SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Doxycyklin EQL Pharma 100 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains doxycycline monohydrate corresponding to 100 mg doxycycline.

Excipient with known effect: Lactose monohydrate 75 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

Greyish- yellow, round biconvex tablet with score line. Diameter 9 mm.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Doxycyklin EQL Pharma is indicated in adults and children over 12 years.

Doxycyklin EQL Pharma is intended for:
Pneumonia caused by *Mycoplasma pneumoniae*, *Chlamydophila psittaci (*ornithosis*)* or *Chlamydophila pneumoniae* (TWAR).
Acute exacerbations in chronic bronchitis.
Urogenital infections caused by *Chlamydia trachomatis.*
Borrelia infections: Erythem migrans in penicillin allergy or signs of dissemination like neuroborreliosis.
In acute sinusitis, Doxycyklin EQL Pharma should be reserved for patients who are hypersensitive to penicillins or have failed in treatment with them.

4.2 Posology and method of administration

Normal dosage:
Adults and children over 12 years old
First day 2 tablets, then 1 tablet daily. If necessary, 2 tablets may be given daily throughout the treatment period.

Neuroborreliosis:
Adults and children over 12 years old
Two tablets 1-2 times daily for 10-14 days. The shorter treatment duration, 10 days, can be used at dosing in the higher range. In these cases, dose reduction (300 mg daily) is recommended if the patient's weight is less than 50 kg.

Doxycyklin EQL Pharma should be swallowed with liquid. The tablets should not be taken in a lying position.

To reduce the risk of gastrointestinal side effects, the tablets should be taken during meals.

Renal impairment
Doxycyklin EQL Pharma can be given in normal dose even in impaired renal function.

In parenteral nutrition, there is minimal risk of impact on nitrogen balance in the concomitant administration of Doxycyklin EQL Pharma.

4.3 Contraindications

Hypersensitivity to the active substance doxycycline, or to tetracyclines or to any of the excipients in the tablet.

4.4 Special warnings and precautions for use

A possible risk of decreased absorption and decreased plasma concentration of doxycycline should be taken into consideration in patients who lack hydrochloric acid production or who are treated with medicines that inhibit hydrochloric acid secretion in the ventricle (see section 4.5).

Severe cutaneous adverse reactions (SCARs)

Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)**,** and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with doxycycline treatment.

Patients should be advised of the signs and symptoms of the severe cutaneous adverse reactions and should seek medical advice from their physician immediately when observing any indicative signs or symptoms. If signs and symptoms suggestive of these reactions appear, doxycycline should be withdrawn immediately and an alternative treatment considered (as appropriate). If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of doxycycline, treatment with doxycycline must not be restarted in this patient at any time.

Photodynamic reactions may occur. Therefore, the patient should avoid direct sun exposure and also artificial UV radiation (eg sunlight, solarium) during treatment. This risk may theoretically last for at least 5 days after completion of treatment due to relatively long half-life and high fat solubility.

Diarrhoea / pseudomembranous colitis caused by *Clostridium difficile* occurs. Therefore, patients with diarrhoea should therefore be carefully monitored.

Caution should be exercised when treating patients with myasthenia gravis who may be at risk of worsening of the condition.

Paediatric population
Children under 8 years of age should only be treated with doxycycline in strict indication due to incorporation into the growing skeleton and risk of *enamel hypoplasia.*

Some patients with spirochete infections may experience a Jarisch-Herxheimer reaction shortly after doxycycline treatment is started. Patients should be reassured that this is a usually self-limiting consequence of antibiotic treatment of spirochete infections.

Doxycyklin EQL Pharma contains lactose monohydrate. 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

The following combinations of Doxycyklin EQL Pharma should be avoided:

Oral divalent iron inhibits the absorption of doxycycline.

Antacids containing di- or trivalent cations form chelate complexes with tetracyclines and impair their absorption. Sodium bicarbonate has been reported to inhibit the absorption of tetracyclines due to change in pH.

Didanosine tablets contain trivalent cations that form chelate complexes with tetracyclines, and the absorption of tetracyclines may thereby deteriorate. Experimental studies are however not available.

Kinapril tablets contain magnesium that like antacids containing di- or trivalent cations form chelate complexes with tetracyclines and the absorption of tetracyclines is thereby impaired.

Concomitant administration with atovaquone significantly reduces the plasma concentration of atovaquone.

The following combinations of Doxycyklin EQL Pharma may require dose adjustment:

Drugs that inhibit the hydrochloric acid secretion in the ventricle, such as proton pump inhibitors, may inhibit the absorption of doxycycline from Doxycyklin EQL Pharma. A study in which healthy subjects were treated with omeprazole 40 mg daily for one week and then took a single dose doxycycline monohydrate resulted in a reduction of doxycycline AUC by 44% and Cmax by 56%. The clinical relevance of the study has not been determined.

Oral *calcium* inhibits the absorption of tetracyclines, and these agents should therefore be administered at least three hours apart

Long-term treatment with *phenobarbital*, *phenytoin* and *carbamazepine* shortens the plasma half-life of doxycycline, which can cause the therapeutic concentration of doxycycline to not be maintained for 24 hours. Doxycyklin EQL Pharma should therefore be given twice daily in these cases.

In a study of 10 patients with brucellosis, *rifampicin* reduced the plasma concentration of doxycycline (probably due to induced metabolism). Two patients did not respond to treatment.

Anticoagulants: Since tetracyclines in long-term therapy have been shown to decrease the activity of prothrombin in plasma, the dose of anticoagulants may need to be reduced.

Alcohol shortens the half-life of doxycycline.

4.6 Fertility, pregnancy and lactation

Fertility
No known effect.

Pregnancy
Studies on animals have not shown any teratogenic effect. In humans use of tetracyclines during a limited number of pregnancies has, at present, not shown any specific malformation. Tetracyclines can cause enamel hypoplasia and discoloration of the teeth during the time when the child's teeth are mineralized (last half of pregnancy, neonatal period and up to about 8 years of age). Tetracyclines are also incorporated into the growing skeleton. During the last half of pregnancy doxycycline should only be given after special consideration.

Breast-feeding
Doxycycline passes into breast milk. Doxycycline may only be used by nursing mothers for a short period of time. Long-term use of doxycycline may result in significant absorption of the breastfeeding infant and is therefore not recommended due to the theoretical risk of dental discoloration and reduced bone growth in the nursing child

4.7 Effects on ability to drive and use machines

Doxycyklin EQL Pharma has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Up to 10% of patients treated with Doxycyklin EQL Pharma tablets may experience side effects. These are usually of gastrointestinal nature and can be minimized if the medicinal product is taken with food.

Within the classification of organ systems, adverse reactions are reported under headings that indicate frequency ranges with the following categories: very common (≥1 / 10), common (≥1 / 100, <1/10), uncommon (≥1 / 1000, <1/100) , rare (≥1 / 10,000, <1/1000), very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Classification		
Blood and lymphatic system disorders	Rare	Trombocytopeni
Immune system	Not known	Jarisch-Herxheimer reaction (see section 4.4)
Nervous system disorders	Rare	Increased intracranial pressure
Gastrointestinal disorders	Common	Nausea, vomiting, diarrhoea
	Rare	Pseudomembranous colitis
	Not known	Oesophagitis/ oesophageal ulcer
Skin and subcutaneous disorders	Uncommon	Skin rash, urticaria, photosensibility
	Rare	Onycholys, erythema multiforme, mucocutaneous syndrome, Stevens-Johnson syndrome, Toxic epidermal necrolysis
	Not known	Drug reaction with eosinophilia and systemic symptoms (DRESS)
General disorders and administration site conditions	Rare	Anaphylactic reaction, anaphylactic shock

When treating with tetracyclines during the time the teeth are mineralized, enamel hypoplasia and discoloration of the teeth can occur. Children under the age of 8 should therefore not be treated with tetracyclines, nor women during the last half of pregnancy.

Fungal overgrowth due to disturbance of the normal microflora occurs as with other broad spectrum antibiotics. This can give, for example glossitis, vaginitis.

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 national reporting system listed in Appendix V.*

4.9 Overdose

Toxicity
Relatively low acute toxicity. However, in the case of renal impairment, the administration of high therapeutic doses has given liver and kidney effects (several letal cases known). Liver injury has been observed primarily in parenteral administration where pregnant women are particularly sensitive.

Symptoms
Nausea, vomiting, diarrhoea. Increased intracranial pressure has been described. In case of impaired renal function, further impairment may occur. Hepatic effects. Risk of enamel hypoplasia in children.

Treatment
If warranted, ventricular drainage, carbon, antacids. Symptomatic treatment. Dialysis can be considered in case of massive exposure and concomitant renal failure.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Tetracyclines, ATC code: J01AA02

Doxycycline is a tetracycline derivative that acts by inhibiting ribosomal protein synthesis and affecting both extra and intracellular pathogens. The effect is mainly bacteriostatic.

Antibacterial spectrum

Sensitive	Betahemolytic streptococci group A, C och G Pneumococci *Staphylococcus aureus* *Moraxella catarrhalis* *Haemophilus influenzae* *Pasteurella multocida* *Fransicella tularensis* and *Brucella* *Borrelia burgdorferi* *Mycoplasma pneumoniae* *Ureaplasma urealyticum* *Chlamydia trachomatis,* *Chlamydophila pneumoniae* *Chlamydophila psittaci* *Rickettsia, Coxiella burnetii*
Intermediate	
Resistent	Betahemolytic streptococci group B, enterococci Gonococci, meningococci Gramnegative intestinal bacteria Pseudomonas Anaerobic bacteria including *Bacteroides fragilis* och *Clostridium difficile*

Resistance is present (1-10%) in pneumococci, *Haemophilus influenzae* and *Staphylococcus aureus* and is common (> 10%) in betahemolytic streptococci group A.

Cross resistance exists between all tetracycline derivatives. The resistance is often plasmid mediated.

The resistance situation varies geographically and information about the local resistance conditions should be obtained through the local microbiological laboratory.

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 doxycycline and are listed here:
https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

5.2 Pharmacokinetic properties

Absorption
Doxycycline is rapidly and almost completely absorbed (approx. 93%). Absorption is affected only marginally by milk and other food.
Bioavailability is approximately 93%. Therapeutic serum concentration (approx. 1 µg / ml) is reached within 30 minutes and maximum serum concentration (approx. 3 µg / ml) within 2-3 hours.

Distribution
High lipid solubility facilitates tissue distribution and therapeutic tissue concentrations are thereby achieved in most organs.
The binding to serum proteins amounts to 80-90%.

Biotransformation
Doxycycline is metabolised to a very small extent.

Elimination
Within 72 hours approximately 40% of the administered doxycycline is excreted in active form with urine and approximately 5% with faeces. Remaining amount is excreted in inactive form, chelated, with faeces. The biological half-life is 18-22 hours

Renal impairment
In case of impaired renal function, excretion in the feces of chelate-bound doxycycline increases. Doxycyklin EQL Pharma can therefore be given in normal dose to patients with impaired renal function. Plasma levels are not significantly affected by hemodialysis.

5.3 Preclinical safety data

Hyperpigmentation of thyroid and tubular renal degeneration has been noted in repeated dose toxicity studies. The clinical relevance of these findings is unknown.

Doxycycline has shown positive results in some genotoxic studies. Related tetracyclines have shown evidence of cancerogenic effects (adrenal and thyroid tumors) in rat studies. At doses greater than 50 mg / kg / day, fertility and reproduction were negatively affected in rats. Doxycycline is known to cross placenta, and literature data indicate that tetracyclines may have a toxic effect on a growing fetus

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Sodium starch glycolate
Hypromellose
Lactose monohydrate
Talc

Magnesium stearate
Colloidal silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

No special storage conditions.

6.5 Nature and contents of container

Al-PVC-PVDC blister with 10 or 15 tablets in packages of 10, 15, 20, 30 and 100 tablets.

6.6 Special precautions for disposal

No special requirements for disposal

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 2013-01-24
Date of latest renewal: 2018-01-24

10. DATE OF REVISION OF THE TEXT

2026-04-22