SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Doxy-Denk 100
Doxy-Denk 200

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: doxycycline

Doxy-Denk 100
Each tablet contains 100 mg doxycycline (as doxycycline hyclate).
Excipient with known effect: each tablet contains 21 mg of lactose monohydrate and less than 1 mmol (23 mg) sodium.

Doxy-Denk 200
Each film-coated tablet contains 200 mg doxycycline (as doxycycline hyclate).
Excipient with known effect: each film-coated tablet contains 55 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Doxy-Denk 100
Tablet
Pale yellow, round, convex tablet without breaking notch.

Doxy-Denk 200
Film-coated tablet
Greenish-yellow, biconvex, round tablets with a score line.
The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Doxycycline is indicated in infections caused by disease pathogens susceptible to doxycycline (see section 5.1), especially:

- infections of the respiratory tract and ENT region
  - acute episodes of chronic bronchitis
  - sinusitis
  - otitis media
  - pneumonia due to mycoplasmas, Rickettsia or Chlamydia
- urogenital tract infections
  - urethritis due to Chlamydia and Ureaplasma urealyticum
  - acute prostatitis
  - uncomplicated gonorrhoea (especially with concomitant Chlamydia infection)
  - infections of the female reproductive organs
  - syphilis in the presence of penicillin allergy
  - urinary tract infections (only when the susceptibility of the pathogen has been confirmed)

- gastrointestinal tract infections
  - cholera
  - Yersinia or Campylobacter infection
  - Shigella infection when susceptibility has been confirmed
- outpatient therapy of biliary tract infections
- skin disorders, including infected severe forms of acne vulgaris and rosacea
- chlamydial conjunctivitis with trachoma
- borreliosis (erythema chronicum migrans or Lyme disease)
- rare infections such as brucellosis, ornithosis, bartonellosis, listeriosis, rickettsiosis, melioidosis, plague, inguinal granuloma
- other disorders:
  - malabsorption syndromes (tropical sprue and Whipple disease)

Official guidelines for appropriate use of antimicrobial active substances should be followed.

4.2 Posology and method of administration

Posology

Adults and adolescents from 12 to 17 years inclusive (with a body weight [BW] less than 70 kg)
- first day: 200 mg doxycycline (as a single dose or 2 divided doses)
- subsequent days: 100 mg doxycycline per day

In severe disorders or patients with a BW of more than 70 kg
- 200 mg doxycycline once daily for the entire treatment duration

Children from 8 to 11 years inclusive (see section 4.4)
Use of doxycycline for the treatment of acute infections in children from 8 to 11 years inclusive should be reviewed carefully and take place only if other medicinal products are not available, are likely to be ineffective or are contraindicated.

In these circumstances, the dose in acute infections is as follows:

Children less than 45 kg
Initial dose: 4.4 mg/kg (as a single dose or 2 divided doses), maintenance dose: 2.2 mg/kg (as a single dose or 2 divided doses).
In severe infections, up to 4.4 mg/kg should be administered throughout the entire treatment duration.

Children more than 45 kg
The same dose as for adults should be administered.

Children from birth to less than 8 years
In view of the risk of tooth discolouration, doxycycline should not be used in children less than 8 years old (see sections 4.4 and 4.8).

The treatment duration depends on the course of the disease and should be continued for at least a further 1-2 days after the disease symptoms have subsided.

Special dosages

Acute gonorrhoeal urethritis in men
200 mg doxycycline daily for 7 days.

Acute gonococcal epididymitis
200 mg doxycycline daily for 10 days.

Acute gonococcal infections in women
200 mg doxycycline daily for at least 7 days.

The success of treatment in a gonococcal infection should be verified by a culture test 3-4 days after the treatment has ended.

Syphilis (primary and secondary form in the presence of penicillin allergy)
300 mg doxycycline daily for 15 days. The dose can be taken all at once.

Skin disorders, including infected severe forms of acne vulgaris and rosacea
100 mg doxycycline daily, generally for 7-21 days.
Thereafter, daily ingestion of 50 mg doxycycline is possible as a maintenance dose for a further 2-3 weeks. Depending on clinical success, long-term treatment with low-dose doxycycline (50 mg daily) can be administered over a period of up to 12 weeks for the treatment of acne. (Special dose strengths of 50 mg doxycycline are available for this.)

Stage I borreliosis (erythema chronicum migrans or Lyme disease)
200 mg doxycycline daily for 2-3 weeks (but at least 14 days).

Use in patients with impaired renal function
It is generally unnecessary to reduce the doxycycline dose in patients with impaired renal function.

Use in patients with impaired hepatic function
(see section 4.4)

Method of administration
Doxycycline should be taken regularly either in the morning with breakfast or at the same time as another meal.
To prevent oesophageal ulceration, the tablet should be taken with a glass of water (not milk) and not immediately before bedtime (see sections 4.4 and 4.8).
Ingestion after or during a meal may decrease the frequency of gastrointestinal disturbance. This has a negligible effect on the rate of absorption.

4.3 Contraindications

- Hypersensitivity to the active substance, to other tetracyclines or to any of the excipients listed in section 6.1.
  Complete cross-allergy exists within the tetracycline group.
- Severe hepatic function disorders
- Pregnancy and lactation (see section 4.6)
- Children less than 8 years (for exceptions, see section 4.4)

4.4 Special warnings and precautions for use

In **severe acute hypersensitivity reactions** or **severe skin symptoms** with a life-threatening generalised reaction (such as exfoliative dermatitis, Lyell's disease) (see section 4.8), treatment with doxycycline must be discontinued immediately and emergency measures initiated without delay.

If severe, persistent diarrhoea occurs during or after discontinuation of doxycycline treatment, a serious and potentially life-threatening form of colitis (**pseudomembranous enterocolitis**), mostly triggered by *Clostridium difficile*, should be suspected. In this case, doxycycline must be discontinued without delay and appropriate treatment initiated immediately. Antiperistaltic agents are contraindicated.

Due to selection, **microbial overgrowth** of unsusceptible pathogens (e.g. Candida) may occur on the skin or mucous membranes, especially in the genital tract and the oral and intestinal mucosa, on

treatment with doxycycline (see section 4.8).
Any infections that occur must be treated.

In sunlight, **phototoxic reactions** due to photosensitisation may occur on exposed areas of skin (see section 4.8), in rare cases also involving the nails (nail detachment with discolouration). Sunbathing in the open or in a solarium should therefore be avoided during doxycycline treatment.

An **increase in benign intracranial pressure** (pseudotumor cerebri) has been reported in adolescents and adults (see sections 4.5 and 4.8). These symptoms subsided rapidly after discontinuation of the medicinal product.

A Jarisch-Herxheimer reaction may occur shortly after initiation of doxycycline treatment in some patients with spirochete infection. Patients should be reassured that this is a usually self-limiting result of antibiotic treatment for spirochete infections.

If, in the presence of a **sexually transmissible disorder**, concomitant syphilis is suspected, appropriate diagnostic measures, including darkfield microscopy, should be taken. Monthly serology tests should be performed for at least 4 months in all such cases.

Caution is required in the treatment of patients with **myasthenia gravis** due to the risk of disease exacerbation.

Tetracyclines can cause exacerbations of **systemic lupus erythematosus**.

Caution is advised in the case of concomitant use of **methoxyflurane anaesthesia** (see section 4.5).

Regular blood, liver and kidney tests should be performed during **long-term use** (i.e. for longer than 21 days). Patients should be monitored for possible vitamin B deficiency during long-term treatment.

Cases of **oesophagitis and oesophageal ulceration** have been reported in patients who have taken medicinal products from the tetracycline group, including doxycycline, in capsule or tablet form. Most of these patients took the medicinal product immediately before bedtime or with insufficient fluid.

Patients with impaired hepatic function
Doxycycline should be administered with caution in patients with impaired hepatic function or in patients who are concomitantly using potentially hepatotoxic medicinal products.
Hepatic dysfunction has been observed. These reactions occurred after both oral and parenteral treatment with tetracyclines, including doxycycline.

Patients with impaired renal function
Tetracyclines can cause nephrotoxic damage or worsen pre-existing renal function impairment (identifiable from an increase in creatinine and urea in the urine) (see section 4.8).

Studies of the serum half-life of doxycycline in patients with normal and impaired renal function have shown no significant difference. Haemodialysis has no influence on the serum half-life of doxycycline.

Paediatric population
Irreversible tooth discolouration (yellow-grey-brown) may occur with use of active substances in the tetracycline group during tooth development (in the last half of pregnancy, in infancy and in children up to 8 years). This side effect is more common on long-term treatment but has also been observed following repeated short-term treatments. Dental enamel hypoplasia has also been reported.
Doxycycline should not be used in children less than 8 years with serious or life-threatening disorders (e.g. Rocky Mountain spotted fever) unless the expected benefit outweighs the risk and no appropriate alternative therapies are available.

Although the risk of irreversible tooth discolouration is low in children from 8 to 11 years inclusive,

use of doxycycline should be reviewed carefully and take place only if other medicinal products are not available, are likely to be ineffective or are contraindicated.

This medicine contains lactose.
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 effect of doxycycline is influenced by the following medicinal products
Doxycycline absorption from the gastrointestinal tract can be impaired by divalent or trivalent cations such as aluminium, calcium (milk, dairy products and calcium-containing fruit juices) and magnesium in antacids or by zinc, bismuth or iron preparations as well as by medicated activated charcoal, colestipol and cholestyramine.
Therefore, such medicinal products and foods should be taken 2-3 hours apart.

The antibiotic rifampicin, inducing substances from the barbiturate class and other anticonvulsants such as carbamazepine, diphenylhydantoin and primidone as well as chronic alcohol abuse can accelerate doxycycline breakdown due to enzyme induction in the liver, which means therapeutically active doxycycline concentrations are not reached at the usual dosage.

Doxycycline influences the effect of the following medicinal products
Doxycycline can enhance the effect of sulphonylurea derivatives (oral antidiabetic drugs). On combined administration, a blood sugar test should be performed and the dose of these medicinal products reduced accordingly, if applicable.

Prolongation of the prothrombin time has been reported in patients taking anticoagulants (e.g. phenprocoumon, warfarin) and doxycycline. As plasma prothrombin activity can be reduced on tetracyclines, a reduction in the dose of the anticoagulant must be considered in patients receiving anticoagulation therapy.

Concomitant use of doxycycline and ciclosporin A may increase the toxic effect of the immunosuppressant. Concomitant administration should take place only with appropriate monitoring.

Concomitant use with methotrexate may enhance the toxicity of the latter.

Other interactions
The combination of potentially nephrotoxic methoxyflurane anaesthesia with doxycycline therapy can lead to renal failure (see section 4.4).

Treatment with doxycycline should be avoided shortly before, during or after acne treatment with isotretinoin and/or other retinoids because both medicinal products can cause reversible increases in intracranial pressure (pseudotumor cerebri; see section 4.8) in rare cases.

There is a risk of an increase in the plasma digoxin concentration on concomitant treatment with digoxin and/or digoxin derivatives due to inactivation of the intestinal reduction of digoxin, which might lead to digoxin intoxication (nausea, vomiting, dizziness, fatigue, cardiac arrhythmia).

As bacteriostatic medicinal products may interfere with bactericidal medicinal products, concomitant ingestion of doxycycline and betalactam antibiotics should be avoided because this may lead to a decrease in antibacterial efficacy.

Concomitant use of theophylline and tetracyclines can increase the frequency of gastrointestinal adverse reactions.

Tetracyclines potentially inhibit the breakdown of secale alkaloids in the liver (occurrence of ergotism

possible in isolated cases).

Interference with laboratory tests
Urine glucose tests may produce false positive results if the copper sulphate (Benedict's) method is used. Urine glucose tests with glucose oxidase reagents may produce false negative results. Due to the influencing of fluorometric determinations, such tests may show false positive increases in urinary catecholamines.

4.6 Fertility, pregnancy and lactation

Pregnancy
Doxycycline is contraindicated in pregnancy. The risks associated with the use of tetracyclines during pregnancy appear to be particularly related to effects on the development of teeth and the skeleton (see section 4.4 on use during tooth development).

The risk of liver damage from taking tetracycline is higher during pregnancy.

Breast-feeding
Tetracyclines are excreted in human milk and are therefore contraindicated in breast-feeding mothers (see section 4.4. on use during tooth development).

4.7 Effects on ability to drive and use machines

As this medicinal product can cause adverse reactions (e.g. visual disturbances), patients should be instructed to be cautious when driving and using machines.

4.8 Undesirable effects

The following undesirable effects have been reported during treatment with tetracyclines, including doxycycline:

The frequencies of adverse reactions are ranked according to the following convention:

Very common	≥ 1/10
Common	≥ 1/100, < 1/10
Uncommon	≥ 1/1,000, < 1/100
Rare	≥ 1/10,000, < 1/1,000
Very rare	< 1/10,000
Not known	cannot be estimated from the available data

Infections and infestations
Rare: Candida colonisation of the skin or mucous membranes (especially in the genital tract and the oral and intestinal mucosa) with symptoms such as stomatitis and pharyngitis, acute inflammation of the external reproductive organs and the vagina in women (vulvovaginitis), as well as anal itching (pruritus ani).

Blood and lymphatic system disorders
Uncommon: blood clotting disorder
Rare: leukocytosis, thrombocytopenia, haemolytic anaemia, neutropenia, eosinophilia, lymphocytopenia, lymphadenopathy, atypical lymphocytes and toxic granulation of granulocytes

Immune system disorders
Common: anaphylactic reactions (including hypersensitivity, Henoch-Schönlein purpura, hypotension, pericarditis, angioedema, exacerbations of systemic lupus erythematosus, asthma, dyspnoea, serum sickness, peripheral oedema, tachycardia

and urticaria)
Rare: anaphylactic shock, drug rash with eosinophilia and systemic symptoms (DRESS)
Not known: Jarisch-Herxheimer reaction (see section 4.4.)

Metabolism and nutrition disorders
Rare: anorexia

Psychiatric disorders and nervous system disorders
Common: headache
Rare: restlessness, anxiety states; paraesthesia; benign intracranial hypertension in adults (pseudotumor cerebri), of which possible symptoms are headaches, nausea, vomiting and potentially visual disturbances (scotoma, diplopia), etc., vision loss due to papillary oedema; impairment or loss of the sense of smell and taste, which was reversible, and also only partially so, in only some cases.
Very rare: seizures

Eye disorders
Very rare: transient myopia

Ear and labyrinth disorders
Rare: tinnitus

Vascular disorders
Rare: flushing

Gastrointestinal disorders
Common: nausea, vomiting, meteorism, steatorrhoea
Uncommon: dyspepsia (indigestion/gastritis), stomatitis and pharyngitis, hoarseness, black hairy tongue, discolouration of permanent teeth with enamel defects if used during dentition
Rare: pseudomembranous colitis - C. difficile-induced diarrhoea, oesophageal ulcerations, oesophagitis, enterocolitis, abdominal pain, diarrhoea, dysphagia, glossitis
Not known: tooth discolouration: reversible discolouration of the surface of permanent teeth have been reported with use of doxycycline.

Hepatobiliary disorders
Rare: hepatic damage, hepatitis, abnormal hepatic function, pancreatitis

Skin and subcutaneous tissue disorders
Very common: photosensitivity reactions with erythema, cutaneous oedema and blister formation
Common: rashes, including maculopapular and erythematous rashes
Rare: severe skin reactions with life-threatening, general reactions (such as erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrosis), nail detachment and discolouration

Musculoskeletal and connective tissue disorders
Uncommon: reversible bone growth retardation when used during pregnancy and in children less than 8 years of age
Rare: myalgia, arthralgia

Renal and urinary disorders
Uncommon: haematuria
Rare: raised BUN values
Very rare: renal damage, such as interstitial nephritis, acute renal failure and anuria

Investigations

Not known: microscopic brownish-black discolouration of the thyroid after long-term treatment (without abnormal thyroid function values)

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.

4.9 Overdose

Doxycycline is not acutely toxic on single oral administration in multiple therapeutic doses. No acute doxycycline intoxication has been reported to date in the literature.
However, there is a risk of parenchymal hepatic and renal damage as well as pancreatitis in overdose.

In the event of an oral overdose of doxycycline, the as-yet-unabsorbed fractions of the substance should be bound to non-absorbable chelate complexes by administration of antacids, magnesium salts or calcium salts. After immediate discontinuation of therapy, symptomatic measures may be indicated. Doxycycline is not adequately removed by dialysis, and haemodialysis or peritoneal dialysis therefore has little effect.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Doxycycline is an antibiotic from the tetracycline group.
ATC code: J01AA02

Mechanism of action
The mechanism of action of doxycycline is based on the inhibition of protein biosynthesis by reversible blockade of the aminoacyl-tRNA binding site at the 30S ribosomal subunit, which interrupts peptide chain elongation. This results in a predominantly bacteriostatic effect.

Relationship between pharmacokinetics and pharmacodynamics
Efficacy depends mainly on the ratio between the AUC (area under the curve) and the minimum inhibitory concentration (MIC) of the pathogen.

Resistance mechanisms
Resistance to doxycycline can be based on the following mechanisms:
- Resistance is mostly based on the presence of efflux pumps, which actively transport tetracyclines from the cell.
- A further mechanism is ribosome resistance proteins, which prevent doxycycline from binding to the ribosome.
- A rare mechanism is enzymatic inactivation of doxycycline. Extensive cross-resistance exists between doxycycline and other tetracyclines. Tetracycline-resistant strains can be susceptible to doxycycline.

Breakpoints
Definitions – **S**: susceptible, standard dosing regime; **I**: susceptible, increased exposure; **R**: resistent.
Doxycycline is tested using the usual dilution series. The following minimum inhibitory concentrations have been determined for susceptible and resistant microorganisms:

EUCAST (European Committee on Antimicrobial Susceptibility Testing) breakpoints (v. 9.0)

Organism	**S**	**R**
Staphylococcus spp.[1)]	≤ 1 mg/L	> 2 mg/L

Streptococcus spp. (groups A, B, C, G) [1)]	≤ 1 mg/L	> 2 mg/L
Streptococcus pneumoniae [1)]	≤ 1 mg/L	> 2 mg/L
Haemophilus influenzae [1)]	≤ 1 mg/L	> 2 mg/L
Moraxella catarrhalis [1)]	≤ 1 mg/L	> 2 mg/L

[1)] Isolates susceptible to tetracycline are always susceptible to doxycycline, but some resistant to tetracycline may also be susceptible to doxycycline. The MIC of doxycycline should be used to determine the doxycycline susceptibility of isolates resistant to tetracycline.

Prevalence of acquired resistance in Germany

The prevalence of acquired resistance among individual species can vary locally and over time. Therefore, local information on the resistance situation is required – particularly for appropriate treatment of severe infections. If the efficacy of doxycycline is questionable due to the local resistance situation, advice on treatment should be sought from experts. Microbiological diagnosis with identification of the pathogen and its susceptibility to doxycycline should be sought, particularly in the event of serious infections or treatment failure.

The prevalence of acquired resistance in Germany based on data over the last 5 years from national resistance monitoring projects and studies (date: April 2019):

Commonly susceptible species
Aerobic Gram-positive microorganisms
Actinomyces israelii°
Listeria monocytogenes°[I]
Staphylococcus aureus (including methicillin-resistant strains)
Tropheryma whippelii°
Aerobic Gram-negative microorganisms
Bartonella henselae°
Borrelia burgdorferi°
Burkholderia mallei°
Burkholderia pseudomallei°
Brucella spp.°
Francisella tularensis°
Haemophilus ducreyi°
Haemophilus influenzae
Moraxella catarrhalis
Pasteurella multocida°
Vibrio cholerae°
Vibrio parahaemolyticus°
Yersinia enterocolitica°
Yersinia pestis°
Anaerobic microorganisms
Propionibacterium acnes°
Other microorganisms
Chlamydia trachomatis °
Chlamydophila pneumoniae°
Chlamydophila psittaci°
Ehrlichia spp.°
Leptospira spp.°
Mycoplasma hominis°
Mycoplasma pneumoniae°

Rickettsia spp.°
Treponema pallidum° Δ
Ureaplasma urealyticum°
Species in which acquired resistance might be a problem during use
Aerobic Gram-positive microorganisms
Staphylococcus epidermidis
Staphylococcus haemolyticus
Staphylococcus hominis
Streptococcus agalactiae+
Streptococcus pneumoniae[2]
Aerobic Gram-negative microorganisms
Campylobacter jejuni
Naturally resistant species
Aerobic Gram-negative microorganisms
Morganella morganii
Proteus spp.
Pseudomonas aeruginosa

The stated categorisations are partly based on data on tetracycline.

°At the time of publication of the tables, no up-to-date data were available. Susceptibility is assumed in the primary literature, standard works and treatment recommendations.

+The resistance rate is over 50% in at least one region.

ΔIn penicillin allergy only

[1]Doxycycline is suitable only for the treatment of oculoglandular or cutaneous listeriosis in penicillin allergy.

[2]Doxycycline is not the agent of choice for the treatment of pneumococcal pneumonia and systemic pneumococcal infections.
Doxycycline is not the agent of choice for infections due to *Escherichia coli* and other *Enterobacteriaceae* species.

5.2 Pharmacokinetic properties

Absorption
Doxycycline is almost completely absorbed (> 90% of a dose) from the upper part of the small intestine following oral administration.
Relevant plasma concentrations are reached after only 30 minutes and peak plasma concentrations after 1-2 hours. Peak plasma concentrations of 3-5.3 mg/l were determined after ingestion of a single 200 mg dose. On administration under therapeutic conditions (200 mg on the 1st day of treatment and 100 mg on subsequent days), steady-state concentrations are reached rapidly and are approximately as high as after administration of a single 200 mg dose.

Similarly high concentrations are obtained after a single intravenous infusion of 200 mg dose.

The plasma half-life in healthy people is approx. 16 ± 6 hours; it may be slightly prolonged in the event of impaired renal function and more severely prolonged in hepatic disorders. Doxycycline protein binding is 80-90%.

Distribution
Distribution is rapid in the healthy body, with relatively low CNS penetration, including through inflamed meninges. A high gallbladder concentration and good tissue diffusion are achieved especially in the liver, kidneys, lungs, spleen, bones and reproductive organs. The apparent volume of distribution of doxycycline is approximately 0.75 l/kg.

Biotransformation
Doxycycline is metabolised to only a small extent (≤ 10% of a dose) in the human body.

Elimination
Excretion takes place mainly in the form of a microbiologically active substance through the intestine (by transintestinal secretion and through the gallbladder) and to a certain extent (30-55%) also through the kidneys. Approx. 41% (range: 22-60%) of a doxycycline dose is recovered in the urine within 24 hours. Due to these pharmacokinetic properties, the doxycycline half-life is not significantly prolonged in patients with severely impaired renal function.

5.3 Preclinical safety data

Acute toxicity
Acute toxicity tests have found no particular sensitivity (see section 4.9).

Chronic toxicity

Tests in various animal species (monkey, rat, dog, hamster) for a period of up to one year have shown no significant pathological changes. Gastrointestinal disorders occurred in the test group that received very high dosages.

Mutagenic and carcinogenic potential
An 18-month study conducted in rats did not reveal evidence of a carcinogenic potential of doxycycline. Doxycycline has not been adequately investigated for mutagenic effects. *In vivo* and *in vitro* tests conducted to date have been negative.

Reproductive toxicity
Teratogenicity studies have been conducted in various animal species (rat, mouse, monkey, rabbit). No congenital abnormalities were shown. In foetuses, tooth discolouration, enamel defects and delayed bone growth due to doxycycline incorporation can occur from the 4th month onwards.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Doxy-Denk 100
Sodium starch glycolate, maize starch, hydrogenated castor oil, lactose monohydrate, silica colloidal anhydrous, magnesium stearate [vegetable], microcrystalline cellulose.

Doxy-Denk 200
Gelatine; lactose monohydrate, macrogol 6000, magnesium stearate [vegetable], maize starch; alkaline butylmethacrylate copolymer (MW: approx. 150 000), silica colloidal anhydrous, talc, quinoline yellow lake, titanium dioxide.

6.2 Incompatibilities

Doxycycline can form chelates with divalent and trivalent cations that are not absorbed in the gastrointestinal tract.

6.3 Shelf life

Doxy-Denk 100
3 years

Doxy-Denk 200

2 years

6.4 Special precautions for storage

Store below 25 °C.

6.5 Nature and contents of container

Doxy-Denk is available in PVC/PE/PVDC/aluminium blisters.

Doxy-Denk 100
Pack size: 20 tablets.

Doxy-Denk 200
Pack size: 8 film-coated tablets.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Denk Pharma GmbH & Co. KG
Prinzregentenstr. 79
81675 München
Germany

8. MARKETING AUTHORISATION NUMBERS IN GERMANY

Doxy-Denk 100
12138.01.00

Doxy-Denk 200
2578.01.00

9. DATE OF FIRST AUTHORISATION IN GERMANY

Doxy-Denk 100
16.02.1990

Doxy-Denk 200
06.09.1982

10. DATE OF REVISION OF THE TEXT

05/2019

11. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription