PACKAGE LEAFLET

Package leaflet: Information for the user

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, pharmacist or nurse.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Clarithromycin is and what it is used for

Clarithromycin contains clarithromycin. 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 soft tissue infections

Clarithromycin is indicated in adults and adolescents 12 years and older.

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

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 domperidone, cisapride (for stomach disorders) or pimozide (for mental health problems) as combining these drugs can sometimes cause serious disturbances in heart rhythm. Consult your doctor for advice on alternative medicines.
- are taking other medicines which 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 oral midazolam (a sedative).
- have abnormally low levels of potassium in your blood (hypokalaemia).
- 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)

You must not be given Clarithromycin if any of the above apply to you. If you are not sure, talk to your doctor or nurse before you are given this medicine.

Warnings and precautions

Talk to your doctor or nurse before being given Clarithromycin if:

- you have heart problems (e.g. heart disease, heart failure, an unusually slow heart rate, or abnormally low levels of magnesium in the blood (hypomagnesaemia))
- you have any liver or kidney problems
- you have, or are prone to, fungal infections (e.g. thrush)
- you are pregnant or breast feeding

Children

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

Other medicines and Clarithromycin

You should **not** be given Clarithromycin if you are taking any of the medicines listed in the section above " You must not be given Clarithromycin".

Tell your doctor 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 (for blood thinning)
- 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 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 , breast-feeding and fertility

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

Pregnancy

Clarithromycin should only be used during pregnancy after a careful benefit/risk assessment.

Breast-feeding

Clarithromycin and its active metabolite are excreted in breast milk. Therefore, diarrhoea and fungus infection of the mucous membranes could occur in the breast-fed infant, so that nursing might have to be discontinued. The possibility of sensitisation should be considered. The benefit of treatment of the mother should be weighed against the potential risk for the infant.

Driving and using machines

Clarithromycin may make you feel dizzy or drowsy. If they affect you in this way do not drive, operate machinery or do anything that requires you to be alert.

Clarithromycin contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per 1 vial, that is to say essentially 'sodium-free'.

3. How Clarithromycin is given to you

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 recommended dose of Clarithromycin for adults and children over 12 years is 1g 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 have

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

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine 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:

- 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, tongue, lips, eyes 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 are signs that your liver may have inflammation and not be working properly.
- severe skin reactions such as painful blistering of the skin, mouth, lips, eyes and genitals (symptoms of a rare allergic reaction called Stevens-Johnson syndrome/toxic epidermal necrolysis)
- 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).

- muscle pain or weakness known as rhabdomyolysis (a condition which causes the breakdown of muscle tissue which can result in kidney damage).

Other side effects include:

Common: (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
- increased sweating

Uncommon: (may include 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
- 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 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: (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)
- 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 overexcitement)
- 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
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. 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.

The doctor and hospital pharmacist are responsible for storing, using and disposing of the Clarithromycin correctly.

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

This medicinal product does not require any special storage conditions.

Reconstituted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 20°C - 25°C and for 24 hours at 2-8°C.

Reconstituted and diluted solution: Chemical and physical in-use stability has been demonstrated for 6 hours at 20°C - 25°C and for 24 hours at 2-8°C.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements

6. Contents of the pack and other information

What Clarithromycin contains

The active substance is clarithromycin. Each vial contains 500 mg clarithromycin (as clarithromycin lactobionate).

- The other ingredient is sodium hydroxide 1N (for pH-adjustment)

What Clarithromycin looks like and contents of the pack

Clarithromycin is a white to off white lyophilized powder for concentrate for solution for infusion, available in 15 ml type-I, clear tubular glass vial stoppered with grey bromobutyl double slotted rubber stopper and sealed with baby blue aluminium seal.

Clarithromycin is available in single pack of 1 vial.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Tillomed Laboratories Limited
220 Butterfield, Great Marlings,
Luton, LU2 8DL
United Kingdom

Manufacturer[1]
Emcure Pharma UK Limited
Basepoint Business Centre,
110 Butterfield Great Marlings
Luton LU2 8DL
United Kingdom

Tillomed Pharma GmbH
Mittelstrasse 5/5A
12529 Schönefeld

[1] Only actual manufacturer stated on printed leaflet.

Germany

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

Germany	Clarithromycin Tillomed 500 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
United Kingdom	Clarithromycin 500 mg Powder for Concentrate for Solution for Infusion
Italy	Claritromicina Tillomed
Austria	Clarithromycin Tillomed 500 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
Czech Republic	Clarithromycin Tillomed
Poland	Klarytromycyna Tillomed

This leaflet was last revised in 03/2020.

The following information is intended for healthcare professionals

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.

Preparation for Use

Reconstitution (Step 1)
Prepare the initial solution of clarithromycin 500mg by adding 10 ml of water for injections to the vial.
Shake until the vial contents have dissolved.
Use only water for injections, as other diluents may cause precipitation during reconstitution. Do not use diluents containing preservatives or inorganic salts. Each ml contains 50 mg clarithromycin.

Dilution (Step 2)
The reconstituted solution (500 mg clarithromycin in 10 ml water for injections) should be added to a minimum of 250 ml of one of the following diluents before administration: dextrose 50 mg/ml (5%) in Lactated Ringer's solution, dextrose 50 mg/ml (5%) solution for infusion, Lactated Ringer's, dextrose 50 mg/ml (5%) in sodium chloride 3 mg/ml (0.3%), Normosol-M in dextrose 50 mg/ml (5%), dextrose 50 mg/ml (5%) in sodium chloride 4.5 mg/ml (0.45%), and sodium chloride 9 mg/ml (0.9%) solution for infusion.

1ml of the prepared solution for infusion in this way contains 2 mg clarithromycin.

IMPORTANT: BOTH DILUENT STEPS (1 and 2) SHOULD BE COMPLETED BEFORE USE.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Shelf life and Storage precautions:

2 years

Reconstituted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 20°C - 25°C and for 24 hours at 2-8°C.

Reconstituted and diluted solution: Chemical and physical in-use stability has been demonstrated for 6 hours at 20°C - 25°C and for 24 hours at 2-8°C.

From a microbiological point of view, unless the method of opening/ reconstitution/ dilution precludes the risk of microbial contamination, 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 not be longer than the times stated above for the chemical and physical in-use stability.