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.
- 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.

This medicine will be referred to as Clarithromycin in the rest of this leaflet

What is in this leaflet:

1. What Clarithromycin is and what it is used for

Clarithromycin contains the active substance clarithromycin, which belongs to a group of medicines called 'macrolide antibiotics'. These are used to kill bacteria or 'germs' that cause infections.

Clarithromycin is used whenever an intravenous (injection into a vein) antibiotic is required to treat severe infections or alternatively if a patient is unable to swallow clarithromycin tablets. It is used to treat infections such as

- Chest infections such as bronchitis and pneumonia
- throat and sinus infections
- skin and tissue infections caused by bacteria.

Clarithromycin is for use in adults and children 12 years and older.

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

You should not be given Clarithromycin:
- if you are allergic to clarithromycin or other macrolide antibiotics such as erythromycin or azithromycin or to any of the other ingredients of this medicine, (listed in section 6)
- if you are taking ergotamine or dihydroergotamine tablets or ergotamine inhalers (used to treat migraine
- if you are taking oral midazolam (a sedative)
- if you are taking terfenadine or astemizole (widely used for hay fever or allergies) or cisapride or pimozide tablets, as combining these drugs whilst receiving Clarithromycin sometimes can cause serious disturbances in heart rhythm

- if someone in your family has a history of heart rhythm disorders (ventricular cardiac arrhythmia, including torsades de pointes) or abnormality of the electrocardiogram (ECG, electrical recording of the heart) called "long QT syndrome".
- if you are taking medicines called ticagrelor or ranolazine (for heart attack, chest pain or angina).
- 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 colchicine (usually taken for gout).
- if you have abnormally low levels of potassium in your blood (hypokalaemia).
- if you have severe liver disease with kidney disease.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before being 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

Take special care with Clarithromycin

- if you have abnormally low levels of magnesium in your blood (hypomagnesaemia) consult your doctor before being given Clarithromycin.

- as prolonged or repeated use of clarithromycin may result in the overgrowth of bacteria and fungi

- if you develop severe or prolonged diarrhoea during or after receiving Clarithromycin.

Children

This product is not suitable for use in children under 12 years of age

You should inform your doctor immediately if you are concerned about your treatment with Clarithromycin.

Other medicines and Clarithromycin
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines

Clarithromycin MUST NOT be used with the following medicines:

- **ergotamine or dihydroergotamine (used to treat migraine) as there is an increased risk of ergotism (fungal poisoning**
- **oral midazolam (a sedative medication)**
- **pimozide (used in the treatment of psychiatric conditions) as there is an increased risk of ventricular arrhythmias (abnormal heart rhythms)**
- **terfenadine or astemizole (widely used for hayfever and allergies)**
- **cisapride (for stomach disorders)**
- **ticagrelor or ranolazine (for heart attack, chest pain or angina)**

- **lovastatin or simvastatin (HMG-CoA reductase inhibitors, commonly known as statins, used to lower levels of cholesterol (a type of fat in the blood). Use with clarithromycin, increases the risk of myopathy (disease resulting in muscle weakness), use with clarithromycin should be avoided.**
- **colchicine (usually taken for gout) clarithromycin increases the risk of colchicine poisoning (side effects include burning in the mouth and throat, fever, vomiting, diarrhoea, abdominal pain and kidney failure, death from respiratory failure can follow)**

If you are taking these medicines you should tell your doctor before you are given Clarithromycin.

Tell your doctor if you are taking any of the following medicines (listed below): -
digoxin, quinidine or disopyramide (used to treat heart conditions)

- carbamazepine, valproate, phenobarbital or phenytoin (drugs used to treat epilepsy)
- theophylline (used to treat breathing difficulties)
- triazolam, alprazolam or midazolam (sedatives)
- cilostazol (used to treat poor circulation)
- methylprednisolone (a corticosteroid)
- vinblastine (used in the treatment of cancer
- 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).
- gliclizide or glimepiride (sulphonylureas used in the treatment of type II diabetes).
- 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))
- ciclosporin, sirolimus and tacrolimus (immune suppressant drug)
- warfarin or other drugs used to thin the blood -use with clarithromycin will enhance the effect of warfarin
- zidovudine etravirine, efavirenz, nevirapine, ritonavir, atazanavir, saquinavir (anti-viral drugs used in the treatment of HIV) - use of clarithromycin tablets reduces absorption of zidovudine and can reduce its effectiveness in treating your viral disease
- 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)
- ranitidine, omeprazole and antacids (used to reduce stomach acid production)
- rifabutin (used in the treatment of some infections)

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 before receiving the 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 they affect you in this way do not drive, operate machinery or do anything that requires you to be alert.

3. How Clarithromycin will be given

Clarithromycin is prepared by your doctor or nurse by dissolving the powder in the vial in sterile water.
The solution prepared is then added to a larger volume of sterile liquid, and this is then given into one of your veins for at least an hour.

The usual dose of Clarithromycin for adults and children over 12 years is 1 gram per day in 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 a more
suitable medicine for your child.

Length of treatment:
Treatment with intravenous clarithromycin shouldbe between 2 to 5 days. The patient should then be switched to oral clarithromycin when necessary.
The total treatment period should not exceed more than 14 days. The usual duration of treatment is 6 to 14 days.

Always use your medicine exactly as your doctor has told you. You should check with your doctor or nurse if you are not sure.

If you are given more Clarithromycin than you should have
This medicine will be given to you by your doctor so it is unlikely that you will receive too much. Your doctor has information on how to recognise and treat an overdose. If you are concerned about your treatment please talk to your doctor.

If a child accidentally swallows some of this medicine, seek medical advice urgently. An overdose of Clarithromycin is likely to cause 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:

- severe or prolonged diarrhoea, which may haveblood 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.
- 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).
- 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).
- leukopenia (low levels of white blood cells - detected during a blood test)
- changes in heart rhythm such as palpitations or an irregular heartbeat, heart attack.
- blood clot that causes sudden blockage in a lung artery (pulmonary embolism)
- 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
- type of heart rhythm disorder (Torsade de pointes, ventricular tachycardia, ventricular
- fibrillation)
- inflammation of the pancreas.
- 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 (jaundice), dark urine, tender abdomen, loss of appetite, pale stools or itchiness of the skin). These may be signs your liver is not working properly
- 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).

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).

Some side effects that have been reported following treatment with clarithromycin are listed below.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor immediately.

Very	• Phlebitis (inflammation of the

Common : may affect more than 1 in 10 people	vein)
Common: may affect up to 1 in 10 people	• headache • difficulty sleeping. • widening of blood vessels. • a change in the way the liver works. • skin rash • increased sweating • tenderness, redness, swelling or pain at the injection site • nausea (feeling sick) • vomiting (being sick) • • dyspepsia (indigestion) • abdominal pains • changes in sense of taste • tenderness or pain at site of injection
Uncommon: may affect up to 1 in 100 people	• oral or vaginal 'thrush' (a fungal infection) • inflammation of the skin characterized by the presence of bullae which are filled with fluid, itchy and painful rash. • exaggerated immune response to a foreign agent. • lack or loss of appetite. • anxiety, nervousness • drowsiness, tiredness, dizziness, shaking or loss of consciousness. • involuntary muscle movements • vertigo • ringing in the ears or hearing loss. • inflammation of the stomach and intestines • asthma: lung disease associated with tightening of air passages, making breathing difficult. • inflammation of the lining of the gullet (oesophagus) and lining of the stomach. • bloating, constipation, wind, burping, dry mouth. • inflammation of the tongue, mouth and lips • raised abnormal kidney and liver function blood test and raised blood tests. • swelling, redness or itchiness of the skin • feeling weak, tired and having

	no energy • joint pains • muscle pain, muscle stiffness 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 • increased prothrombin time (the time taken for blood to clot is increased)
Rare: may affect up to 1 in 1,000 people	• hypoglycaemia (low blood glucose levels) • hearing loss (normally reversible)
Very rare (inc. isolated cases): may affect up to 1 in 10,000 people	• muzziness (confused, muddled, blurred state of mind) • dizziness
Not Known (frequency cannot be estimated from the available data): frequency cannot be estimated from the available data	• pseudomembranous colitis (infection of the colon caused by bacteria). • bacterial infection of the outer layers of the skin. • thrombocytopenia (decreased numbers of platelets- type of blood cell) • 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 over excitement) • convulsions (fits) • loss of taste or smell or inability to smell properly. • paraesthesia, more commonly known as ‘pins and needles’. • disease of the muscle • deafness • loss of blood (haemorrhage) • discolouration of the tongue or teeth. • acne • skin reaction with red scaly rash with bumps under the skin and blisters (exanthematous pustulosis).

Reporting of side effects
If you or your child gets 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 HPRA Pharmacovigilance Earlsfort Terrace IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

5. By reporting side effects you can help provide more information on the safety of this medicine.**ow to store Clarithromycin**

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

Do not store above 30°C. The reconstituted solution will be stored for up to 6 hours at 25°C. Keep the vials in the outer carton in order toprotect from light. The expiry date is stated on the end-flap of the carton, please make sure this has not expired. The doctor will also check that the product does not show signs of visible damage or discoloration. Medicines should not be disposed of viawastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment. This product should only be used in a hospital environment and will be safely disposed of by your doctor.

6. Contents of the pack and other information

What Clarithromycin contains:
The active substance is clarithromycin 500 mg. When reconstituted and diluted, the final solution has a concentration of 2 mg/ml of clarithromycin.

The other ingredient is lactobionic acid.

What Clarithromycin looks like and contents of the pack:

Clarithromycin is a white to off-white powder and when dissolved is a clear solution.

This medicinal product is presented in glass containers called vials.
Each vial contains 500 mg of clarithromycin.The product is supplied in cartons each containing one vial.

Marketing Authorisation Holder:
Martindale Pharmaceuticals Ltd
Bampton Road, Harold Hill, Romford,
Essex RM3 8UG
United Kingdom

Manufacturer:
Laboratorios Alcala
Farma, S.L.
Avenida de Madrid 82
28802 Alcalá de Henares,
Madrid,

Spain

Product licence numbers: PA 0361/025/001

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If you would like any more information, or would like the leaflet in a different format, please contact medical information at the above address.

TECHNICAL PRESCRIBINIG INFORMATION

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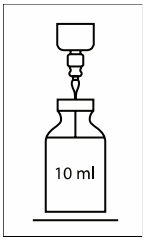
Clarithromycin

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

Recommended Administration
Clarithromycin should not be given as a bolus or an intramuscular injection.

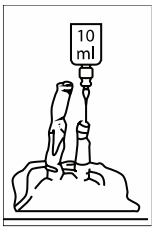
Clarithromycin should be administered into one of the larger proximal veins as an IV infusion over 60 minutes, using a solution concentration of about 2mg/ml.

STEP 1
• Add 10 ml sterilised Water for Injections into the vial and Shake
• May be stored from 5°C up to room temperature



DO NOT USE
• Diluents containing preservatives
• Diluents containing inorganic salts

STEP 2
• Add 10ml from Step 1 to 250ml of a suitable diluent (see below)
• This provides a 2mg/ml solution



DO NOT USE
• Solution strengths greater than 2mg/ml (0.2%)
• Rapid infusion rates (< 60 minutes)

Recommended Diluents
• Dextrose 50 mg/ml (5%) solution for infusion in Lactated Ringer's Solution
• Dextrose 50 mg/ml (5%) solution for infusion
• Lactated Ringer's Solution
• Dextrose 50 mg/ml (5%) in Sodium Chloride 3 mg/ml (0.3%) solution for infusion
• Dextrose
• Dextrose 50 mg/ml (5%) in Sodium Chloride 4.5 mg/ml (0.45%) solution for infusion
• Sodium Chloride 9 mg/ml (0.9%) solution for infusion.

Compatibility with other IV additives has not been established.

Recommended Dosage
Intravenous therapy may be given for 2 to 5 days and should be changed to oral clarithromycin therapy when appropriate. The total duration of treatment should not exceed more than 14 days.

Adults: The recommended dosage of Clarithromycin is 1.0 gram daily, divided into two 500 mg doses, appropriately diluted as described below.

Children: At present, there are insufficient data to recommend a dosage regime for routine use in children.
Adolescents & Elderly: As for adults.

Renal Impairment: In patients with renal impairment who have creatinine clearance less than 30ml/min, the dosage of clarithromycin should be reduced to one half of the normal recommended dose.

Shelf life
4 years unopened.

Reconstituted/Diluted Solutions: Chemical and physical in use stability has been demonstrated for 6 hours at 25ºC.

From a microbiological point of view, the reconstituted and diluted 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 8ºC, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Storage
As packaged for sale: Do not store above 30ºC. Store in the original container as the powder is sensitive to light. See carton and vial for expiry date. The product should not be used after this date.

Product licence numbers: PA 0361/025/001