Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Doxycycline 100 mg hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains doxycycline hyclate equivalent to 100 mg doxycycline.
Excipient with known effect
Each hard capsule contains 98.8 mg lactose (as monohydrate).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard capsule
Ivory yellow hard capsule (24.4 mm in length).

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Doxycycline has been found clinically effective in the treatment of a variety of infections caused by susceptible strains of Gram-positive and Gram-negative bacteria and certain other micro-organisms.

Respiratory tract infections:
Pneumonia and other lower respiratory tract infections due to susceptible strains of *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Klebsiella pneumoniae, Moraxella catarrhalis* and other organisms.
Mycoplasma pneumoniae.
Treatment of chronic bronchitis, sinusitis.

Urinary tract infections:
Infections caused by susceptible strains of Klebsiella species, Enterobacter species, *Escherichia coli*, *Streptococcus faecalis* and other organisms.

Sexually transmitted diseases:
Infections due to *Chlamydia trachomatis* including uncomplicated urethral, endocervical or rectal infections. Non-gonococcal urethritis caused by *Ureaplasma urealyticum* (T-mycoplasma).
Doxycycline is also indicated in infections due to *Calymmatobacteriumgranulomatis*. Doxycycline is an alternative drug in the treatment of gonorrhoea and syphilis.
Since Doxycycline is a member of the tetracycline series of antibiotics, it may be expected to be useful in the treatment of infections which respond to other tetracyclines, such as:

Ophthalmic infections:
Doxycycline is indicated in the treatment of trachoma, although the infectious agent is not always eliminated, as judged by immunofluorescence.
Inclusion conjunctivitis may be treated with oral Doxycycline alone or in combination with topical agents.

Rickettsial infections:
Rocky Mountain spotted fever, typhus group, Q fever and Coxiella endocarditis.

Other infections:
Psittacosis, brucellosis (in combination with streptomycin), cholera, bubonic plague, louse and tick-borne relapsing fever including stage 1 and stage 2 Lyme disease, leptospirosis, tularaemia glanders, chloroquine-resistant falciparum malaria and acute intestinal amoebiasis (as an adjunct to amoebicides). Infections due to susceptible strains of *Bacteroides* species, *Listeria* species and *Bacillus anthracis*.
Doxycycline is an alternative drug in the treatment of leptospirosis, gas gangrene and tetanus.

Doxycycline is indicated for prophylaxis in the following conditions: Scrub typhus, travellers' diarrhoea (enterotoxigenic *Escherichia coli*), leptospirosis, malaria and cholera.

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

4.2 Posology and method of administration

Posology:
Adults and children aged 12 years to less than 18 years:
The usual dose of Doxycycline for the treatment of acute infections in adults and children aged 12 years to less than 18 years is 200 mg on the first day (administered as a single dose or divided into two equal doses with a 12 hour interval), followed by a maintenance dose of 100 mg/day. In the management of more severe infections (particularly chronic infections of the urinary tract), 200 mg daily should be given throughout the treatment period.
Children aged 8 years to less than 12 years (see section 4.4):
The use of Doxycycline for the treatment of acute infections in children aged 8 years to less than 12 years should be carefully justified in situations where other drugs are not available, are not likely to be effective or are contraindicated.
In such circumstance, the doses for the treatment of acute infections are:

- For children 45 kg or less - Initial dose: 4.4 mg/kg (in single or 2 divided doses) with maintenance dose: 2.2 mg/kg (in single or 2 divided doses). In the management of more severe infections, up to 4.4 mg/kg should be given throughout treatment.
- For children, over 45 kg - dose administered for adults should be used.

Children aged from birth to less than 8 years:
Doxycycline should not be used in children aged younger than 8 years due to the risk of teeth discolouration (section 4.4 and 4.8).
Dosage recommendations in specific infections:

Sexually transmitted diseases
100 mg twice daily for 7 days is recommended in the following infections: uncomplicated urethral, endocervical or rectal infection caused by Chlamydia trachomatis, non-gonococcal urethritis caused by Ureaplasma urealyticum.
Uncomplicated gonococcal infections (except anorectal infections in men) Doxycycline 100 mg twice daily for 7 days together with intramuscular ceftriaxone.

Acute epididymo-orchitis caused by Chlamydia trachomatis or Neisseria gonorrhoea
Doxycycline 100 mg twice daily for 10 days together with intramuscular ceftriaxone.

Primary and secondary syphilis
Non-pregnant penicillin-allergic patients who have primary or secondary syphilis can be treated with the following regimen: doxycycline 100 mg orally twice daily for two weeks, as an alternative to penicillin therapy.

Louse and tick-borne relapsing fevers and louse borne typhus
A single dose of 100 to 200 mg according to severity.

Early Lyme disease (Stage 1 and 2)
100 mg twice daily for 10-30 days according to clinical signs, symptoms and response.

Chloroquine-resistant falciparum malaria
200 mg daily for at least 7 days. Due to the potential severity of the infection, a rapid-acting schizonticide such as quinine should always be given in conjunction with Doxycycline; quinine dosage recommendations vary in different areas.

Prophylaxis of malaria
100 mg daily in adults. Prophylaxis can begin 1-2 days before travel to malarious areas. It should be continued daily during travel in the malarious areas and for 4 weeks after the traveller leaves the malarious area.

For the treatment and selective prophylaxis of cholera in adults
300 mg as a single dose.

For the prevention of scrub typhus
200 mg as a single dose, once weekly.

For the prevention of travellers' diarrhoea in adults
200 mg on the first day of travel (administered as a single dose or as 100 mg every 12 hours) followed by 100 mg daily throughout the stay in the area. Data on the use of the drug prophylactically are not available beyond 21 days.

For the treatment of leptospirosis
100 mg twice daily for 7 days.

For the prevention of leptospirosis
200 mg once each week throughout the stay in the area and 200 mg at the completion of the trip. Data on the use of the drug prophylactically are not available beyond 21 days.

Infections due to susceptible strains of Bacillus anthracis
Adults: 100 mg of doxycycline, by mouth, twice a day for 60 days.

Paediatric population
See sections 4.3 and 4.4.

Use in the elderly
Doxycycline may be prescribed in the usual dose with no special precautions. No dosage adjustment is necessary in the presence of renal impairment.

Use in patients with impaired hepatic function
Doxycycline should be administered with caution to patients with hepatic impairment or those receiving potentially hepatotoxic drugs.

Use in patients with renal impairment
Studies to date have indicated that administration of Doxycycline at the usual
recommended doses does not lead to accumulation of the antibiotic in patients with renal impairment.

Rocky Mountain spotted fever
Doxycycline is the first line treatment for adults and children of all ages:
Adults: 100 mg every 12 hours.
Children: weighing less than 45 kg: 2.2 mg/kg body weight given twice a day. Children weighing 45 kg or more should receive the adult dose (see section 4.4 paediatric population).

Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Minimum course of treatment is 5-7 days.

Method of administration
Doxycycline capsules are for oral administration only.
The capsules should be taken with an adequate amount of fluid (at least 100 ml of water). This should be done in the sitting or standing position and the patient should be advised to remain upright for at least thirty minutes after taking a dose.
Doxycycline capsules should be taken well before bedtime to reduce the risk of oesophageal irritation and ulceration.
If gastric irritation occurs, it is recommended that Doxycycline capsules be given with food or milk. Studies indicate that the absorption of Doxycycline is not notably influenced by simultaneous ingestion of food or milk.
Exceeding the recommended dosage may result in an increased incidence of side effects. Therapy should be continued at least 24-48 hours after symptoms and fever have subsided.
When used in streptococcal infections, therapy should be continued for 10 days to prevent the development of rheumatic fever or glomerulonephritis.

4.3 Contraindications

Hypersensitivity to the active substance or other tetracyclines, or to any of the excipients listed in section 6.1.
Obstructive oesophageal disorders, such as stricture or achalasia.
Pregnancy: Doxycycline is contraindicated in pregnancy. It appears that the risks associated with the use of tetracyclines during pregnancy are predominantly due to effects on teeth and skeletal development (see section 4.4 regarding use during tooth development).
Nursing mothers: Tetracyclines are excreted into milk and are therefore contra- indicated in nursing mothers (see section 4.4 regarding use during tooth development).

Paediatric population: Doxycycline is contraindicated in children under the age of 8 years. As with other tetracyclines, Doxycycline forms a stable calcium complex in any bone-forming tissue. A decrease in the fibula growth rate has been observed in prematures given oral tetracyclines in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued. (See above about use during tooth development).

4.4 Special warnings and precautions for use

Paediatric population: The use of drugs of the tetracycline class during tooth development (last half of pregnancy; infancy and childhood to the age of 8 years) 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. Use Doxycycline in paediatric patients aged younger than 8 years only when the potential benefits are expected to outweigh the risks in severe or life-threatening conditions (e.g. Rocky Mountain spotted fever), only when there are no adequate alternative therapies.
Although the risk of permanent teeth staining is rare in children aged 8 years to less than 12 years, the use of Doxycycline should be carefully justified in situations where other drugs are not available, are not likely to be effective or are contraindicated.
Use in patients with impaired hepatic function: Doxycycline should be administered with caution to patients with hepatic impairment or those receiving potentially hepatotoxic drugs. Abnormal hepatic function has been reported rarely and has been caused by both the oral and parenteral administration of tetracyclines, including Doxycycline.
Use in patients with renal impairment: Excretion of Doxycycline by the kidney is about 40%/72 hours in individuals with normal renal function. This percentage excretion may fall to a range as low as 1-5%/72 hours in individuals with severe renal insufficiency (creatinine clearance below 10 mL/min). Studies have shown no significant difference in the serum half-life of Doxycycline in individuals with normal and severely impaired renal function.
Haemodialysis does not alter the serum half-life of Doxycycline. The anti-anabolic action of the tetracyclines may cause an increase in blood urea. Studies to date indicate that this anti-anabolic effect does not occur with the use of Doxycycline in patients with impaired renal function.
Skin reaction: Severe skin reactions, such as exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in patients receiving doxycycline (see section 4.8). If severe skin reactions occur, doxycycline should be discontinued immediately and appropriate therapy should be instituted**.**
Photosensitivity: Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines, including Doxycycline.
Patients likely to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with tetracycline drugs and treatment should be discontinued at the first evidence of skin erythema.
Microbiological overgrowth: The use of antibiotics may occasionally result in over-growth of non susceptible organisms. Constant observation of the patient is essential. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.
General: Benign intracranial hypertension (pseudotumor cerebri) has been associated with the use of tetracyclines including doxycycline. Benign intracranial hypertension (pseudotumor cerebri) is usually transient, however cases of permanent visual loss secondary to benign intracranial hypertension (pseudotumor cerebri) have been reported with tetracyclines including doxycycline. If visual disturbance occurs during treatment, prompt ophthalmologic evaluation is warranted. Since intracranial pressure can remain elevated for weeks after drug cessation patients should be monitored until they stabilize. Concomitant use of isotretinoin and doxycycline should be avoided because isotretinoin is also known to cause benign intracranial hypertension (pseudotumor cerebri).
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including doxycycline, and has ranged in severity from mild to life-threatening. It is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.
Clostridium difficile associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including doxycycline, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.
C. difficile produces toxins A and B which contribute to the development of CDAD.

Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Oesophagitis Cases of oesophageal injuries (oesophagitis and ulceration), sometimes serious, have been reported. Patients should be instructed to take doxycycline capsules with plenty of water (at least 100ml), remain upright and not take their treatment before going to bed (see section 4.2). Withdrawal of doxycycline and investigation of oesophageal disorder should be considered if symptoms such as dyspepsia or retrosternal pain occur. Caution is required in the treatment of patients with known oesophageal reflux disorders.
Venereal disease When treating venereal disease where co-existent syphilis is suspected, proper diagnostic procedures, including dark-field examinations, should be utilised. In all such cases monthly serological tests should be made for at least four months.
Beta-haemolytic streptococci infections Infections due to a group A beta-haemolytic streptococci should be treated for at least 10 days.
Jarisch-Herxheimer reaction 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.
Myasthenia gravis Due to a potential for weak neuromuscular blockade, care should be taken in administering tetracyclines to patients with myasthenia gravis.
Systemic lupus erythematosusTetracyclines can cause exacerbation of SLE (see section 4.8).
Excipients
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

There have been reports of prolonged prothrombin time in patients taking warfarin and doxycycline. Because the tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving Doxycycline in conjunction with penicillin.
The absorption of doxycycline is impaired by concurrently administered antacids containing aluminium, calcium, magnesium or other drugs containing these cations; oral zinc, iron salts or bismuth preparations.
The serum half-life of doxycycline is shortened when patients are concurrently receiving alcohol, barbiturates, carbamazepine or phenytoin.
A few cases of pregnancy or breakthrough bleeding have been attributed to the concurrent use of tetracyclines with oral contraceptives.
The concurrent use of tetracyclines and methoxyflurane has been reported to result in fatal renal toxicity.

Laboratory Test Interactions
False elevations of urinary catecholamine levels may occur due to interference with the fluorescence test.

4.6 Fertility, pregnancy and lactation

Pregnancy
Doxycyline has not been studied in pregnant patients. It should not be used in pregnancy unless, in the judgement of the physician, it is essential for the welfare of the patient. (see section 4.3 about use during tooth development).

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.

Breast-feeding
Tetracyclines are present in the milk of lactating women who are taking a drug of this kind and should therefore not be used in nursing mothers (see section 4.3 about use during tooth development).

4.7 Effects on ability to drive and use machines

The effect of Doxycycline on the ability to drive or operate heavy machinery has not been studied. There is no evidence to suggest that Doxycycline may affect these abilities.

4.8 Undesirable effects

The following adverse reactions have been observed in patients receiving tetracyclines, including doxycycline.

System organ class	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1000 to <1/100)**	**Rare (≥1/10,000 to <1/1000)**	**Not known (Frequency cannot be estimated from the available data)**
Blood and lymphatic system disorders			Haemolytic anaemia, neutropenia, thrombocytopenia, eosinophilia	
Immune system disorders	Hypersensitivity (including anaphylactic shock, anaphylactic reaction, anaphylactoid reaction, angioedema, exacerbation of systemic lupus, erythemato sus, pericarditis, serum sickness, Henoch-Schonlein purpura, hypotension, dyspnoea, tachycardia, peripheral oedema and urticaria)		Drug reaction with Eosinophilia and Systemic Symptoms DRESS), Jarisch-Herxheimer reaction[b] (see section 4.4)	
Endocrine disorders			Brown-black microscopic discolouration of thyroid glands	
Metabolism and Nutrition disorders			Decreased appetite	
Nervous system disorders	Headache		Benign intracranial hypertension (pseudotumorcerebri) [a], fontanelle bulging	
Ear and labyrinth disorders			Tinnitus	
Eye disorders			Visual disturbance[d]	
Vascular disorders			Flushing	
Gastrointestinal disorders	Nausea/vomiting	Dyspepsia (Heartburn/gastritis)	Pancreatitis, Pseudomembranous colitis, *Clostridium difficile* colitis, oesophageal ulcer, oesophagitis, enterocolitis, inflammatory lesions (with monilial overgrowth) in the	Tooth discolouration[e]

			anogenital region, dysphagia, abdominal pain, diarrhoea, glossitis	
Hepatobiliary disorders			Hepatotoxicity hepatitis, hepatic function abnormal	
Skin and subcutaneous tissue disorders	Photosensitivity reaction, rash including maculopapular and erythematous rashes		Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, dermatitis exfoliative, photoonycholysis, skin hyperpigmentation[c]	
Musculoskeletal and connective tissue disorders			Arthralgia, myalgia	
Renal and urinary disorders			Blood urea increased	

a In association with tetracyclines, including doxycycline, benign intracranial hypertension has been reported with possible symptoms of headache, vomiting, visual disturbances including blurred vision, scotoma, diplopia or permanent loss of vision. The manifestation of clinical symptoms, including headache or visual disturbances, should suggest a possible diagnosis of intracranial hypertension. If an increase in intracranial pressure is suspected during treatment with tetracyclines, administration should be discontinued.
b In the setting of spirochete infections treated with doxycycline.
c With chronic use of doxycycline.
d Associated with Benign intracranial hypertension (pseudotumor cerebri).
e Reversible and superficial discolouration of permanent teeth has been reported with the use of doxycycline but frequency cannot be estimated from available data.

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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Acute overdosage with antibiotics is rare. In the event of overdosage discontinue medication. Gastric lavage plus appropriate supportive treatment is indicated. Dialysis does not alter serum half-life and thus would not be of benefit in treating cases of overdosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: tetracyclines, ATC code: J01AA02
Doxycycline is primarily bacteriostatic and is believed to exert its antimicrobial effect by the inhibition of protein synthesis. Doxycycline is active against a wide range of Gram-positive and Gram-negative bacteria and certain other micro-organisms.

Doxycycline has a high degree of lipid solubility and a low affinity for calcium. It is highly stable in normal human serum. Doxycycline will not degrade into an epianhydro form.
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

Tetracyclines are readily absorbed and are bound to plasma proteins in varying degrees. They are concentrated by the liver in the bile and excreted in the urine and faeces at high concentrations and in a biologically active form. Doxycycline is virtually completely absorbed after oral administration. Studies reported to date indicate that the absorption of doxycycline, unlike certain other tetracyclines, is not notably influenced by the ingestion of food or milk.

Following a 200 mg dose, normal adult volunteers averaged peak serum levels of 2.6 micrograms/ml of doxycycline at 2 hours decreasing to 1.45 micrograms/ml at 24 hours.

Studies have shown no significant difference in serum half-life of Doxycycline (range 18 to 22 hours) in individuals with normal or severely impaired renal function.
Haemodialysis does not alter the serum half-life of Doxycycline.

Children and Adolescents (2 to 18 years of age)
Population pharmacokinetic analysis of sparse concentration-time data of doxycycline following standard of care intravenous (IV) and oral dosing in 44 paediatric patients (2-18 years of age) showed that allometrically-scaled clearance (CL) of doxycycline in paediatric patients ≥ 2 to ≤ 8 years of age (median [range] 3.58 [2.27-10.82] L/h/70 kg, N=11) did not differ significantly from paediatric patients > 8 to 18 years of age (3.27 [1.11-8.12] L/h/70 kg, N=33). For paediatric patients weighing ≤ 45 kg, body weight normalized doxycycline CL in those ≥ 2 to ≤ 8 years of age (median [range] 0.071 [0.041-0.202] L/kg/h, N=10) did not differ significantly from those >8 to 18 years of age (0.081 [0.035-0.126] L/kg/h, N=8). In paediatric patients weighing >45 kg, no clinically significant differences in body weight normalized doxycycline CL were observed between those ≥ 2 to ≤ 8 years (0.050 L/kg/h, N=1) and those > 8 to 18 years of age (0.044 [0.014-0.121] L/kg/h, N=25). No clinically significant difference in CL between oral and IV dosing was observed in the small cohort of paediatric patients who received the oral (N=19) or IV (N=21) formulation alone.

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

Capsule contents
Lactose monohydrate
Maize starch
Magnesium stearate
Capsule shell
Gelatin
Titanium dioxide (E 171)
Iron oxide yellow (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store below 30 °C. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

PVC/Alu or PVdC/PVC//Alu blisters
Pack sizes: 1, 5, 6, 8, 10, 12, 14, 20, 28, 30, 42, 50, 56, 60, 84, 90, 100 and 112 hard capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Activase Pharmaceuticals Limited
Boumpoulinas 11
Nicosia
1060
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8 MARKETING AUTHORISATION NUMBER

PA1567/006/002

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Date of First Authorisation: 9th January 2026

10 DATE OF REVISION OF THE TEXT