

PACKAGE LEAFLET: Information for the user

DOXYDERMA

Tablets – 100 mg

(Doxycycline monohydrate)

Read this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, talk to your doctor or pharmacist.

In this leaflet:

1. What is Doxyderma and what is it used for?
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1. WHAT IS DOXYDERMA AND WHAT IS IT USED FOR?

Doxyderma is a broad-spectrum antibiotic of the tetracycline group.

Doxyderma is indicated for infections caused by pathogens sensitive to doxycycline, especially by:

- Infections of the respiratory airways and ear-nose-throat area
 - acute exacerbations of chronic bronchitis
 - sinusitis
 - inflammation of the middle ear (Otitis media)
 - certain forms of pulmonary inflammation (pneumonia) caused by mycoplasma, rickettsia or chlamydia

- Genitourinary tract infections
 - urethritis caused by Chlamydia and Ureaplasma urealyticum
 - acute prostatitis
 - uncomplicated gonorrhea (especially with concurrent chlamydial infection)
 - infections of the female genital organs
 - syphilis, when there is penicillin allergy
 - urinary tract infection (only in case of proven sensitivity of the pathogen)
- Infections of the gastrointestinal tract
 - Cholera
 - infections caused by *Yersinia* or *Campylobacter*
 - *Shigella* infection in proved sensitivity
- Outpatient treatment of biliary tract infections
- Skin diseases, also infected severe forms of acne vulgaris and rosacea
- Conjunctivitis caused by chlamydia and trachoma
- Diseases caused by *Borrelia* such as erythema chronicum migrans and Lyme disease (mainly caused by infections from bites)
- Rare infections such as brucellosis, ornithosis, bartonellosis, listeriosis, rickettsiosis, melioidosis, plague, inguinal granuloma
- Other diseases:
 - malabsorption syndrome (diseases associated with dyspepsia) for example tropical Sprue and Whipple's disease.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE DOXYDERMA?

Do not take Doxyderma:

- if you are hypersensitive (allergic) to doxycycline monohydrate, other tetracyclines or to any other excipients of Doxyderma;
- if you suffer from severe disorders of liver function.

Take special care with Doxyderma

Please talk to your doctor or pharmacist before taking Doxyderma.

Known infections caused by staphylococci, streptococci, pneumococci should not be treated with doxycycline because the resistance (sensitivity of the pathogen from the drug) situation is unfavorable.

During concomitant use of Doxyderma with some other antidiabetics and anticoagulants (see „Taking Doxyderma with other medicines“), the blood sugar control and coagulation parameters should be performed and if it is necessary doses of these drugs should be reduced.

Effects on laboratory tests

The detection of glucose, proteins, urobilinogen and catecholamines in the urine, can be disturbed by taking tetracyclines.

Skin and annexes

Under sunlight, it may through light-sensitizing come to phototoxic reactions of the exposed areas of the skin (see „Possible side effects“). Thus, sunbathing outdoors or in tanning beds should be avoided during treatment with Doxyderma.

Inform your doctor about your treatment with Doxyderma before submitting to anesthesia (see „Taking Doxyderma with other medicines“).

Special instructions

If the treatment lasts more than 21 days, regular tests of the blood, liver and kidney function should be performed. Please control the success of treatment 3-4 days after its completion in the case of a gonococcal infection to avoid the return of the disease.

Use in children and elderly

Children under 8 years old should not be treated with Doxyderma (see „Pregnancy and breast-feeding“).

For elderly, there are no specific instructions.

Taking Doxyderma with other medicines

Tell your doctor or pharmacist if you are taking / using, have recently taken / used or are planning to take / use other medicines, including medicines taken without a prescription.

Which drugs affect the action of Doxyderma?

The absorption of doxycycline from the gastro-intestinal tract can be affected by 2- or 3-valent cations such as aluminum and magnesium (which are in antacids), or calcium (which is in milk and its products) or by iron preparations and by charcoal and cholestyramine (drug

that reduces high cholesterol blood levels). Therefore, such pharmaceutical or food containing these elements should be taken in a time interval of 2 to 3 hours.

The antibiotic rifampicin, barbiturates (drug used as a sedative or hypnotic) and other antiepileptics (carbamazepine, diphenylhydantoin and primidone) and chronic alcohol abuse can accelerate the metabolism of doxycycline (due to enzyme induction in the liver). In these conditions Doxyderma is not effective because blood levels are not achieved.

How does Doxyderma affect the effect of other drugs?

Doxycycline may increase the effect of sulfonylurea (oral antidiabetics) and anticoagulants (dicumarol type) (see „Take special care with Doxyderma”). In combined administration a control should be performed on the blood sugar or the coagulation parameters and if necessary, appropriate dose reduction of these drugs are made.

Doxyderma may increase the damaging effect (toxic) of cyclosporin A (drug for suppression of the immune system).

Other interactions

The combination of a potentially nephrotoxic methoxyflurane for anesthesia with doxycycline therapy can lead to kidney failure (see „Take special care with Doxyderma”). Shortly before, during or after acne treatment with isotretinoin, treatment with Doxyderma should not be started because in rare cases both drugs can cause increases of intracranial pressure (Pseudotumor cerebri) which is reversible after completion of the treatment.

Concomitant administration of Doxyderma with some other antibiotics (beta-lactam antibiotics such as penicillins, cephalosporins) should be avoided because in the laboratory test it is observed a weakening (antagonist) effect of the antibacterial effect.

The concomitant use of Doxyderma with theophylline (drug used to treat asthma) may increase the incidence of side effects in the gastrointestinal tract.

Taking Doxyderma with food and drinks

Please do not consume milk, its products and fruit juices containing calcium simultaneously with Doxyderma. You should leave an interval time of 2-3 hours after your daily dose (see “Taking Doxyderma with other medicines”).

Keep in mind that in case of prolonged alcohol abuse, metabolism of doxycycline is accelerated. Thus Doxyderma is not effective because blood levels are not achieved.

Pregnancy and breastfeeding

If you are pregnant or breast-feeding, or if you think you are pregnant or are planning to become pregnant, consult your doctor or pharmacist before using this medicine.

Doxyderma can be used during pregnancy and breastfeeding, and in infants and children up to 8 years only if there is a very strict indication, because the accumulation of doxycycline may cause irreversible tooth discoloration, enamel defects and reversible delay of bone growth in fetuses since 4 months old and in children up to 8 years old.

Effects on ability to drive and use machines

During treatment with Doxyderma temporary myopia may occur, which may cause insecurity in driving or using machines.

3. HOW TO TAKE DOXYDERMA?

Always take Doxyderma exactly as your doctor has told you. Ask your doctor or pharmacist if you are not sure.

Unless otherwise prescribed by the doctor, the usual dose is:

Adolescents over 50 kg and adults under 70 kg body weight take 2 tablets of Doxyderma 100 mg (equivalent to 200 mg of doxycycline) on the first day and in the following days take 1 tablet of Doxyderma 100 mg (equivalent to 100 mg of doxycycline).

Adults over 70 kg body weight take 2 tablets of Doxyderma 100 mg (equivalent to 200 mg of doxycycline) daily.

This medicine is not recommended for use in children under 50 kg (from 8 years: 4 mg / kg body weight on the first day and 2 mg / kg body weight on the following days), because of its dosage strength.

Special dosage recommendations:

- Acute gonorrheal urethritis (urethritis associated with gonorrhea) in men: 2 tablets of Doxyderma 100 mg daily (equivalent to 200 mg of doxycycline) for 7 days.

- Acute gonococcal epididymitis: 2 tablets of Doxyderma 100 mg daily (equivalent to 200 mg of doxycycline) for 10 days.
- Acute gonococcal infection in women: 2 tablets of Doxyderma 100 mg daily (equivalent to 200 mg of doxycycline) for at least 7 days.

The success of treatment for a gonococcal infection should be checked by a cultural control 3 to 4 days after treatment.

- Syphilis (primary and secondary form by penicillin allergy): 3 tablets of Doxyderma 100 mg daily (equivalent to 300 mg of doxycycline, can be taken all at once) for 15 days.
- Skin diseases, also infected severe forms of acne vulgaris and rosacea: 1 tablet of Doxyderma 100 mg daily (equivalent to 100 mg of doxycycline), usually 7 - 21 days. Then the daily intake of 50 mg doxycycline as maintenance therapy for other 2 to 3 weeks is possible. Depending on the clinical success, for acne therapy, a long-term treatment with low-dose doxycycline (50 mg daily) carried out over a period of up to 12 weeks is possible.
- Lyme disease (Stage I): 2 tablets of Doxyderma 100 mg daily (equivalent to 200 mg of doxycycline), for 2-3 weeks (at least for 14 days).

Patients with impaired renal function

Generally, in patients with impaired renal function, it is not necessary to reduce the dose of doxycycline.

Duration of treatment

The duration of treatment depends on the type, gravity, and the course of the disease.

Generally, Doxyderma is taken for 5 – 21 days. Your doctor will decide on the duration of your treatment (see also “Special dosage recommendations”).

If infections caused by β -hemolytic streptococci which are known to be sensitive to doxycycline is treated, the treatment should last at least 10 days to prevent delayed damage (such as rheumatic fever or glomerulonephritis).

For the duration of treatment at the specific dosage recommendations, see below:

- acute gonorrheal urethritis in men: 7 days
- acute gonococcal epididymitis: 10 days
- acute gonococcal infection in women: at least 7 days

- syphilis (primary and secondary forms by penicillin allergy): 15 days
- Lyme disease (stage I): 2 to 3 weeks.

Method of administration

Doxyderma should be taken either regularly in the morning with breakfast or simultaneously with another meal with plenty of water (no milk or its products).

The intake during a meal time can reduce the frequency of gastrointestinal disorders.

To avoid errors during use, always take tablets with plenty of water in a sitting or standing position. After about 10-15 minutes after taking, drink fluids again!

Please tell your doctor or pharmacist if you think the effect of Doxyderma is too strong or too weak.

If you take more Doxyderma than you should

There are no known poisoning events with Doxyderma.

As in the case of overdose, there is a risk of liver and kidney impairments as well as pancreatitis. Inform your doctor if you suspect for overdose to seek advice on the risk and the appropriate measures.

If you forget to take Doxyderma

If you forget once to take Doxyderma, wait until the next day and take the dose at the usual time.

If you stop taking Doxyderma

You may risk the success of the treatment. Please talk to your doctor or pharmacist before you stop treatment with Doxyderma.

If you have any other questions about the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, doxycycline can cause side effects, although not every patient gets them.

For the evaluation of side effects, the following frequencies are used:

Very common	affects more than 1 in 10 users
Common	affects up to 1 in 10 users
Uncommon	affects up to 1 in 100 users
Rare	affects up to 1 in 1.000 users
Very rare	affects up to 1 in 10.000 users
Unknown	Frequency cannot be estimated from the available data

Side effects or important signs from which you have to show caution and measures that should be taken if get any of them:

If you notice any of the following side effects, do not take Doxyderma anymore and ask your doctor immediately.

The Jarisch-Herxheimer reaction which causes fever, chills, headache, muscle pain, and skin rash is usually self-limiting. This occurs shortly after starting doxycycline treatment for infections with spirochete such as Lyme disease.

Common side effects:

- gastrointestinal disturbances in the form of heartburn, stomach pressure, vomiting, bloating, fatty stools and mild diarrhea. The consumption of the substance after or with meals may reduce these undesirable effects to a certain extent, the absorption rate is thus only marginally impaired.

Uncommon side effects:

- bleeding disorders;
- allergic reactions such as generalized rash, erythema, urticaria, pruritus, erythema multiforme, reversible localized swelling of the skin, mucous membranes or joints (angioedema), asthma, anaphylactic shock, fixed drug eruption on genitals and other body regions and a serum sickness-like reaction with fever, headache and joint pain;
- mouth and esophagus inflammation, hoarseness, swelling;
- hematuria;

- irreversible tooth discoloration and enamel damage and a reversible bone growth delay in administration of doxycycline in children under 8 years. In addition, literature reports exist about tooth discoloration in adults after long-term use of doxycycline. The exact mechanism of this side effect in adults is unclear.

Rare side effects:

- the following haematological changes are reversible: leukocytopenia, leukocytosis, thrombocytopenia, anemia, lymphocytopenias, lymphadenopathy, atypical lymphocytes and toxic granulations of the granulocytes;
- severe acute hypersensitivity symptoms such as facial edema, tongue swelling, internal laryngeal swelling with narrowing of the airways, tachycardia, dyspnea (shortness of breath), low blood pressure to threatening shock and cardiac arrest; when these phenomena occur, which can be life threatening, immediate medical attention is required (see "Countermeasures for side effects");
severe skin symptoms with life-threatening systemic reactions (such as exfoliative dermatitis, Lyell syndrome); within the tetracycline group there is a complete cross-allergy;
- restlessness, anxiety;
- intracranial pressure (Pseudotumor cerebri), which is reversible after cessation of therapy; it manifests itself through headaches, nausea, vomiting and possibly a visual impairment by papilledema; paresthesia;
- tachycardia;
- myalgia, arthralgia;
- renal damage, such as interstitial nephritis, acute renal failure and anuria; tetracyclines can cause nephrotoxic damage or may worsen a pre-existing renal impairment (indicated by an increase in creatinine and urea serum);
- disruption or loss of smell and taste sensation, which were only a few cases and only partially reversible;
- skin and subcutaneous tissue disorders: allergic reactions to doxycycline rarely occur. Under sunlight, it may through light-sensitizing come to phototoxic reactions of the exposed areas of the skin (with symptoms of a severe sunburn, such as redness, swelling, blistering, discoloration), rarely with the involvement of the nails (nail peeling and

discoloration). Sunbathing outdoors or in tanning beds should be avoided during doxycycline treatment.

Very rare side effects:

- seizures (after oral administration of doxycycline, a case of an epileptic seizure has been reported; by intravenous administration this side effect has been described in several cases);
- pseudomembranous enterocolitis (see "Countermeasures for side effects"), black hairy tongue.

Infections and infestations

During therapy with doxycycline, as a result of selectivity, colonization of the skin or mucous membranes by *Candida* (particularly of the genital tract and the oral and intestinal mucosa) may occur, with symptoms like inflammation of the mucous membranes of the mouth and pharynx (glossitis, stomatitis), acute inflammation of the external genital organs and the vagina in women (vulvovaginitis), and itching in the anal region (pruritus ani).

Hepatobiliary disorders

In overdose there is the risk of liver damage or pancreatitis.

During pregnancy there is an increased risk of liver damage by tetracycline administration.

Countermeasures for side effects

Pseudomembranous colitis

Here is a cessation of therapy with Doxyderma to consider depending on the indication and an appropriate treatment may be initiated immediately (e.g. administration of specific antibiotics / chemotherapeutics, whose effectiveness has been clinically proven). Drugs which inhibit the intestinal movement (peristalsis) are contraindicated.

Severe acute hypersensitivity reactions (e.g. anaphylaxis)

In this case the treatment with Doxyderma must be stopped immediately and the usual appropriate emergency measures (e.g., antihistamines, corticosteroids, sympathomimetics and possibly ventilation) must be initiated.

Please inform your doctor or pharmacist if any of the side effects gets serious, or if you notice any side effects not listed in this leaflet.

5. HOW TO STORE DOXYDERMA?

Keep out of the sight and reach of children!

Do not store above 30°C.

Do not use this medicine after the expiry date marked in blister and in carton box.

6. OTHER INFORMATION

What Doxyderma contains:

The active substance is Doxycycline monohydrate.

1 tablet contains 104.1 mg of doxycycline monohydrate equivalent to 100 mg of doxycycline.

The other excipients are:

microcrystalline cellulose, sodium starch glycolate, hydrogenated vegetable oil, povidone, colloidal anhydrous silica, magnesium stearate.

Contents of the pack

Box with 10 and 20 tablets.

Marketing authorisation holder and manufacturer

PROFARMA sh.a.,

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Tirana, Albania.

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