Package leaflet: Information for the user

CO-AMOXICLAV 500MG/100MG AND 1000MG/200MG POWDER FOR SOLUTION FOR INJECTION OR INFUSION

Amoxicillin/clavulanic acid

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

The name of your medicine is Co-amoxiclav 500mg/100mg or 1000mg/200mg Powder for Solution for Injection or Infusion. In the rest of this leaflet it is called Co-amoxiclav Injection.

What is in this leaflet

1. What Co-amoxiclav injection is and what it is used for

Co-amoxiclav is an antibiotic and works by killing bacteria that cause infections. It contains two different medicines called amoxicillin and clavulanic acid. Amoxicillin belongs to a group of medicines called "penicillins" that can sometimes be stopped from working (made inactive). The other active component (clavulanic acid) stops this from happening.

Co-amoxiclav is used in adults and children to treat the following infections:
- severe ear, nose and throat infections
- respiratory tract infections
- urinary tract infections
- skin and soft tissue infections including dental infections
- bone and joint infections
- intra-abdominal infections
- genital organ infections in women.

Co-amoxiclav is used in adults and children to prevent infections associated with major surgical procedures.

2. What you need to know before you are given Co-amoxiclav injection

You should not have Co-amoxiclav:
- if you are allergic to amoxicillin, clavulanic acid, penicillin or any of the other ingredients of this medicine (listed in section 6)
- if you have ever had a severe allergic reaction to any other antibiotic. This can include a skin rash or swelling of the face or neck

- if you have ever had liver problems or jaundice (yellowing of the skin) when taking an antibiotic.

Do not take Co-amoxiclav if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before having Co-amoxiclav.

Warnings and Precautions
Talk to your doctor, pharmacist or nurse before having this medicine if you:
- have glandular fever
- are being treated for liver or kidney problems
- are not passing water regularly.

If you are not sure if any of the above apply to you, talk to your doctor, pharmacist or nurse before taking Co-amoxiclav.

In some cases, your doctor may investigate the type of bacteria that is causing your infection. Depending on the results, you may be given a different strength of Co-amoxiclav or a different medicine.

Conditions you need to look out for
Co-amoxiclav can make some existing conditions worse, or cause serious side effects. These include allergic reactions, convulsions (fits) and inflammation of the large intestine. You must look out for certain symptoms while you are taking Co-amoxiclav, to reduce the risk of any problems. See *'Conditions you need to look out for'* in **Section 4.**

Blood and urine tests
If you are having blood tests (such as red blood cell status tests or liver function tests) or urine tests (for glucose), let the doctor or nurse know that you are taking Co-amoxiclav. This is because Co-amoxiclav can affect the results of these types of tests.

Other medicines and Co-amoxiclav
Tell your doctor, pharmacist or nurse if you are using, have recently used or might use any other medicines. This includes medicines that can be bought without a prescription and herbal medicines.

If you are taking allopurinol (used for gout) with Co-amoxiclav, it may be more likely that you will have an allergic skin reaction.

If you are taking probenecid (used for gout), your doctor may decide to adjust your dose of Co-amoxiclav.

If medicines to help stop blood clots (such as warfarin) are taken with Co-amoxcilav then extra blood tests may be needed.

Co-amoxiclav can affect how methotrexate (a medicine used to treat cancer or rheumatic diseases) works.

Co-amoxiclav can affect how mycophenolate mofetil (a medicine used to prevent the rejection of transplanted organs) works.

If you are a transplant patient taking mycophenolate mofetil talk to your doctor.

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, pharmacist or nurse for advice before taking this medicine.

Driving and using machines
Co-amoxiclav can have side effects and the symptoms may make you unfit to drive. Do not drive or operate machinery unless you are feeling well.

Co-amoxiclav contains sodium and potassium:
500 mg/100 mg powder for injection or infusion
- Co-amoxiclav 500 mg/100 mg contains approximately 31.4 mg (1.4 mmol) of sodium. This should be considered if you are on a controlled sodium diet.
- Co-amoxiclav 500 mg/100 mg contains approximately 19.6 mg (0.5 mmol) of potassium. This should be considered by patients with kidney problems or patients on a controlled potassium diet.

1000 mg/200 mg powder for injection or infusion
- Co-amoxiclav 1000 mg/200 mg contains approximately 62.9 mg (2.7 mmol) of sodium. This should be considered if you are on a controlled sodium diet.
- Co-amoxiclav 1000 mg/200 mg contains approximately 39.3 mg (1.0 mmol) of potassium. This should be considered by patients with kidney problems or patients on a controlled potassium diet.

3. How to use Co-amoxiclav injection

You will never give yourself this medicine. A qualified person, like a doctor or a nurse, will give you this medicine.

The recommended doses are:
500 mg/100 mg, 1000 mg/200 mg powder for injection or infusion

Adults, and children weighing 40 kg and over

Standard dose	1000 mg/200 mg every 8 hours.
To stop infections during and after surgery	1000 mg/200 mg before the surgery when you are given your anaesthetic. The dose can differ depending on the type of operation you are having. Your doctor may repeat the dose if your surgery takes longer than 1 hour.

Children weighing less than 40 kg
- All doses are worked out depending on the child's bodyweight in kilograms

Children aged 3 months and over:	25 mg/5 mg for each kilogram of bodyweight every 8 hours.
Children aged less than 3 months or weighing less than 4 kg	25 mg/5 mg for each kilogram of body weight every 12 hours.

Patients with kidney and liver problems

- If you have kidney problems you may be given a different dose. A different strength or a different medicine may be chosen by your doctor.
- If you have liver problems your doctor will keep a close check on you and you may have more regular liver function tests.

How Co-amoxiclav will be given to you

- Co-amoxiclav will be given as an injection into a vein or by intravenous infusion.
- Make sure you drink plenty of fluids while having Co-amoxiclav.
- You will not normally be given Co-amoxiclav for longer than 2 weeks without the doctor reviewing your treatment.

If more Co-amoxiclav is given to you than recommended

It is unlikely you will be given too much, but if you think you have been given too much Co-amoxiclav, tell your doctor, pharmacist or nurse immediately. Signs may be an upset stomach (feeling sick, being sick or diarrhoea) or convulsions.

If you have any further questions about how this product is given, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects below may happen with this medicine.

Conditions you need to look out for

Allergic reactions:

- skin rash
- inflammation of blood vessels *(vasculitis)* which may be visible as red or purple raised spots on the skin, but can affect other parts of the body
- fever, joint pain, swollen glands in the neck, armpit or groin
- swelling, sometimes of the face or mouth *(angioedema)*, causing difficulty in breathing
- collapse.
- chest pain in the context of allergic reactions, which may be a symptom of allergy triggered cardiac infarction (Kounis syndrome)

Contact a doctor immediately if you get any of these symptoms. **Stop taking Co-amoxiclav**

Inflammation of large intestine

Inflammation of the large intestine, causing watery diarrhoea usually with blood and mucus, stomach pain and/or fever.

Acute inflammation of the pancreas (acute pancreatitis)

If you have severe and on-going pain in the stomach area this could be a sign of acute pancreatitis.

Drug-induced enterocolitis syndrome (DIES):

DIES has been reported mainly in children receiving amoxicillin/clavulanate. It is a certain kind of allergic reaction with the leading symptom of repetitive vomiting (1-4 hours after drug administration). Further symptoms could comprise abdominal pain, lethargy, diarrhoea and low blood pressure.

Contact your doctor as soon as possible for advice if you get these symptoms.

Common side effects
These may affect up to 1 in 10 people
- thrush (*candida* - a yeast infection of the vagina, mouth or skin folds)
- diarrhoea

Uncommon side effects
These may affect up to 1 in 100 people
- skin rash, itching
- raised itchy rash *(hives)*
- feeling sick (nausea), especially when taking high doses
- vomiting
- indigestion
- dizziness
- headache

Uncommon side effects that may show up in your blood tests:
- increase in some substances *(enzymes)* produced by the liver

Rare side effects
These may affect up to 1 in 1000 people
- skin rash, which may blister, and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge – *erythema multiforme)* if you notice any of these symptoms contact a doctor urgently.
- swelling and redness along a vein which is extremely tender when touched

Rare side effects that may show up in your blood tests:
- low number of cells involved in blood clotting
- low number of white blood cells

Frequency not known
Frequency cannot be estimated from the available data.
- Allergic reactions (see above)
- Inflammation of the large intestine (see above)
- Inflammation of the membranes surrounding the brain and spinal cord (*aseptic meningitis*)
- Serious skin reactions:
    - a widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals *(Stevens-Johnson syndrome)*, and a more severe form, causing extensive peeling of the skin (more than 30% of the body surface – *toxic epidermal necrolysis)*
    - widespread red skin rash with small pus-containing blisters *(bullous exfoliative dermatitis)*

- a red, scaly rash with bumps under the skin and blisters *(exanthemous pustulosis*)
- flu-like symptoms with a rash, fever, swollen glands, and abnormal blood test results (including increased white blood cells (eosinophilia) and liver enzymes) (Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS))
- Rash with blisters arranged in a circle with central crusting or like a string of pearls (linear IgA disease)

Contact a doctor immediately if you get any of these symptoms
- inflammation of the liver *(hepatitis*)
- jaundice, caused by increases in the blood of bilirubin (a substance produced in the liver) which may make your skin and whites of the eyes appear yellow
- blood takes longer to clot
- convulsions (in people taking high doses of Co-amoxiclav or who have kidney problems)

Side effects that may show up in your blood or urine tests:
- severe reduction in the number of white blood cells
- low number of red blood cells *(haemolytic anaemia)*
- crystals in urine leading to acute kidney injury

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 the national reporting system listed below:

Ireland:
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 Co-amoxiclav

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. The expiry date refers to the last day of that month.

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 Co-amoxiclav contains
The active substances are amoxicillin (a penicillin) and clavulanic acid.

There are no other ingredients

What Co-amoxiclav looks like and contents of the pack
Co-amoxiclav injection is available in two strengths, 500/100mg and 1000/200mg, and is available in packs of 10 glass vials.
Co-amoxiclav 500/100mg vials each contain 500mg of amoxicillin (as sodium salt) with 100mg of clavulanic acid (as potassium salt).
Co-amoxiclav 1000/200mg vials each contain 1000mg of amoxicillin (as sodium salt) with 200mg of clavulanic acid (as potassium salt).

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Pinewood Laboratories Limited., Ballymacarbry, Clonmel, Co. Tipperary, Ireland
Manufacturer: CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK

These medicinal products are authorized in the Member States of the EEA under the following names:
Co-amoxiclav 500mg/100mg and 1000mg/200mg Powder for Solution for Injection or Infusion

Leaflet Revised: February 2023

INFORMATION FOR HEALTHCARE PROFESSIONALS
Co-amoxiclav 500mg/100mg Powder for Solution for Injection or Infusion
Co-amoxiclav 1000mg/200mg Powder for Solution for Injection or Infusion
Please refer to the Summary of Product Characteristics (SmPC) for further details on this product.

Qualitative and Quantitative Composition
500/100mg Injection
Each vial contains 500mg amoxicillin (as sodium salt) and 100mg clavulanic acid (as potassium salt)

1000/200mg Injection
Each vial contains 1000mg amoxicillin (as sodium salt) and 200mg clavulanic acid (as potassium salt).

Refer to Section 6.6 for method of reconstitution

For a full list of excipients, see section 6.1.

Pharmaceutical Form
Powder for solution for injection or infusion.

Co-amoxiclav Powder for Solution for Injection or Infusion is a white or almost white powder.

Therapeutic Indications
Co-amoxiclav is indicated for the treatment of the following infections in adults and children (see sections 4.2, 4.4 and 5.1):

- Severe infections of the ear, nose and throat (such as mastoiditis, peritonsillar infections, epiglottitis and sinusitis when accompanied by severe systemic signs and symptoms)
- Acute exacerbations of chronic bronchitis (adequately diagnosed)
- Community acquired pneumonia
- Cystitis
- Pyelonephritis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis
- Intra-abdominal infections
- Female genital infections

Prophylaxis against infections associated with major surgical procedures in adults, such as those involving the:

- Gastrointestinal tract
- Pelvic cavity
- Head and neck
- Biliary tract surgery

Consideration should be given to the official guidance on the appropriate use of antibacterial agents

Posology and Method of Administration
Co-amoxiclav Injection is for intravenous use.

Method of Administration
Co-amoxiclav may be administered either by slow intravenous injection over a period of 3 to 4 min directly into a vein or via a drip tube or by infusion over 30 to 40 min.Co-amoxiclav is not suitable for intramuscular administration.

Children aged less than 3 months should be administered Co-amoxiclav by infusion only. Treatment with Co-amoxiclav may be initiated by the use of an intravenous preparation and completed with an appropriate oral presentation as considered appropriate for the individual patient.

Posology
Adults and children ≥ 40kg
For treatment of infections as indicated in section 4.1: 1000 mg/ 200 mg every 8 hours

For surgical prophylaxis	For procedures less than 1 hour in duration, the recommended dose of Co-amoxiclav is 1000 mg/200 mg to 2000 mg/200 mg given at induction of anaesthesia (Doses of 2000 mg/200 mg can be achieved by using an alternative intravenous formulation of Co-amoxiclav). For procedures greater than 1 hour in duration, the recommended dose of Co-amoxiclav is 1000 mg/200 mg to 2000 mg/200 mg given at induction of anaesthesia, with up to 3 doses of 1000 mg/200 mg in 24 hours. Clear clinical signs of infection at operation will require a normal course of intravenous or oral therapy postoperatively.

Children < 40 kg
Recommended doses:

- *Children aged 3 months and over:* 25 mg/ 5 mg per kg every 8 hours
- *Children aged less than 3 months or weighing less than 4 kg:* 25 mg/5 mg per kg every 12 hours.

Elderly
No dose adjustment is considered necessary.

Renal impairment
Dose adjustments are based on the maximum recommended level of amoxicillin.

No dose adjustment is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.

Adults and children ≥ 40kg

CrCl: 10-30 ml/min	Initial dose of 1000 mg/200 mg and then 500 mg/100 mg given twice daily
CrCl < 10 ml /min	Initial dose of 1000 mg/200 mg and then 500 mg/100 mg given every

	24 hours
Haemodialysis	Initial dose of 1000 mg/ 200 mg and then followed by 500 mg/100 mg every 24 hours, plus a dose of 500 mg/100 mg at the end of dialysis (as serum concentrations of both amoxicillin and clavulanic acid are decreased).

Children < 40 kg

CrCl: 10 to 30 ml/min	25 mg/5 mg per kg given every 12 hours
CrCl < 10 ml /min	25 mg/5 mg per kg given every 24 hours
Haemodialysis	25 mg/5 mg per kg given every 24 hours, plus a dose of 12.5 mg/2.5 mg per kg at the end of dialysis (as serum concentrations of both amoxicillin and clavulanic acid are decreased).

Hepatic impairment
Dose with caution and monitor hepatic function at regular intervals (see sections 4.3 and 4.4).

Pharmaceutical Particulars
List of Excipients
None

Incompatibilities
Co-amoxiclav Injection should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates or with intravenous lipid emulsions.
Co-amoxiclav Injection should not be mixed with infusions containing glucose, dextran or bicarbonate.
If co-amoxiclav is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside can occur under these conditions.
This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Shelf Life
As packed for sale: two years.
The product should be used immediately after opening. Discard any unused solution.

Special Precautions for Storage
Do not store above 25°C.
Keep the vial in the outer carton in order to protect from light.

Nature and Contents of Container
500/100mg Injection
Clear 10ml glass vials (Ph.Eur. Type II) with a grey bromobutyl stopper and aluminiumpropylene flip-off cap.

1000/200mg Injection
Clear 20ml glass vials (Ph.Eur Type II) with a red chlorobutyl stopper and aluminium-propylene flip-off cap.

Special Precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements.

Preparation of solutions for intravenous injection

500 mg/100 mg powder for solution for injection or infusion
Water for Injection Ph.Eur. is the normal solvent.
Co-amoxiclav 500/100 mg should be dissolved in 10 ml of solvent. This yields approximately 10.5 ml of solution for single-dose use. A transient pink colouration may or may not develop during reconstitution. Reconstituted solutions are normally colourless or a pale straw colour.

1000 mg/200 mg powder for solution for injection or infusion
Water for Injection Ph.Eur. is the normal solvent. Co-amoxiclav 1000 mg/200 mg should be dissolved in 20 ml of solvent. This yields approximately 20.9 ml of solution for single-dose use. A transient pink colouration may or may not develop during reconstitution. Reconstituted solutions are normally colourless or a pale straw colour.

Co-amoxiclav should be administered within 20 min of reconstitution.

Preparation of solutions for intravenous infusion
Co-amoxiclav vials are not suitable for multi-dose use.

500 mg/100 mg powder for solution for injection or infusion
Co-amoxiclav should be reconstituted as described above for injection. Without delay the reconstituted solution should be added to 50 ml of infusion fluid using a minibag or in-line burette.

1000 mg/200 mg powder for solution for injection or infusion
Co-amoxiclav should be reconstituted as described above for injection. Without delay the reconstituted solution should be added to 100 ml of infusion fluid using a minibag or in-line burette.

Marketing Authorisation Holder
Pinewood Laboratories Limited., Ballymacarbry, Clonmel, Co. Tipperary, Ireland
Marketing Authorisation Number
500/100mg Injection PA 0281/226/001
1000/200mg Injection PA 0281/226/002

Date of First Authorisation/Renewal of Authorisation
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