Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Minox 50 mg Film-Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains Minocycline 50 mg as Minocycline Hydrochloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Round, yellow-brown tablets with a smooth surface.

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. Typical indications include:

- ear, nose and throat infections
- respiratory tract infections such as pneumonia, bronchiectasis,
- lung abscess, acute and chronic bronchitis
- prostatitis, venereal diseases (gonorrhoea)
- urinary tract infections
- pelvic inflammatory disease (salpingitis, oophoritis)
- skin and soft tissue infections
- acne
- ophthalmological infections
- nocardiosis,
- prophylactic treatment of asymptomatic meningococcal carriers.
- preventative treatment before and after surgery
- actinomycosis, anthrax patients, with a penicillin allergy

4.2 Posology and method of administration

Route of Administration: Oral

Administration:

Unlike earlier tetracyclines, absorption of Minocycline is not significantly impaired by food or moderate amounts of milk. In severe infections, treatment should be continued for up to three days after characteristic symptoms of the infection have subsided.

Because of the incidence of rheumatic fever or glomerulonephritis following streptococcal infection, therapy should be continued for 10 days even though symptoms have subsided. Treatment of acne vulgaris should be continued for a maximum of six weeks.

Recommended Dosage Schedule:

Adults:

1. Routine antibiotic use: 200mg daily in divided doses.
2. Acne Vulgaris: 50mg twice daily. Treatment of acne should be continued for a minimum of six weeks and where possible limited to a maximum of six months. Treatment should only be continued if there is a satisfactory response and if liver function and ANF is monitored (see Contra-indication & Warnings).
3. Gonorrhoea: In adult males, 200mg initially, followed by 100mg every 12 hours for a minimum of 4 days with post therapy cultures within 2-3 days. Adult females may require therapy for 10-14 days at the same dosage indicated for males.
4. Prophylaxis of asymptomatic meningococcal carriers: 100mg twice daily for 5 days usually followed by a course of rifampicin.

Children:

For children above 8 years of age the recommended dosage of Minocycline is one 50mg tablet every 12 hours. Minocycline is not recommended for children under 8 years old.

Elderly:

Minocycline may be used at the normal recommended dosage in elderly patients even with mild to moderate renal impairment.

4.3 Contraindications

Minox 50 should not be administered to patients:

- who are hypersensitive to the active substance, other similar antibiotics such as tetracyclines or doxycycline, or to any of the excipients listed in section 6.1
- with systemic lupus erythematosus
- with severe hepatic dysfunction
- with complete kidney failure
- who are pregnant or breast-feeding
- children under 8 years of age

4.4 Special warnings and precautions for use

Minocycline should be used with caution in patients with mild to moderate hepatic dysfunction and in conjunction with alcohol or other potentially hepatotoxic drugs.

Rare cases of auto-immune hepatotoxicity (including acute liver failure), 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, Minox should be discontinued.

Cross-resistance between tetracyclines may develop in micro-organisms and cross sensitisation in patients. Minox should be discontinued if there are symptoms of overgrowth of resistant organisms e.g. enteritis, glossitis, stomatitis, vaginitis, pruritis and/or staphylococcal enteritis.

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 extreme renal insufficiency, reduction of dosage and monitoring of renal function may be required. The anti-anabolic action of tetracyclines may cause an increase in blood urea nitrogen (BUN). In patients with significantly impaired renal function, higher serum levels of tetracyclines may lead to azotaemia, hyperphosphataemia and acidosis. If renal impairment exists, even unusual oral and parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity.

Minocycline may cause hyperpigmentation at various body sites (see sec 4.8). Hyperpigmentation may present regardless of dose or duration of therapy but develop more commonly during long term treatment. Patients should be advised to report any unusual pigmentation without delay and Minox should be discontinued. People with a darker skin often exhibit more intense hyperpigmentation than individuals with fair skin.

Minocycline should not be used by patients sensitive to sunlight or artificial light (e.g. sunbeds).

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.

Caution is advised in patients with myasthenia gravis as tetracyclines can cause weak neuromuscular blockade.

Cases of abnormal thyroid function, such as thyroiditis, thyroid nodule, goiter and thyroid cancer, have been reported in patients taking minocycline during the post marketing period (see sec 4.8). When minocycline therapy is given over prolonged periods, monitoring for signs of thyroid cancer should be considered.

Symptoms of vestibular nature have been observed during treatment with minocycline. These symptoms occur more frequently in women than in men and are reversible. When dizziness occurs, it may be desirable to adjust the dosage. Caution is required particularly in patients suffering from Meniere's syndrome. When vestibular symptoms and other side effects occur, such as visual disturbances, hallucinations and scotoma, treatment with minocycline should be terminated.

Clostridium difficile associated diarrhoea (CDAD) has been reported with the use of nearly all antibacterial agents, including minocycline hydrochloride, and may range in severity from mild diarrhoea to fatal colitis.

Use in the elderly

Clinical studies of minocycline did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently than younger subjects.
Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy.

Use in children

Tetracyclines may cause a yellow to brown discolouration of the teeth and enamel hypoplasia in the developing foetus or child and therefore Minocycline should only be administered if considered essential to pregnant or lactating women and to children under eight years of age. The treatment period should be as short as feasible and repeated courses should be avoided.

Laboratory monitoring:
Periodic laboratory evaluations of organ system function, including haematopoietic, renal and hepatic, should be conducted.

4.5 Interaction with other medicinal products and other forms of interaction

Absorption of Minocycline is impaired by the concomitant administration of iron salts and by antacids containing sucralfate, calcium, magnesium, aluminium, bismuth and zinc salts and quinapril which contains a magnesium carbonate excipient. Do not take these medicines simultaneously. It is recommended that any indigestion remedies, vitamins, or other supplements containing these are taken at least 3 hours before or after a dose of Minox.

Avoid concomitant use with kaolin Activated charcoal and ion exchangers have a negative effect on the absorption when administered concomitantly.

Tetracycline therapy should not be used in conjunction with penicillin or cephalosporin antibiotics. Bacteriostatic drugs may interfere with the bactericidal action of penicillin.

Tetracyclines depress plasma prothrombin activity and reduced doses of concomitant anticoagulants may be necessary.

Diuretics may aggravate nephrotoxicity by volume depletion.

Unlike earlier tetracyclines, absorption of minocycline is not significantly impaired by food or moderate amounts of milk.

There is an increased risk of ergotism when ergot alkaloids or their derivatives are given with tetracyclines.

Administration of isotretinoin or other systemic retinoids or retinol should be avoided shortly before, during and shortly after minocycline therapy. Each of these agents alone has been associated with pseudotumour cerebri (benign intracranial hypertension) (see 4.4 Special warnings and precautions for use).

4.6 Fertility, pregnancy and lactation

Minox 50 should only be administered to pregnant and lactating women if considered essential by the physician. 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.

Minocycline, like other tetracycline-class antibiotics, crosses the placenta and may cause foetal harm when administered to a pregnant woman. In addition, there have been post-marketing reports of congenital abnormalities including limb reduction. If minocycline is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to the foetus.

Minocycline could cause permanent discolouration and under development of tooth enamel.
This adverse reaction is more common during long term use of the drugs but has been observed following repeated short term courses.

Use in 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

Patients who experience light-headedness, dizziness and vertigo whilst taking Minox 50 should refrain from driving or operating machinery.

4.8 Undesirable effects

The adverse reactions considered at least possibly related to treatment are listed below sorted by MedDRA system organ class. Frequencies are defined as very common (≥ 1/10); common (> 1/100 to < 1/10); uncommon (> 1/1000 to <1/100); rare (> 1/10 000 to < 1/1000); very rare (< 1/10 000). Not known (frequency cannot be estimated from available data)

Infections and infestations:
Very rare: Oral and anogenital candidiasis, vulvovaginitis.

Blood and lymphatic system disorders:
Rare: Eosinophilia, leucopenia, neutropenia, thrombocytopenia.
Very rare: Haemolytic anaemia, pancytopenia.
Not known: Agranulocytosis, prothrombin activity may be depressed.

Immune system disorders:
Uncommon: Urticaria, angioneurotic oedema
Rare: Polyarthralgia, anaphylactic reaction, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus, hypersensitivity/eosinophilic pneumonitis
Not known: Serum sickness-like reaction, autoimmune disorders like vasculitis and lupus erythematosus/lupus-like reactions; drug rash with eosinophilia and systemic symptoms (DRESS) syndrome, most often with hepatic, pulmonary and renal involvement; severe acute hypersensitivity reaction up to anaphylactic shock (see section 4.4).

Endocrine disorders:
Very rare: Abnormal thyroid function, including thyroiditis, thyroid nodule, goiter and thyroid cancer. Brown-black discolouration of the thyroid.

Metabolism and nutrition disorders:
Rare: Anorexia.

Nervous system disorders:
Common: Dizziness (light-headedness).
Rare: Headache, hypaesthesia, paraesthesia, pseudotumour cerebri, vertigo.
Very rare: Bulging fontanelle.
Not known: Convulsions, sedation.

Eye disorders:
Not known: Visual disturbances, scotoma and double vision. Pigmentation of the cornea, sclera and retina has been observed.

Ear and Labyrinth disorders:
Not known: Vestibular disturbances, impaired hearing, tinnitus.

Cardiac disorders:
Very rare: Myocarditis, pericarditis.

Respiratory, thoracic and mediastinal disorders:
Rare: Cough, dyspnoea.
Very rare: Bronchospasm, exacerbation of asthma, pulmonary eosinophilia.
Not known: Pneumonitis.

Gastrointestinal disorders:
Rare: Diarrhoea, nausea, stomatitis, discolouration of teeth (including adult tooth discolouration), vomiting.
Very rare: Dyspepsia, dysphagia, enamel hypoplasia, enterocolitis, oesophagitis, esophageal ulceration, glossitis, pancreatitis, pseudomembranous colitis. There are also reports of: Oral cavity discolouration (including tongue, lip and gum).

Hepatobiliary disorders:
Rare: Increased liver enzymes, hepatitis, rare cases of autoimmune toxicity (see Section 4.4 Special warnings and precautions for use).
Very rare: Hepatic cholestatis, hepatic failure (including fatalitie) hyperbilirubinaemia, jaundice.
Not known: Autoimmune hepatitis.

Skin and subcutaneous tissue disorders:
Rare: Alopecia, erythema multiforme, erythema nodosum, fixed drug eruption, hyperpigmentation of skin, photosensitivity, pruritis, rash, urticaria.
Very rare: Angioedema, exfoliative dermatitis, hyperpigmentation of nails, Stevens-Johnson Syndrome, toxic epidermal necrolysis, vasculitis.

Musculoskeletal, connective tissue and bone disorders:
Rare: Arthralgia, lupus-like syndrome, myalgia.
Very rare: Arthritis, bone discolouration, cases of or exacerbation of systemic lupus erythematosus (SLE) (see Section Special warnings and precautions for use), joint stiffness, joint swelling.

Renal and urinary disorders:
Rare: Increased BUN
Very rare: Acute renal failure, interstitial nephritis.

Reproductive system and breast disorders:
Very rare: Balanitis.

General disorders and administration site conditions:
Uncommon: Fever.
Very rare: Discolouration of secretions.

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.
- Eosinophilia and systemic symptoms (DRESS) in patients treated for acne. Early recognition of DRESS symptoms, specialist referral and immediate discontinuation of minocycline are recommended. Post marketing data show that fatal cases of eosinophilia and systemic symptoms (DRESS) have occurred in patients with acne treated with minocycline.

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 black/blue/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.

Hepato-biliary system
In common with other tetracyclines increases in liver function test values and rarely hepatitis, and acute liver failure have been reported. This may or may not be associated with autoantibodies. In prolonged therapy (>6 months) periodic liver function tests and anti-nuclear factor assays should be performed.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms:
Dizziness, nausea and vomiting are the adverse effects most commonly seen with overdose.

Treatment:
Discontinue Minox. There is no specific antidote to Minocycline Hydrochloride – Gastric lavage plus appropriate supportive treatment should be instituted in cases of overdosage.
Minocycline is not removed in significant quantities by haemodialysis or peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Codes: JO1AA08

General anti-infective for systemic use: Antibacterials for systemic use: Tetracyclines

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

Typical indications include, ear, nose and throat infections, acute and chronic bronchitis, bronchiectasis, lung abscess, pneumonia prostatitis, venereal disease, urinary tract infections, salpingitis, skin and soft tissue infections, acne, ophthalmological infections, nocardiosis, prophylactic treatment of asymptomatic meningococcal carriers.

5.2 Pharmacokinetic properties

Minocycline hydrochloride is readily absorbed from the gastro-intestinal tract and is not significant affected by the presence of food or moderate amounts of milk, although absorption is impaired by the concomitant administration of iron salts or antacids containing calcium, magnesium or aluminium salts. As Minocycline hydrochloride is more lipid-soluble than doxycycline and other tetracyclines it is widely distributed in body tissues and fluids, including the cerebrospinal fluid. About 75% of Minocycline hydrochloride in the circulation is bound to plasma proteins; its half-life ranges from 11 to 23 hours. The plasma half-life tends to be prolonged in patients with severe renal impairment.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone K25
Sodium Starch Glycolate (Type A)
Microcrystalline Cellulose
Colloidal Anhydrous Silica
Magnesium Stearate

Film-coating

Hypromellose 6mPa.s
Titanium Dioxide (E171)
Yellow Ferric Oxide (172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25 °C.

Store in the original package.

6.5 Nature and contents of container

Minox 50mg Film-coated Tablets are packed in blisters of PVC/Aluminium. The blisters are packed in an outer cardboard carton in pack sizes of 10, 50 and 100 tablets.

Not all pack sizes may be marketed.

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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Rowex Ltd.
Bantry
County Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/013/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th May 1986

Date of last renewal: 9th May 2006

10 DATE OF REVISION OF THE TEXT

September 2016