SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Minocycline Tablets BP 100mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Minocycline Hydrochloride PhEur equivalent to 100mg anhydrous minocycline.

Excipients with known effect:
Each 100mg tablet contains 228.00 mg lactose. Also contains Sunset yellow (E110).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Orange film-coated tablets.

Orange, circular, biconvex film-coated tablets, impressed “C” on one face and the identifying letters “M” “N” on either side of a central division line on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Minocycline is indicated for the treatment of the following infections:

1) Gonorrhoea.
2) Non-gonococcal urethritis.
3) Prostatitis.
4) 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.
5) Acute and chronic bronchitis.
6) Bronchiectasis.
7) Lung abscess.
8) Pneumonia.
9) Ear, nose and throat infections.
10) Urinary tract infections.
11) Pelvic inflammatory disease (eg salpingitis, oophoritis).
12) Skin and soft tissue infections caused by minocycline sensitive organisms.

13) Ophthalmic infections.
14) Nocardiosis.
15) Prophylactic treatment of asymptomatic meningococcal carriers.
16) 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: 200mg daily in divided doses.
Acne: 50mg twice daily. Treatment should continue for a minimum of six weeks.
Gonorrhoea: Males: 200mg initially followed by 100mg 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: 100mg twice daily for five 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: 50mg every 12 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 heriditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Minocycline tablets contain sunset yellow (E110), which may cause allergic reactions.
- *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
- *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.
- *Use in Hepatic Dysfunction:* Minocycline should be used with caution in patients with hepatic dysfunction and in conjunction with alcohol and other hepatotoxic drugs.
- *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 or pre-existing SLE, minocycline should be discontinued.
- *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 cases of severe renal insufficiency, reduction of dosage and monitoring of renal function may be required.

- *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 *eg* glossitis, stomatitis, vaginitis, pruritus ani or staphylococcal enteritis.
- *Myasthenia Gravis:* Tetracyclines can cause weak neuromuscular blockade - use with caution in Myasthenia Gravis.
- 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.
- *Hyperpigmentation:* As with other tetracyclines, minocycline may cause hyperpigmentation at various body sites (see also sections 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 photosensitivity occurs, patients should be warned to avoid direct exposure to natural or artificial light and to discontinue therapy at the first sign of discomfort.

4.5 Interaction with other medicinal products and other forms of interaction

Anticoagulants
Plasma prothrombin activity is depressed by tetracyclines. Reduced doses of any concomitant anticoagulants may be necessary.

ACE inhibitors, antacids and adsorbants
Tetracyclines bind to di-/tri-valent cations. Absorption from the gastrointestinal tract is impaired by the concomitant administration of 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.

Diuretics
Diuretics may aggravate nephrotoxicity by volume depletion.

Antibacterials
Minocycline should not be used with penicillins.

Ergotamine and ergometrine
There is an 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).

Laboratory tests
Minocycline may affect urinary urobilinogen excretion tests by reducing bacterial converters of bilirubin to urobilinogen. Minocycline 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
Animal studies have indicated that tetracyclines cross the placenta. Tetracyclines have been found in foetal tissues and can have toxic effects on the developing foetus (related to retardation of skeletal development). Studies on animals treated during early pregnancy also indicate embryotoxicity. The use of tetracyclines during the last half of pregnancy, when the teeth are developing, may cause permanent discoloration of the teeth (more common with long-term or repeated short-term use). Enamel hypoplasia has also been reported.

Breast-feeding
Tetracyclines have been detected 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

Dizziness, vertigo, headache, light-headedness, visual disturbances, tinnitus 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 is defined using the following convention:

Common: (≥1/100 to <1/10)
Uncommon: (≥1/1,000 to <1/100)
Rare: (≥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.
Blood and lymphatic system disorders Rare Very rare Not known	Eosinophilia, leucopenia, neutropenia, thrombocytopenia Haemolytic anaemia, pancytopenia. Agranulocytosis
Immune system disorders Rare Not known	Anaphylaxis/anaphylactoid reaction (including shock and fatalities). Hypersensitivity, pulmonary infiltrates, anaphylactoid purpura**,** polyarteritis nodosa.
Endocrine disorders Very rare	Abnormal thyroid function, brown-black discolouration of the thyroid.
Metabolism and nutrition disorders Rare	Anorexia.
Nervous system disorders Common Rare Very rare Not known	Dizziness (lightheadedness). Headache, hypaesthesia, paraesthesia, intracranial hypertension, vertigo. Bulging fontanelle. Convulsions, sedation.
Ear and labyrinth disorders	

Rare	Impaired hearing, tinnitus.
Cardiac disorders Rare	Myocarditis, pericarditis.
Respiratory, thoracic and mediastinal disorders Rare Very rare Not known	Cough, dyspnoea. Bronchospasm, exacerbation of asthma, pulmonary eosinophilia. Pneumonitis.
Gastrointestinal disorders Rare Very rare	Diarrhoea, nausea, stomatitis, discolouration of teeth, vomiting. Dyspepsia, dysphagia, enamel hypoplasia, enterocolitis, oesophagitis, oesophageal ulceration, glossitis, pancreatitis, pseudomembranous colitis.
Hepatobiliary disorders Rare Very rare Not known	Increased liver enzymes, hepatitis, autoimmune hepatoxicity (see section 4.4). Hepatic cholestatis, hepatic failure (including fatalities), hyperbilirubinaemia, jaundice. *Autoimmune hepatitis
Skin and subcutaneous tissue disorders Rare Very rare Not known	Alopecia, erythema multiforme, erythema nodosum, fixed drug eruption, hyperpigmentation of skin, photosensitivity, pruritis, rash, urticaria, vasculitis. Angioedema, exfoliative dermatitis, hyperpigmentation of nails, Stevens-Johnson Syndrome, toxic epidermal necrolysis. Drug rash with eosinophilia and systemic symptoms (DRESS)
Musculoskeletal and connective tissue disorders Rare	Arthralgia, lupus-like syndrome, myalgia.

Very rare	Arthritis, bone discolouration, cases of or exacerbation of systemic lupus erythematosus (SLE) (see section 4.4), joint stiffness, joint swelling.
Renal and urinary disorders Rare	Increased serum urea, acute renal failure, interstitial nephritis.
Reproductive system and breast disorders Very rare	Balanitis.
General disorders and administration site conditions Uncommon Very rare	Fever Discolouration of secretions.

* Autoimmune hepatitis: See section 4.4.

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.xlsx

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 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

The tablets also contain: hydroxypropylcellulose (E463), maize starch, magnesium stearate, lactose, methylated spirits.

The coating contains: hypromellose (E464), propylene glycol, purified talc, purified water, methylated spirits, titanium dioxide (E171), sunset yellow (E110), quinoline yellow (E104).

6.2 Incompatibilities

None known

6.3 Shelf life

Shelf-life

Three years from the date of manufacture.

Shelf-life after dilution/reconstitution

Not applicable.

Shelf-life after first opening

Not applicable.

6.4 Special precautions for storage

Store below 25°C in a dry place.

Protect from light.

6.5 Nature and contents of container

The product containers are rigid injection moulded polypropylene or injection blow-moulded polyethylene containers and snap-on polyethylene lids; in case any supply difficulties should arise the alternative is amber glass containers with screw caps and polyfoam wad or cotton wool.

The product may also be supplied in blister packs in cartons:
a) Carton: Printed carton manufactured from white folding box board.
b) Blister pack: (i) 250µm white rigid PVC. (ii) Surface printed 20µm hard temper aluminium foil.

Pack sizes: 28's, 30's, 50's, 56's, 60's, 84's, 90's, 100's, 112's, 120's, 168's, 180's, 500's, 1000's
Not all pack sizes may be marketed.

Product may also be supplied in bulk packs, for reassembly purposes only, in polybags contained in tins, skillets or polybuckets filled with suitable cushioning material. Bulk packs are included for *temporary* storage of the finished product before final packaging into the proposed marketing containers.
Maximum size of bulk packs: 50,000.

6.6 Special precautions for disposal and other handling

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Accord-UK Ltd
(Trading style: Accord)
Whiddon Valley
Barnstaple
Devon
EX32 8NS

8 MARKETING AUTHORISATION NUMBER

PL 00142/0357

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/07/1993 / 14/11/2003

10 DATE OF REVISION OF THE TEXT

11/12/2024