

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Minocycline Tablets BP 100 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 115.85 mg of minocycline hydrochloride (dihydrate) equivalent to 100 mg of minocycline.

Excipients with known effect:

Each 100mg tablet contains 35.75 mg lactose.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

The product is presented in the form of buff coloured, biconvex, film coated tablet, engraved with company logo on one side and A494 on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Minocycline is a broad spectrum antibiotic used for the treatment of infections caused by tetracycline-sensitive organisms. Some tetracycline-resistant strains of staphylococci are also sensitive.

It is indicated for the treatment of the following infections:

- Gonorrhoea
- Non-gonococcal urethritis
- Prostatitis
- Moderate to severe acne; use in moderate acne only if topical treatment is ineffective, if acne is extensive or hard to reach and if there is a high risk of scarring.
- Acute and chronic bronchitis
- Bronchiectasis
- Lung abscess
- Pneumonia
- Ear, nose and throat infections
- Urinary tract infections

- Pelvic inflammatory disease e.g. salpingitis, oophoritis.
- Skin and soft tissue infections caused by minocycline sensitive organisms
- Ophthalmological infections
- Nocardiosis
- Prophylactic treatment of asymptomatic meningococcal carriers
- Pre and post-operative prophylaxis of infection.

For sensitive organisms, see section 5.1

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

Adults:

Routine antibiotic use: 200 mg daily in divided doses.

Acne: 50 mg twice daily. Treatment should continue for a minimum of six weeks.

Gonorrhoea: males: 200 mg initially followed by 100 mg every 12 hours for a minimum of 4 days with post-therapy cultures within 2-3 days.
females may require more prolonged therapy.

Prophylaxis of asymptomatic meningococcal carriers: 100 mg twice daily for 5 days, usually followed by a course of rifampicin.

If, after six months, there is no satisfactory response minocycline should be discontinued and other therapies considered. If minocycline is to be continued for longer than six months, patients should be monitored at least three monthly intervals thereafter for signs and symptoms of hepatitis or SLE (see section 4.4.)

Special populations

Renal impairment: Minocycline may be used at the normal recommended dosage in mild to moderate renal impairment, however caution is advised in patients with severe renal impairment.

Hepatic impairment:

Minocycline should be used with caution in patients with hepatic impairment.

Elderly:

Care is required if Minocycline is given to the elderly. Dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Paediatric population:

Children over 12 years: 50 mg every twelve hours.
Children under 12 years: Not recommended.

Method of Administration

For oral administration. To reduce the risk of oesophageal irritation and ulceration, the tablets should be swallowed whole with plenty of fluid, while sitting or standing. Unlike earlier tetracyclines, absorption of minocycline is not significantly impaired by food or moderate amounts of milk.

4.3 Contraindications

- Hypersensitivity to the active substance, to tetracyclines or to any of the excipients listed in section 6.1.
- Systemic Lupus Erythematosus
- Pregnancy and lactation
- Children under 12 years.
- Complete renal failure

4.4 Special warnings and precautions for use

- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Use in Hepatic Dysfunction: Caution should be exercised when administering to patients with hepatic dysfunction and in conjunction with alcohol or other potentially hepatotoxic drugs.
- Breathing difficulties: Cases of breathing difficulties including dyspnoea, bronchospasm, exacerbation of asthma, pulmonary eosinophilia and pneumonitis (see section 4.8) have been reported with minocycline use. If patients develop breathing difficulties, they should seek urgent medical advice and minocycline should be discontinued.
- Cross-sensitivities: Cross-resistance between tetracyclines may develop in micro-organisms and cross-sensitisation in patients. Minocycline should be discontinued if there are signs/symptoms of overgrowth of resistant organisms, enteritis e.g. glossitis, stomatitis, vaginitis, pruritus ani or staphylococcal enteritis.
- Paediatric population: The use of tetracyclines during tooth development in children under the age of 12 years may cause permanent discoloration (see above). Enamel hypoplasia has been reported.
- Renal Impairment: Clinical studies have shown that there is no significant drug accumulation in patients with renal impairment when they are treated with minocycline in the recommended doses. In patients with severe renal impairment, dose reduction and monitoring of renal function may be required.
- Myasthenia Gravis: Caution is advised in patients with myasthenia gravis as tetracyclines can cause weak neuromuscular blockade.
- Auto-immune Disorders: Rare cases of auto-immune hepatotoxicity and isolated cases of systemic lupus erythematosus (SLE) and also exacerbation or pre-existing SLE have been reported. If patients develop signs or symptoms of SLE or hepatotoxicity, or suffer exacerbation of pre-existing SLE, minocycline should be discontinued.

- **Hyperpigmentation:** As with other tetracyclines, minocycline may cause hyperpigmentation at various body sites (see section 4.2 and 4.8). Hyperpigmentation may present regardless of dose or duration of therapy but develops more commonly during long term treatment. Patients should be advised to report any unusual pigmentation without delay and minocycline should be discontinued. This is generally reversible on cessation of therapy.
- **Photosensitivity:** If a photosensitivity reaction occurs, patients should be warned to avoid direct exposure to natural or artificial light and to discontinue therapy at the first signs of skin discomfort.
- **Intracranial hypertension:** As with other tetracyclines, bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults have been reported. Presenting features were headache and visual disturbances including blurring of vision, scotoma and diplopia. Permanent vision loss has been reported. Treatment should cease if evidence of raised intracranial pressure develops.
- **Lactose:** Minocycline Tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

- ACE inhibitors Antacids and Adsorbants - Tetracyclines bind to di-/tri-valent cations. Absorption from the gastrointestinal tract is impaired by the concomitant administration of antacids, iron, calcium, aluminium, magnesium bismuth and zinc salts (interactions with specified salts, antacids, kaolin, bismuth containing ulcer-healing drugs, quinapril which contains a magnesium carbonate excipient). Dosages should be maximally separated. Absorption of tetracyclines is not significantly impaired by food, milk and milk products.
- Antibacterials - minocycline should not be used with penicillins.
- Anticoagulants - tetracyclines depress plasma prothrombin activity and reduced dosages of concomitant anticoagulants may be necessary
- Diuretics – may aggravate nephrotoxicity by volume depletion.
- Ergotamine and ergometrine – increased risk of ergotism.
- Oral Contraceptives - both can induce hyperpigmentation.
- Retinoids - Administration of isotretinoin should be avoided shortly before, during and shortly after minocycline therapy. Each drug alone has been associated with pseudotumor cerebri (benign intracranial hypertension) (see section 4.4 Special warnings and precautions)
- Laboratory tests - may affect urinary urobilinogen excretion tests by reducing bacterial converters of bilirubin to urobilinogen. May also produce an interference fluorescence in the Hungarty methods for measuring urinary catecholamines.

4.6 Fertility, pregnancy and lactation

Minocycline use during pregnancy and lactation is contraindicated.

Pregnancy and lactation

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). Studies on animals treated during early pregnancy also indicate embryotoxicity.

The use of tetracycline during the (last half of pregnancy), when the teeth are developing, may cause permanent discoloration of the teeth more common during long-term or repeated short-term use. Enamel hypoplasia has also been reported.

Breast-feeding

Tetracyclines have been found in the milk of lactating women. Permanent tooth discoloration may occur in the developing infant and enamel hypoplasia has been reported.

4.7 Effects on ability to drive and use machines

Light headedness, headache, visual disturbances, dizziness, tinnitus, vertigo and impaired hearing (rarely) have occurred following administration of minocycline. Patients should be warned of these effects and the possible hazard of driving or operating machinery, if affected.

4.8 Undesirable effects

Adverse reactions are listed in the Table in CIOMS frequency categories under MedDRA system/organ classes:

The frequency of adverse reactions Minocycline Tablets is defined using the following convention:

Common: ($\geq 1/100$ to $< 1/10$)

Uncommon: ($\geq 1/1,000$ to $< 1/100$)

Rare: ($\geq 1/10,000$ to $< 1/1,000$)

Very Rare: ($< 1/10,000$)

Not known: (cannot be estimated from the available data)

MedDRA system organ class	Adverse Drug Reaction
Infections and Infestations	Very Rare: Oral and anogenital candidiasis, vulvovaginitis.
<u>Blood and Lymphatic System Disorders</u>	Rare: Eosinophilia, leucopenia, neutropenia, thrombocytopenia. Very Rare: Haemolytic anaemia, pancytopenia. Not known: Agranulocytosis
<u>Immune System Disorders</u>	Rare: Anaphylaxis /anaphylactoid reaction (including shock and fatalities). Not known: Hypersensitivity, pulmonary infiltrates, anaphylactoid purpura, polyarteritis nodosa.

<u>Endocrine Disorders</u>	Very Rare: Abnormal thyroid function, brown-black discolouration of the thyroid.
<u>Metabolism and Nutrition Disorders</u>	Rare: Anorexia.
<u>Nervous System Disorders</u>	Common: Dizziness (light-headedness). Rare: Headache, hypaesthesia, paraesthesia, intracranial hypertension, vertigo. Very Rare: Bulging fontanelle. Not known: convulsions, sedation.
<u>Ear and Labyrinth Disorders</u>	Rare: Impaired hearing, tinnitus.
<u>Cardiac Disorders</u>	Rare: Myocarditis, pericarditis.
<u>Respiratory, Thoracic and Mediastinal Disorders</u>	Rare: Cough, dyspnoea. Very Rare: Bronchospasm, exacerbation of asthma, pulmonary eosinophilia. Not known: Pneumonitis.
<u>Gastrointestinal Disorders</u>	Rare: Diarrhoea, nausea, stomatitis, discolouration of teeth vomiting. Very Rare: Dyspepsia, dysphagia, enamel hypoplasia, enterocolitis, oesophagitis, oesophageal ulceration, glossitis, pancreatitis, pseudomembranous colitis.
<u>Hepatobiliary Disorders</u>	Rare: Increased liver enzymes, hepatitis, autoimmune hepatotoxicity. (See Section 4.4 Special warnings and precautions for use). Very Rare: Hepatic cholestasis, hepatic failure (including fatalities), hyperbilirubinaemia, jaundice. Not known: Autoimmune hepatitis*.
<u>Skin and Subcutaneous Tissue Disorders</u>	Rare: Alopecia, erythema multiforme, erythema nodosum, fixed drug eruption, hyperpigmentation of skin, photosensitivity, pruritis, rash, urticaria, vasculitis. Very Rare: Angioedema, exfoliative dermatitis, hyperpigmentation of nails,

	Stevens-Johnson Syndrome, toxic epidermal necrolysis. Not known: Drug rash with eosinophilia and systemic symptoms (DRESS)
<u>Musculoskeletal and Connective Tissue Disorders</u>	Rare: Arthralgia, lupus-like syndrome, myalgia. Very Rare: Arthritis, bone discolouration, cases of or exacerbation of systemic lupus erythematosus (SLE) (See Section 4.4 Special warnings and precautions for use), joint stiffness, joint swelling.
<u>Renal and Urinary Disorders</u>	Rare: Increased serum urea, acute renal failure, interstitial nephritis.
<u>Reproductive System and Breast Disorders</u>	Very Rare: Balanitis.
<u>General Disorders and Administration Site Conditions</u>	Uncommon: Fever. Very Rare: Discolouration of secretions.

* Autoimmune hepatitis: See Section 4.4 Special warnings and precautions for use.

The following syndromes have been reported. In some cases involving these syndromes, death has been reported. As with other serious adverse reactions, if any of these syndromes are recognised, the drug should be discontinued immediately:

- Hypersensitivity syndrome consisting of cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more of the following: hepatitis, pneumonitis, nephritis, myocarditis, pericarditis. Fever and lymphadenopathy may be present.
- Lupus-like syndrome consisting of positive antinuclear antibody, arthralgia, arthritis, joint stiffness or joint swelling, and one or more of the following: fever, myalgia, hepatitis, rash, vasculitis.
- Serum sickness-like syndrome consisting of fever, urticaria or rash, and arthralgia, arthritis, joint stiffness or joint swelling. Eosinophilia may be present.
- Hyperpigmentation of various body sites including the skin, nails, teeth, oral mucosa, bones, thyroid, eyes (including sclera and conjunctiva), breast milk, lacrimal secretions and perspiration has been reported. This blue/black/grey or muddy-brown discolouration may be localised or diffuse. The most frequently reported site is in the skin. Pigmentation is often reversible on discontinuation of the drug, although it may take several months or may persist in some cases. The generalised muddy-brown skin pigmentation may persist, particularly in areas exposed to the sun.

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 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

Dizziness, nausea and vomiting are the adverse effects most commonly seen with overdose. Gastric lavage plus appropriate supportive treatment. Antacids and calcium salts will reduce absorption of minocycline but there is no specific antidote. Minocycline is not removed in significant quantities by haemodialysis or peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, tetracyclines, ATC code: J01A A08

Minocycline is a broad spectrum antibiotic used for the treatment of infections caused by tetracycline-sensitive organisms. Some tetracycline-resistant strains of *Staphylococci* are also sensitive.

Minocycline should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

Mechanism of action

Minocycline inhibits protein synthesis in susceptible bacteria. In common with other tetracyclines it is primarily bacteriostatic and has a similar spectrum of activity to other tetracyclines.

Susceptibility testing breakpoints

MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for minocycline and are listed here:

https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xls

Susceptibility

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable. Minocycline is usually active *in vitro* against *Propionibacterium acnes*, which is implicated in the pathogenesis of acne.

Resistance

Bacterial resistance to the tetracyclines is now common in some species and usually involves cross-resistance between the different tetracyclines.

5.2 Pharmacokinetic properties

Absorption:

Minocycline is readily absorbed from the GI tract and is not significantly affected by the presence of food or moderate amounts of milk as other tetracyclines. Absorption may be impaired by the concomitant administration of iron salts or antacids containing calcium, magnesium or aluminium salts. Normal doses of 200mg followed by 100mg every 12 hours produced plasma concentrations within the range of 1-4µg/ml.

Distribution:

Minocycline is reported to be more lipid-soluble than doxycycline and the other tetracyclines and to be widely distributed in body tissues and fluids, High concentrations being achieved in the hepatobiliary tract, lungs, sinuses and tonsils, as well as in tears, saliva, and sputum. Penetration into the cerebrospinal fluid. is relatively poor, although a higher ratio of CSF to blood concentrations has been reported with minocycline than with doxycycline. It crosses the placenta and diffuses into milk of nursing mothers. About 75% of minocycline in the circulation is bound to plasma proteins. The plasma half-life tends to be prolonged in patients with severe renal impairment. It has a lower renal clearance than doxycycline and its plasma half-life ranges from 11-23 hours.

Biotransformation:

In contrast to most tetracyclines, minocycline appears to undergo some metabolism in the liver, mainly to 9-hydroxyminocycline. It is also excreted in bile.

Elimination:

About a third of the drug may be excreted unchanged and although figures vary widely, about a third of this unchanged drug may appear in the urine and two thirds in the faeces.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Microcrystalline Cellulose
Starch 1500

Stearic Acid
Magnesium Stearate
Colloidal Silicon Dioxide

Film coating materials

Component of Opadry[®] film coating system 03B86981 BROWN

Titanium dioxide (E171)
Iron Oxide Yellow (E172)
Iron Oxide Red (E172)
Iron Oxide Black (E172)
Macrogol
Hypromellose

6.2 Incompatibilities

None

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C. Protect from light and moisture.

6.5 Nature and contents of container

The pack sizes for this product are 28, 50, 100, 250, 500 and 1000 tablets.

The product is packed in opaque plastic containers comprising of polypropylene tubes and polyethylene made tamper-evident closures.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special instructions for use/handling

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Ltd

Key House, Sarum Hill,
Basingstoke, RG21 8SR, UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0229

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

29/03/2004

10 DATE OF REVISION OF THE TEXT

11/08/2025