of new bone formation and recent calcification. The biological half life of demeclocycline is 12 hours.

Elimination
Tetracyclines are excreted in the urine and faeces.

5.3. Preclinical Safety Data

There are no other preclinical safety data of relevance to the prescriber apart from those already detailed in the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Powdered Cellulose, magnesium stearate, Colloidal Anhydrous Silica.

Capsule body and cap: titanium dioxide (E171), yellow iron oxide (E172), red iron oxide (El72), erythrosine (El27), gelatin.

Printing on capsule: Shellac NF E904, Purified water, Propylene glycol (E1520), Dehydrated Alcohol, Strong ammonia solution, Potassium Hydroxide, Isopropyl Alcohol and black iron oxide (E172)

6.2. Incompatibilities

None.

6.3. Shelf Life

36 months

6.4 Special precautions for storage

Do not store above 25°C.
Blister pack-Store in original package in order to protect from light and moisture.
Container/Bottle - Keep the container/bottle tightly closed in the outer carton in order to protect from light and moisture

6.5 Nature and contents of container

Polypropylene containers - 20, 28 or 100 capsules.

Screw capped glass bottles - 100 capsules.

Blister pack - 20 capsules.

HDPE ø 45 mm round 50 ml plastic container containing 28 capsules

6.6. Instruction for Use/Handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Ltd
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69 Old Broad Street,
London, EC2M 1QS,
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8. MARKETING AUTHORISATION NUMBER

PL 12762/0154

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

8 March 2004

10 DATE OF REVISION OF THE TEXT

30/11/2023