PACKAGE LEAFLET: INFORMATION FOR THE USER
Clarithromycin 500mg, powder for concentrate for solution for infusion
Clarithromycin

Read all of this leaflet carefully before you start using 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 or pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

The name of your medicine is Clarithromycin 500mg, powder for concentrate for solution for infusion, which will be referred to as Clarithromycin throughout this leaflet.

What is in this leaflet

1. WHAT CLARITHROMYCIN IS AND WHAT IT IS USED FOR
Clarithromycin is an antibiotic that belongs to a group of medicines called macrolides. Antibiotics stop the growth of bacteria which 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 caused by bacteria such as:
- Chest infections like acute bronchitis and pneumonia
- Throat and sinus infections
- Skin and tissue infections.

2. WHAT YOU NEED TO KNOW BEFORE RECEIVING CLARITHROMYCIN

Do not receive Clarithromycin:
- If you (or your child) are allergic to clarithromycin, other macrolides (similar antibiotics such as erythromycin, azithromycin), or any of the other ingredients of this medicine (listed in Section 6). An allergic reaction may include rash, itching, difficulty in breathing or swelling of the face, lips, throat or tongue
- If you are taking ergotamine like drugs or dihydroergotamine (used to treat migraine and low blood pressure)
- If you are taking cisapride or domperidone (used to treat stomach disorders)
- If you are taking pimozide (used to treat mental illness)
- If you are taking terfenadine or astemizole (used to treat hay fever or allergy)
- If you 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)
- If you are taking oral midazolam (a sedative)
- If you are taking colchicine (used to treat gout)
- If you have abnormally low levels of potassium or magnesium in your blood (a condition known as hypokalaemia or hypomagnesaemia)
- If you have severe liver disease and kidney disease
- If you have an irregular heart rhythm or if you are taking medicines which are known to cause serious disturbances in heart rhythm
- If you taking medicines called ticagrelor or ranolazine (for heart attack, chest pain or angina)
- If you or someone in your family has a history of heart rhythm disorders (ventricular cardiac

arrhythmia, including torsade de pointes) or abnormality of electrocardiogram (ECG, electrical recording of the heart) called “long QT syndrome”
- If you are taking a medicine containing lomitapide.

If any of the above applies to you, consult your doctor for advice on alternative medicines.

Warnings and precautions:
Talk to your doctor or pharmacist or nurse before being given Clarithromycin:
- If you have any liver or kidney problems
- If you are pregnant or breast feeding
- If you have, or are prone to, fungal infections (e.g. thrush)
- If you have heart disease or (bradycardia) slow heart beat
- If you have myasthenia gravis (weakness of muscles)
- If you have any disturbance in heart rhythm.

If any of these apply to you, consult your doctor before being given Clarithromycin. If you develop severe or prolonged diarrhoea during or after receiving this medicine, consult your doctor immediately (see section ‘Possible side effects’).

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

Other medicines and Clarithromycin:
Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.
Especially if you are taking any of the medicines listed below:
- Digoxin, quinidine or disopyramide (used to treat heart conditions)
- Ibrutinib (for cancer treatment)
- Warfarin or any other anticoagulant e.g. dabigatran, rivaroxaban, apixaban (used to thin the blood)
- Carbamazepine, valproate, phenobarbital or phenytoin (used to treat epilepsy)
- Theophylline (used to treat breathing difficulties such as asthma)
- Triazolam (used to induce sleep)
- Alprazolam (used to treat moderate to severe anxiety)
- Midazolam (used in anaesthesia)
- Cilostazol (used to treat poor circulation)
- Atorvastatin, Simvastatin or lovastatin (used to treat high cholesterol)
- Nateglinide, Pioglitazone, Repaglinide, Rosiglitazone or Insulin (used to lower blood glucose levels)
- Methylprednisolone (used to treat inflammation)
- Vinblastine (used for the treatment of cancer)
- Sildenafil, Vardenafil and Tadalafil (used to treat impotence)
- Cyclosporin, or Tacrolimus (used to reduce the activity of the patient’s immune system)
- Zidovudine (used to treat viral infections)
- Rifabutin (used in treatment of some infections)
- Etravirine, Ritonavir, Efavirenz, Nevirapine, Atazanavir, Saquinavir (used to treat HIV infection)
- Colchicine (used to treat gout)
- Pimozide (to treat mental problems)
- Rifampicin (used to treat tuberculosis (TB))
- Fluconazole, Itraconazole (used to treat fungal Infections)
- Verapamil, Amlodipine, Diltiazem (used to treat hypertension)
- Tolterodine (used for treatment of urge Incontinence and/or increased urinary frequency)
- Cisapride (for stomach disorders)
- Astemizole, terfenadine (used to treat allergies)
- Ergotamine or dihydroergotamine (for migraine)
- St. John's Wort (a herbal product used to treat depression)
- Quetiapine or other atypical antipsychotic drugs (used to treat psychotic disorders).

Please tell your doctor if you are taking oral contraceptive pills and diarrhoea or vomiting occurs, as you may need to take extra contraceptive precautions such as using a condom.

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 taking this medicine.

Driving and using machines

Do not drive or use machines, if you suffer from one of the following side effects: dizziness, confusion or disorientation. No studies on the effects on the ability to drive and use machines have been performed.

3. HOW CLARITHROMYCIN IS GIVEN

Dosage:

Clarithromycin may be given for 2 to 5 days by intravenous infusion. The total duration of treatment should not exceed more than 14 days.

Adults and adolescents:

The recommended dose is 1.0 gram daily of Clarithromycin powder for solution for infusion (appropriately diluted), administered as two separate 500mg doses at 12 hourly intervals.

Method and Route of administration:

Clarithromycin will be given to you by a doctor or nurse. Clarithromycin is prepared by dissolving the powder in the vial in sterile water. The solution obtained is added to a larger volume of sterile liquid, and this is then infused (like being given a blood transfusion) into one of your veins for at least an hour.

If you receive more Clarithromycin than you should

Your doctor or nurse will know how much infusion to give you. If you think you have been given too much Clarithromycin you should talk to your nurse or doctor. An overdose with Clarithromycin is likely to cause 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 any of the side effects listed below gets serious, or if you notice any side effects not listed in this leaflet, please contact your doctor immediately. The chance of having side effects may also depend on whether you take Clarithromycin alone, or with any other medicines. Some of the side effects of Clarithromycin can be serious. If you suffer from any of the following symptoms you should contact your doctor straight away:

- Sudden wheeziness or chest tightness, breathing difficulties, swelling of eyelids, face or lips or collapse (fainting) as these may be symptoms of an acute allergic reaction to your medicine
- 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 diarrhoea (this could indicate that you are suffering from a condition called "Pseudomembranous colitis")
- Blistering of the skin, mouth, eyes and genital organs which could indicate a severe adverse reaction
- 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)
- Contact a doctor immediately if you experience a serious skin reaction: a red, scaly rash with bumps under the skin and blisters (exanthematous pustulosis). The frequency of this side effect is not known (cannot be estimated from the available data)
- Muscle pain or weakness known as rhabdomyolysis (a condition which causes the breakdown of muscle tissue which can result in kidney damage).

The following side effects have been reported:

Common (may affect up to 1 in 10 people)

- Feeling sick or being sick, indigestion
- Inflammation, tenderness or pain at the site of injection

- Pain in your stomach
- Your teeth or tongue may become discoloured or you may notice a bitter or metallic taste in your mouth
- Oral thrush
- Headaches
- Smell alteration
- Flushing
- Loose stools
- Abnormal liver function tests
- Rash
- Increased sweating
- Increased blood urea nitrogen
- Difficulty in sleeping.

Uncommon (may affect up to 1 in 100 people)
- Reduction in the number of white cells
- Decreased appetite
- Nervousness
- Problems with your liver such as inflammation or raised liver enzymes
- Increase in time for your blood to clot
- Pain in your joints or muscles, loss of muscle tissue
- Jaundice
- Allergic reactions ranging from urticaria to mild skin eruptions and angioedema to anaphylaxis
- Skin infection characterized by pain, redness, swelling
- Fungal infection (signs of which include redness, itching and discomfort)
- Gastritis (feeling or being sick, loose stools)
- Vaginal thrush (a fungal infection)
- Loss of consciousness
- Diminished voluntary movements and the presence of involuntary movements
- Drowsiness
- Involuntary muscle contractions
- 'Spinning' sensation, difficulty hearing
- The heart suddenly stops beating, palpitations, irregular heart beats
- Bleeding from the nose
- Blockage of the main artery of the lung (symptoms include chest pain, shortness of breath or coughing up blood)
- Inflammation of the lining of the oesophagus (gullet), heartburn, the lining of the stomach becomes inflamed or swollen, abdominal distension, pain in the rectum, dry mouth, passing gas, constipation
- Muscle stiffness
- Pain, fever, weakness, fatigue
- Abnormal kidney function tests
- Feeling anxious.

Rare (may affect up to 1 in 1,000 people)
- 'Ringing' in the ears (tinnitus)
- Uncontrolled shaking of your body (fits or seizures).

Very rare (may affect up to 1 in 10,000 people)
- Reduction of platelets in your blood which may cause bruising or your nose or gums to bleed
- Changes in heart rhythm
- Loss of hearing (which returns after stopping treatment)
- Inflammation of the eye (mainly occurring in patients who take rifabutin (an antibiotic) at the same time)
- Inflammation of the pancreas or infection of the intestine (caused by bacteria)

- Liver failure
- Numbness, tingling or prickling of the skin
- Dizziness or loss of balance
- Inflammation of the kidneys
- Sudden onset of a severe rash or blistering or peeling skin. This may be associated with a high fever and joint pains (Stevens Johnson syndrome / Toxic epidermal Necrolysis).

Not known (frequency cannot be estimated from the available data)
- Inflammation causing abdominal pain or diarrhoea due to a bacterial infection (Clostridium difficile colitis)
- Skin infection characterized by pain, redness, swelling
- Bacterial infection characterized by brown, scaly skin patches
- Severe reduction in number of white blood cells which makes infections more likely
- Serious allergic reaction which causes difficulty in breathing or dizziness
- Low blood sugar (especially in patients taking medicines to treat diabetes)
- Loss of sense of smell, taste and/or hearing
- Life-threatening irregular heartbeat
- Bleeding (when taken with warfarin)
- Liver failure
- Yellowing of the skin or whites of the eyes caused by liver or blood problems
- Acne
- Muscle weakness, breakdown of muscle
- Kidney failure
- Feeling elated or over-excited, which causes unusual behavior
- Abnormal urine colour
- Haemorrhage
- Seeing things or hearing things, feeling confused or disorientated
- Bad dreams
- Depression.

Reporting of side effects
If you get any of the 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 HPRA Pharmacovigilance. Website: www.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 of the product. The expiry date refers to the last day of that month. Do not store above 30°C. Store in the original container in order to protect from light. For in use storage times of the reconstituted solution, please see the section on shelf life in the information intended for medical and healthcare professionals only. Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION
What Clarithromycin contains
The active substance is clarithromycin. Each vial contains 500mg clarithromycin (as lactobionate). Each millilitre of final reconstituted/diluted solution for infusion contains 2mg clarithromycin (as lactobionate). The other ingredient is lactobionic acid.

What Clarithromycin looks like and contents of the pack
Type I clear glass vial with a Ph.Eur. Type I bromobutyl stopper with aluminium cap. Vials are packed in Units of 1, 4 and 6. Not all pack sizes may be marketed. Pack size: 500mg.

Marketing Authorization Holder:
Amdipharm Limited,
Temple Chambers, 3 Burlington Road,
Dublin 4, Ireland
Manufacturer:
LABORATORIOS ALCALA FARMA, S.L., Avenida de Madrid, 82, Alcalá de Henares, Madrid, 28802, Spain.

This medicinal product is authorised in the Member States of the EEA under the following Names:
Ireland: Clarithromycin 500 mg, powder for Concentrate for solution for infusion.
United Kingdom: Clarithromycin 500 mg, powder for Concentrate for solution for infusion.

This leaflet was last revised in October 2021.

The following information is intended for medical or healthcare professionals only:

Recommended Administration:
Clarithromycin 500 mg, powder for concentrate for solution for infusion should be administered into one of the larger proximal veins as an IV infusion over 60 minutes, using a solution concentration of about 2mg/ml.
Clarithromycin should not be given as a bolus or by intramuscular injection.

Step A. Preparation of the vial solution
Inject 10 ml of water for injections into a vial containing the product. Shake until the vial contents have dissolved. Use only water for injections for the dissolution. Other solvents may result in the formation of a precipitate.

Do not use solutions of inorganic salts or solutions containing preservatives. Store the solution at a temperature between 2 and 8°C and use within 48 hours.

Step B. Preparation of infusion solution
Make up 10ml of the vial solution prepared in step A (containing 500 mg clarithromycin lactobionate) to 250 ml using one of the following solutions:

0.9% Sodium Chloride

5% Dextrose

5% Dextrose in 0.3% sodium chloride

5% Dextrose in 0.45% sodium chloride

5% Dextrose in Ringer's lactate solution and Ringer's lactate solution.

Compatibility with other IV additives has not been established.

Infusion solution prepared in this way contains 2mg / ml of clarithromycin lactobionate. Store the solution at a temperature between 2 and 8°C and use within 48 hours.

IMPORTANT: BOTH DILUENT STEPS (A and B) SHOULD BE COMPLETED BEFORE USE.

Dosage:
Clarithromycin may be given for 2 to 5 days by intravenous infusion. The total duration of treatment should not exceed more than 14 days.
Adults and adolescents: The recommended dose is 1.0 gram daily of Clarithromycin powder for solution for infusion (appropriately diluted), administered as two separate 500 mg doses at 12 hourly intervals.
Children under 12 years should not be given Clarithromycin IV. Your doctor will prescribe another suitable medicine for your child.
Renal Impairment:
Patients with severe renal impairment, with creatinine clearance less than 30ml/min, the dosage of clarithromycin should be reduced to one half of the normal recommended dose.

Shelf life
Unopened vials: 4 years

After reconstitution in 10 ml water for injections: Chemical and physical in-use stability has been demonstrated for **24 hours at 25°C and for 48 hours at 5°C.** From a microbiological point of view, the product should be diluted immediately. If not diluted 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° C to 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.**
After dilution to 250 ml in an appropriate diluent: Chemical and physical in-use stability has been demonstrated for **6 hours at 25°C and for 48 hours at 5°C**. From a microbiological point of view, the solution for infusion 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° C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.**

Storage
Do not store above 30°C. Store in the original container in order to protect from light. See carton and vial for expiry date. The products should not be used after this date.

Product Licence number: Ireland PA 1142/022/001