SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sebomin 100mg MR Capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 100mg anhydrous minocycline (as the hydrochloride).

For excipients, see 6.1

3. PHARMACEUTICAL FORM

Prolonged-release capsule, hard.

Orange opaque, hard gelatin capsules (size 2) printed “C” and “MR” in white.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The treatment of 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.

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

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

4.2 Posology and method of administration

Posology

Adults: One 100mg capsule every 24 hours.
Children over 12 years: One 100mg capsule every 24 hours.
Children under 12 years: Sebomin MR is not recommended.
Elderly: No special dosing requirements.

Treatment of acne should be continued for a minimum of 6 weeks. If there is no satisfactory response to Sebomin MR after six months, the treatment should be discontinued and other therapies considered. If Sebomin MR is to be continued for longer than six months, patients should be monitored at least three monthly thereafter for signs and symptoms of hepatitis or SLE or unusual pigmentation of the skin. (see Special warnings and precautions for use).

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.

Method of Administration:

For oral administration. To reduce the risk of oesophageal irritation and ulceration, the capsules should be swallowed whole with plenty of fluid, while sitting or standing. They should not be taken with food as this affects the absorption of minocycline.

4.3 Contraindications

- Known hypersensitivity to tetracyclines or to any of the excipients.
- Pregnancy and lactation
- Children under 12 years
- Complete renal failure.

4.4 Special warnings and precautions for use

Hypersensitivity pneumonitis: Pulmonary infiltrates and eosinophilia have been reported with monicycline. In most cases the pneumonitis resolved when minocycline was stopped but steroids may be needed in some cases, and residual lung damage can occur. Patients should be advised that if they develop breathing difficulties they should stop taking minocycline and immediately contact a physician.

Use in Hepatic Dysfunction: Minocycline should be used with caution in patients with hepatic dysfunction and in conjunction with alcohol and other hepatotoxic drugs. It is recommended that alcohol consumption should remain within the Government's recommended limits.

Auto-immune Disorders: Rare cases of auto-immune hepatotoxicity and isolated cases of systemic lupus erythematosus (SLE) and also exacerbation of

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.

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, e.g. enteritis, 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 be 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.

The capsule shell contains sunset yellow (E110), which can cause allergic - type reactions including asthma. Allergy is more common in those people who are allergic to aspirin.

Use in children: The use of tetracyclines during tooth development in children under the age of 12 years may cause permanent discolouration (see above). Enamel hypoplasia has also been reported.

4.5 Interaction with other medicinal products and other forms of interaction

- ACE Inhibitors - absorption of minocycline decreased by quinapril tablets (which contains magnesium carbonate).
- Antacids and Adsorbants - absorption of minocycline is impaired by the concomitant administration of antacids, iron, calcium, aluminium, magnesium and zinc salts (interactions with specified salts, antacids and kaolin). Dosages should be maximally separated. It is recommended that any indigestion remedies, vitamins, or other supplements containing these salts are taken at least 3 hours before or after a dose of minocycline.
- Antibacterials - minocycline should not be used with penicillins.
- Anticoagulants - tetracyclines depress plasma prothrombin activity and reduced dosages of concomitant anticoagulants may be necessary
- Atovaquone – tetracyclines reduce plasma concentrations of atovaquone.
- Colestipol and colestyramine – possible reduced absorption of tetracyclines by colestipol and colestyramine.
- Diuretics – may aggravate nephrotoxicity by volume depletion.
- Ergotamine and ergometrine – increased risk of ergotism.
- Methysergide – increased risk of ergotism with concurrent methysergide.
- Oral Contraceptives - both can induce hyperpigmentation.
- Oral iron – the absorption of tetracyclines is reduced by oral iron; the absorption of oral iron is decreased by tetracyclines.
- Oral typhoid vaccine – antibacterials inactivate oral typhoid vaccine. Antibacterials should be avoided for 3 days before and after oral typhoid vaccination.
- 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 4.4 Special warnings and precautions)
- Ulcer healing Drugs – absorption of minocycline decreased by sucralfate and bismuth salts.
- 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 Pregnancy and lactation

Pregnancy:
Results of animal studies indicate that tetracyclines cross the placenta and 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.

Minocycline should not therefore be used in pregnancy unless considered essential.

The use of drugs of the tetracycline class during tooth development (last half of pregnancy) may cause permanent discolouration 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.

Lactation:
Tetracyclines have been found in the milk of lactating women who are taking a drug in this class. Permanent tooth discolouration may occur in the developing infant and enamel hypoplasia has been reported.

4.7. Effects on ability to drive and use machines

Headache, light-headedness, visual disturbances, dizziness, tinnitus and vertigo and rarely impaired hearing have occurred with minocycline and patients should be warned about the possible hazards of driving or operating machinery during treatment. Patients should be warned that they should not drive, operate machinery or take part in any activities where, if affected, they could put themselves or others at risk.

4.8 Undesirable effects

Common: ≥1%
Uncommon: ≥0.1% and < 1%
Rare: ≥0.01% and < 0.1%
Very Rare: < 0.01%

MedDRA system organ class	Symptom
Blood and lymphatic system disorders Rare Very rare Isolated reports	 Eosinophilia, leucopenia, neutropenia, thrombocytopenia Haemolytic anaemia, pancytopenia. Agranulocytosis
Cardiac disorders Rare	Myocarditis, pericarditis.
Ear and labyrinth disorders Rare	Impaired hearing, tinnitus.
Endocrine disorders Very rare	Abnormal thyroid function, brown-black discolouration of the thyroid.
Gastrointestinal disorders Rare Very rare	 Diarrhoea, nausea, stomatitis, discolouration of teeth, vomiting. Dyspepsia, dysphagia, enamel hypoplasia,

MedDRA system organ class	Symptom
	enterocolitis, oesophagitis, oesophageal ulceration, glossitis, pancreatitis, pseudomembranous colitis.
General disorders and administration site conditions Uncommon Very rare	 Fever Discolouration of secretions.
Hepatobiliary disorders Common Rare Very rare Not known	 Increases in liver function test values Increased liver enzymes, hepatitis, autoimmune hepatoxicity. (See Section 4.4 Special warnings and Special precautions for use). Hepatic cholestatis, hepatic failure (including fatalities), hyperbilirubinaemia, jaundice. *Autoimmune hepatitis
Immune system disorders Rare Isolated reports	 Anaphylaxis/anaphylactoid reaction (including shock and fatalities), polyarteritis nodosa. Hypersensitivity, pulmonary infiltrates, anaphylactoid purpura.
Infections and infestations Very rare	 Oral and anogenital candidiasis, vulvovaginitis.
Metabolism and nutrition disorders Rare	 Anorexia.
Musculoskeletal and connective tissue disorders Rare Very rare	 Arthralgia, lupus-like syndrome, myalgia. 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.
Nervous system disorders Common Rare	 Dizziness (lightheadedness). Headache, hypaesthesia, paraesthesia, intracranial hypertension, vertigo.

MedDRA system organ class	Symptom
Very rare Isolated reports	Bulging fontanelle. Convulsions, sedation.
Renal and urinary disorders Rare	Increased serum urea, acute renal failure, interstitial nephritis.
Reproductive system and breast disorders Very rare	Balanitis.
Respiratory, thoracic and mediastinal disorders Common Rare Very rare Isolated reports	 Wheezing. Cough, dyspnoea. Bronchospasm, exacerbation of asthma, pulmonary eosinophilia. Pneumonitis.
Skin and subcutaneous tissue disorders Common Rare Very rare Not known	 Maculopapular and erythematous rashes. 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)

* 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

4.9 Overdose

Dizziness, nausea and vomiting are the adverse effects most commonly seen with overdose. There is no specific antidote. In cases of overdose, discontinue medication, treat symptomatically and with appropriate supportive measures. Minocycline is not removed in significant quantities by haemodialysis or peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotheraputic group: Tetracycline, ATC code: J01A A08

Sebomin MR contain the active ingredient minocycline as minocycline hydrochloride, a semi-synthetic derivative of tetracycline.
Minocycline has a long serum half-life and can be administered at 12 hour intervals, the modified release form can be given once daily.

Minocycline interferes with the third stage of bacterial protein synthesis. After amino acids are activated and attached to t-RNA (transfer RNA), the resulting amino acyl-t-RNA migrates to the bacterial ribosome for synthesis of proteins. Minocycline binds to the 30s subunit on the ribosome and inhibits binding of the aminoacyl-t-RNA molecules.
There is also evidence that minocycline may cause alterations in the cytoplasmic membrane, thereby allowing leakage of nucleotides and other compounds from the cell. This would explain the rapid inhibition of DNA replication that ensues when cells are exposed to concentrations of minocycline greater than that needed to inhibit protein synthesis.
In higher concentration, minocycline inhibits mammalian protein synthesis and may aggravate pre-existing renal functional impairment. The drug may interfere with parenteral nutrition in post operative patients by inhibiting utilization of amino acids for protein synthesis.
Minocycline is reported to be active against both Gram negative and Gram positive organisms.

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

5.2 Pharmacokinetic properties

Absorption

Oral bioavailability for minocycline has been reported to be 90%.
One report has demonstrated that food did not significantly affect the absorption of minocycline following 50 mg oral doses. However, another study reported that minocycline absorption was decreased by 77%, 27% and 13% when given with iron, milk and food.

Distribution

Total protein binding of minocycline has been reported to be in the order of 76%.
Other sites of distribution of minocycline include the following:
AQUEOUS HUMOR
Minocycline administered orally with a loading dose of 200 mg followed by 2 doses of 100 mg 12 hours apart produce adequate drug concentration in the aqueous humor of noninflamed eyes. The plasma to aqueous humor ratio was approximately 2:1.
CEREBROSPINAL FLUID
Minocycline has been reported to cross the blood/brain barrier to a higher degree than doxycycline. However, passage of either drug has been shown to be significantly decreased in patients with uninflamed meninges.
GINGIVAL FLUID
The mean gingival crevicular fluid drug concentration of 8.03 +/- 1.64 mcg/ml was reported after 7 days of oral minocycline 200 mg in patients with

moderate to severe periodontal disease. Mean serum concentration was 2.58 +/- 0.32 mcg/ml.
JOINT FLUID CONCENTRATIONS
Following 200 mg oral doses of minocycline, joint fluid levels 3 to 12 hours following the dose were 0.43 to 0.88 mcg/ml.
SALIVA/TEARS
Minocycline achieved significant levels in saliva and tears sufficient to inhibit most strains of meningococci. Following oral doses of 100 mg every 12 hours for 5 days, the concentration of drug in saliva and tear equalled or was greater than the average MIC for meningococci for up to 12 hours after the dose. Two hours following an oral dose, concentrations of minocycline in saliva and tears were at 0.3 mcg/mL and 0.4 mcg/mL, respectively.

SINUS SECRETIONS
Following a dose of 100 mg twice daily for 4 days in patients with sinusitis a sinus level of 1.06 mcg/5 mL was found. The mean minocycline serum level was 3.16 mcg/ml, giving a sinus secretion to serum level ratio of 0.34:1.

Metabolism

An inactive metabolite, 9-hydroxyminocycline has been isolated.

Elimination

Minocycline has a very low renal clearance as compared to other tetracyclines. However, urinary concentrations approximating 10 times that of serum are attained for the first 4 to 6 hours following an oral dose.
Minocycline is excreted 19% in the faeces, this level is much lower than most other tetracyclines.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

glycerol monostearate 40-55,
microcrystalline cellulose 101 (E460(i)),
povidone K-30 (E1201),
purified talc (E553b).

Capsule shell

gelatin,
purified water,
titanium dioxide (E171),
sunset yellow (E110),
quinoline yellow (E104),

Printing ink

shellac (E904),
ethyl alcohol,
isopropyl alcohol,
propylene glycol,
butyl alcohol,
povidone (E1201),
sodium hydroxide,
titanium dioxide (E171).

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

24 months.

6.4 Special Precautions for Storage

Do not store above 30°C.
Polypropylene container - store in the original container,
PVC/aluminium blister pack - keep container in the outer carton.

6.5 Nature and Contents of Container

PVC/aluminium blister pack in outer cardboard container
28, 30, 56, 60, 84, 90
Polypropylene container with polyethylene cap
100, 112, 120, 200, 250, 500

Not all pack sizes may be marketed.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

PL 00142/0526

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19/03/2009

10 DATE OF REVISION OF THE TEXT

19/11/2024