PACKAGE LEAFLET

Package leaflet: Information for the patient

Clarithromycin 500 mg Powder for concentrate for solution for infusion

Clarithromycin

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse 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 you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

The name of your medicine is Clarithromycin 500 mg Powder for concentrate for solution for infusion. In the rest of this leaflet Clarithromycin 500 mg Powder for concentrate for solution for infusion is called Clarithromycin.

1. What Clarithromycin is and what it is used for

Clarithromycin contains the active ingredient clarithromycin (as clarithromycin lactobionate). Clarithromycin belongs to a group of medicines called macrolide antibiotics.
Antibiotics stop the growth of bacteria (bugs) that cause infections.

Clarithromycin is used whenever an intravenous (injection into the vein) antibiotic is required to treat severe infections or, alternatively, if a patient cannot swallow clarithromycin tablets.

It is used to treat infections such as:
1. Chest infections such as bronchitis and pneumonia
2. Throat and sinus infections
3. Skin and tissue infections

Clarithromycin is used in adults and children 12 years and older.

2. What you need to know before you are given Clarithromycin

You must not be given Clarithromycin if you:
- are allergic to clarithromycin, other macrolide antibiotics such as erythromycin or azithromycin, or any of the other ingredients of this medicine (listed in section 6).
- are taking medicines called ergot alkaloid tablets (e.g. ergotamine or dihydroergotamine) or use ergotamine inhalers for migraine.
- are taking medicines called terfenadine or astemizole (widely taken for hay fever or allergies) or cisapride (for stomach disorders) or pimozide (for mental health problems)

as combining these medicines can sometimes cause serious disturbances in heart rhythm. Ask your doctor for advice on alternative medicines.
- are taking other medicines that are known to cause serious disturbances in heart rhythm.
- are taking lovastatin or simvastatin (HMG-CoA reductase inhibitors, commonly known as statins, used to lower levels of cholesterol (a type of fat) in the blood).
- are taking a medicine containing lomitapide.
- are taking oral midazolam (a sedative).
- have abnormally low levels of potassium or magnesium in your blood (hypokalaemia or hypomagnesaemia).
- have severe liver disease with kidney disease.
- or someone in your family has a history of heart rhythm disorders (ventricular cardiac arrhythmia, including torsades de pointes) or abnormality of electrocardiogram (ECG, electrical recording of the heart) called "long QT syndrome".
- are taking medicines called ticagrelor or ranolazine (for heart attack, chest pain or angina).
- are taking colchicine (usually taken for gout).

Warnings and precautions
Talk to your doctor, nurse or pharmacist before you are given Clarithromycin:
- if you have heart problems (e.g. heart disease, heart failure, an unusually slow heart rate, or low levels of magnesium in the blood)
- if you have any liver or kidney problems
- if you have, or are prone to, fungal infections (e.g. thrush)
- if you are pregnant or breast feeding

Children
Clarithromycin is not suitable for use in children under 12 years of age.

Other medicines and Clarithromycin
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines as your dose may need to be changed or you may need to have regular tests performed:

- digoxin, quinidine or disopyramide (for heart problems)
- warfarin or any other anticoagulant e.g. dabigatran, rivaroxaban, apixaban (for thinning the blood)
- carbamazepine, valproate, phenobarbital or phenytoin (for epilepsy)
- atorvastatin, rosuvastatin (HMG-CoA reductase inhibitors, commonly known as statins, and used to lower levels of cholesterol (a type of fat) in the blood). Statins can cause rhabdomyolysis (a condition which causes the breakdown of muscle tissue which can result in kidney damage) and signs of myopathy (muscle pain or muscle weakness) should be monitored.
- nateglinide, pioglitazone, repaglinide, rosiglitazone or insulin (used to lower blood glucose levels)
- gliclazide or glimepiride (sulphonylureas used in the treatment of type II diabetes)
- theophylline (used in patients with breathing difficulties such as asthma)
- triazolam, alprazolam or intravenous or oromucosal midazolam (sedatives)
- cilostazol (for poor circulation)
- methylprednisolone (a corticosteroid)
- vinblastine (for the treatment of cancer)
- ciclosporin, sirolimus and tacrolimus (immune suppressants)
- etravirine, efavirenz, nevirapine, ritonavir, zidovudine, atazanavir, saquinavir (anti-viral drugs used in the treatment of HIV)
- rifabutin, rifampicin, rifapentine, fluconazole, itraconazole (used in the treatment of certain bacterial infections)

- tolterodine (for overactive bladder)
- verapamil, amlodipine, diltiazem (for high blood pressure)
- sildenafil, vardenafil and tadalafil (for impotence in adult males or for use in pulmonary arterial hypertension (high blood pressure in the blood vessels of the lung))
- St John's Wort (a herbal product used to treat depression)
- quetiapine or other antipsychotic medicines.
- other macrolide medicines
- lincomycin and clindamycin (lincosamides - a type of antibiotic)

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before receiving this medicine as the safety of clarithromycin in pregnancy or breast-feeding is not known.

Driving and using machines
Clarithromycin may make you feel dizzy or drowsy. If this medicine affects you in this way do not drive, operate machinery or do anything that requires you to be alert.

Clarithromycin contains less than 23 mg sodium (1 mmol) per 500 mg i.e. essentially "sodium-free".

3. How Clarithromycin is given

Clarithromycin is prepared by your doctor or nurse by dissolving the powder in the vial in sterile water. The solution obtained is added to a larger volume of sterile liquid. Clarithromycin is given to you slowly through a needle, into your vein over a period of at least an hour.

The usual dose of Clarithromycin for adults and children over 12 years is 1.0 g per day, split into two doses, for 2 to 5 days. Your doctor will work out the correct dose for you.

Children under 12 years should not be given Clarithromycin. Your doctor will prescribe another suitable medicine for your child.

If a child accidentally swallows some of this medicine, seek medical advice urgently.

If you are given more Clarithromycin than you should
As Clarithromycin is given to you by a doctor, an overdose is unlikely but symptoms may include vomiting and stomach pains.

4. Possible side effects

Like all medicines, Clarithromycin can cause side effects although not everybody gets them.
If you suffer from any of the following at any time during your treatment tell your doctor immediately as your treatment may need to be stopped:
- a red, scaly rash with bumps under the skin and blisters (symptoms of exanthematous pustulosis). The frequency of this side effect is not known (cannot be estimated from the available data).
- rare allergic skin reactions which cause severe illness with ulceration of the mouth, lips and skin which causes severe illness with rash, fever and inflammation of internal organs (DRESS).

- severe or prolonged diarrhoea, which may have blood or mucus in it. Diarrhoea may occur over two months after treatment with clarithromycin, in which case you should still contact your doctor.
- a rash, difficulty breathing, fainting or swelling of the face and throat. This is a sign that you may have developed an allergic reaction.
- yellowing of the skin (jaundice), skin irritation, pale stools, dark urine, tender abdomen or loss of appetite. These may be signs that your liver may not be working properly.
- severe skin reactions such as blistering of the skin, mouth, lips, eyes and genitals (symptoms of a rare allergic reaction called Stevens- Johnson syndrome/toxic epidermal necrolysis).
- muscle pain or weakness known as rhabdomyolysis (a condition which causes the breakdown of muscle tissue which can result in kidney damage).

Common side effects (may affect up to 1 in 10 people):
- inflammation, tenderness or pain at the site of the injection
- difficulty sleeping
- changes in sense of taste
- headache
- widening of blood vessels
- stomach problems such as feeling sick, vomiting, stomach pain, indigestion, diarrhoea
- a change in the way the liver works
- skin rash
- increased sweating

Uncommon side effects (may affect up to 1 in 100 people):
- high temperature
- swelling, redness or itchiness of the skin
- oral or vaginal 'thrush' (a fungal infection)
- inflammation of the stomach and intestines
- decrease of the levels of blood platelets (blood platelets help stop bleeding)
- decrease in white blood cells (leukopenia)
- decrease in neutrophils (neutropenia)
- stiffness
- chills
- increase of eosinophils (white blood cells involved in immunity)
- exaggerated immune response to a foreign agent
- lack or loss of appetite
- anxiety, nervousness
- drowsiness, tiredness, dizziness or shaking
- involuntary muscle movements
- vertigo
- ringing in the ears or hearing loss
- chest pain or changes in heart rhythm such as palpitations or an irregular heartbeat
- asthma: lung disease associated with tightening of air passages, making breathing difficult
- nose bleed
- blood clot that causes sudden blockage in a lung artery (pulmonary embolism)
- inflammation of the lining of the gullet (oesophagus) and lining of the stomach
- anal pain
- inflammation of the tongue, mouth and lips
- bloating, constipation, wind, burping
- dry mouth
- situation where the bile (fluid made by the liver and stored in the gallbladder) cannot flow from the gallbladder to the duodenum (cholestasis)
- inflammation of the liver

- inflammation of the skin characterized by the presence of the bullae which are filled with fluid, itchy and painful rash
- muscle spasms, muscle pain or loss of muscle tissue. If you suffer from myasthenia gravis (a condition in which the muscles become weak and tire easily), clarithromycin may worsen these symptoms.
- raised abnormal kidney and liver function blood test and raised blood tests
- feeling weak, tired and having no energy

Not known side effects (frequency cannot be estimated from the available data):
- inflammation of the colon
- bacterial infection of the outer layers of the skin
- reduction in the level of certain blood cells (which can make infections more likely or increase the risk of bruising or bleeding)
- swelling of the lips and eyes
- confusion, loss of bearings, hallucinations (seeing things), change in sense of reality or panicking, depression, abnormal dreams or nightmares and mania (feeling of elation or over-excitement)
- convulsion (fits)
- paraesthesia, more commonly known as 'pins and needles'
- loss of taste or smell or inability to smell properly
- type of heart rhythm disorder (Torsade de pointes, ventricular tachycardia)
- loss of blood (haemorrhage)
- inflammation of the pancreas
- discolouration of the tongue or teeth
- change in the levels of products made by the liver, inflammation of the liver or an inability of the liver to function properly (you may notice yellowing of the skin, dark urine, pale stools or itchiness of the skin)
- Stevens-Johnson syndrome: skin condition that causes painful blisters and sores of the skin and mucous membranes, especially in the mouth
- acne
- change in the levels of products produced by the kidney, inflammation of the kidney or an inability of the kidney to function properly (you may notice tiredness, swelling or puffiness in the face, abdomen, thighs or ankles or problems with urination)

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:
For UK: Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
For IE: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2, Tel: +353 1 6764971; Fax: +353 1 6762517, Website: www.hpra.ie; E-mail: medsafety@hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Clarithromycin

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not use this medicine if you notice that the solution is not clear and/or has particles in it.

Reconstituted solution: The solution should be stored for either 48 hours at 5±3ºC or for 24 hours (at 25±2ºC) once reconstituted in 10 mL water for injections.

Reconstituted and further diluted solution: The solution should be stored for either 6 hours (at 25±2ºC) or 48 hours at (5±3ºC) once diluted in 250 mL of appropriate diluent.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

6. Contents of the pack and other information

What Clarithromycin contains

- The active substance is clarithromycin. Each vial contains 500 mg of clarithromycin (as clarithromycin lactobionate). After reconstitution in 10 mL of water for injection, reconstituted solution contains 50 mg/mL of clarithromycin (as clarithromycin lactobionate). After further dilution to 250 mL in an appropriate diluent, each millilitre (mL) of the final diluted solution contains about 1.92 mg of clarithromycin.
- The other ingredients are; lactobionic acid and sodium hydroxide (*for pH adjustment*).

This medicine contains less than 23mg sodium (1mmol) per 500mg i.e. It is essentially "sodium-free".

What Clarithromycin looks like and contents of the pack

Clarithromycin is available in glass vials of 20 mL closed with rubber closures and sealed with aluminium flip-off caps. Each vial contains 500 mg of clarithromycin (as clarithromycin lactobionate).
Each pack contains 1, 4, 6, 10 or 50 vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Noridem Enterprises Ltd., Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus.
Manufacturer responsible for batch release: DEMO S.A. PHARMACEUTICAL INDUSTRY, 21st Km National Road Athens-Lamia, 14568 Krioneri, Attiki, Greece, **T**: +30 210 8161802, **F**: +30 2108161587.

This medicinal product is authorised in the Member States of the EEA under the following names:

Portugal:	Claritromicina Noridem
United Kingdom:	Clarithromycin 500 mg Powder for concentrate for solution for infusion
Ireland:	Clarithromycin 500 mg Powder for concentrate for solution for infusion

Germany:	Clarithromycin Noridem 500 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung

This leaflet was last revised in 03/2023.

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The following information is intended for healthcare professionals only:

Clarithromycin 500 mg Powder for concentrate for solution for infusion

Clarithromycin

Refer to the Summary of Product Characteristics for the full prescribing information.
Method of administration
Refer to the summary of product characteristics for posology information.

Clarithromycin should not be given as a bolus or an intramuscular injection.
Clarithromycin should be administered into one of the larger proximal veins as an IV infusion over 60 minutes, using a solution concentration of about 2 mg/mL.

White or almost white, crystalline lyophilized powder to be reconstituted and further diluted before intravenous (IV) administration.

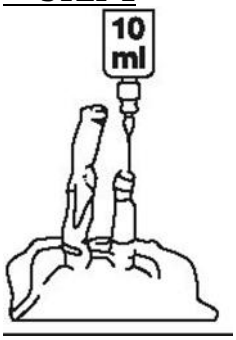
Preparation of the solution for infusion is a two-step process:

STEP 1

Step 1 consists of preparation of the reconstituted solution.
Inject 10 mL of water for injections into the vial containing the product. Shake until the vial contents have dissolved. 1 mL of the vial solution prepared in this way contains 50 mg clarithromycin (as clarithromycin lactobionate).
After reconstitution the solution should be clear.

DO NOT USE
• Diluents containing preservatives

STEP 2



Step 2 consists of the further dilution of the reconstituted solution to a concentration suitable for infusion.
Make up 10 mL of the vial solution prepared in Step 1 (containing 500 mg clarithromycin (as clarithromycin lactobionate)) to 250 mL of a suitable diluent (see below).
1 mL of the infusion solution prepared in this way contains about 1.92 mg clarithromycin (as clarithromycin lactobionate).
DO NOT USE

• Diluents containing inorganic salts	• Solution strengths greater than 2 mg/mL (0.2 %) • Rapid infusion rates (< 60 minutes) Failure to observe these precautions may result in pain along the vein

Physicochemical stability after reconstitution: Chemical and physical in-use stability has been demonstrated for 48 hours at 5±3ºC and for 24 hours (at 25±2ºC) at a final clarithromycin concentration of 50 mg/mL.	Physicochemical stability after reconstitution and further dilution: Chemical and physical in-use stability has been demonstrated for 6 h (at 25±2ºC) or 48 h at (5±3ºC) at a final clarithromycin concentration of 1.92 mg/mL.

Microbiological stability

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Recommended Diluents

5% dextrose in Lactated Ringer's Solution, 5% dextrose, Lactated Ringer's solution, 5% dextrose in 0.3% sodium chloride, 5% dextrose in 0.45% sodium chloride or 0.9% sodium chloride. Compatibility with other IV additives has not been established.

Storage (unopened medicinal product)

This medicinal product does not require any special storage conditions.
Do not use this medicine after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.

Disposal

Any antibiotic residual solution as well as all materials that have been used for administration should be disposed of in accordance with local requirements.