PACKAGE LEAFLET: INFORMATION FOR THE USER

Co-amoxiclav 2000 mg/200 mg powder for solution for 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 any 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.

What is in this leaflet

1. What Co-amoxiclav is and what it is used for
2. What you need to know before you are given Co-amoxiclav
3. How Co-amoxiclav is given
4. Possible side effects
5. How to store Co-amoxiclav
6. Contents of the pack and other information

1. What Co-amoxiclav 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 also 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

You should not have Co-amoxiclav
- if you are allergic to amoxicillin, clavulanic acid or penicillin.
- 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 throat.
- if you have ever had liver problems or jaundice (yellowing of the skin) when taking an antibiotic.

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

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given 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 you are given 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 using 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 amoxicillin/clavulanic acid can affect the results of these types of tests.

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

- If you are taking allopurinol (used for gout) with Co-amoxiclav, it may be more likely that you'll 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-amoxiclav, then extra blood tests may be needed.
- Co-amoxiclav can affect how methotrexate works (methotrexate is a medicine used to treat cancer or rheumatic diseases).
- Co-amoxiclav can affect how mycophenolate mofetil (a medicine used to prevent the rejection of transplanted organs) works.

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
Co-amoxiclav 2000 mg/200 mg contains approximately 125.9 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 6.29% of the recommended maximum daily dietary intake of sodium for an adult.

Co-amoxiclav contains potassium
Co-amoxiclav 2000 mg/200 mg contains approximately 39.3 mg (1 mmol) of potassium. To be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

3. How Co-amoxiclav is given

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:

<u>Adults, and children weighing 40 kg and over</u>

Standard dose	1000 mg/100 mg every 8 to 12 hours
Higher dose	1000 mg/100 mg every 8 hours or 2000 mg/200 mg every 12 hours For very severe infections, the dose may be increased up to 2000 mg/200 mg every 8 hours.
To stop infections during and after surgery	1000 mg/100 mg to 2000 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 40kg
All doses are worked out depending on the child's bodyweight in kilograms

Children aged 3 months and over	50 mg/5 mg for each kilogram of body weight every 8 hours
Children aged less than 3 months or weighing less than 4 kg	50 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 is for intravenous use and will be given by intravenous infusion
- Make sure you drink plenty of fluids while being treated with 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 (fits).

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. The side effects listed below may occur 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 throat (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 mucous, 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 (may affect up to 1 in 10 people)
- thrush (candida - a yeast infection of the vagina, mouth or skin folds)
- diarrhoea

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

<u>Uncommon side effects that may show up in your blood tests</u>
- increase in some substances (enzymes) produced by the liver

Rare side effects (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)
- Crystals in urine leading to acute kidney injury
- inflammation of the protective membrane surrounding the brain and spinal cord (*aseptic meningitis*). Symptoms may include fever, nausea, vomiting, headache, stiff neck, rash and extreme sensitivity to light
- 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*)
- Rash with blisters arranged in a circle with central crusting or like a string of pearls (linear IgA disease)
- 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))

➔ 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
- inflammation of tubes in the kidney
- blood takes longer to clot
- convulsions (in people using 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

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 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 Co-amoxiclav

Co-amoxiclav is for use in hospital only and the expiry date and storage instructions stated on the label are for the doctor, nurse or pharmacist's information. The doctor, pharmacist or nurse will make up your medicine. It should be used within 15 minutes of reconstitution.

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 vial and the carton after "EXP". The expiry date refers to the last day of that month.

Do not store above 25°C

Shelf-life after dilution or reconstitution
Reconstituted vials (before dilution for infusion)
The reconstituted solution (1 vial in 20 ml of water for injection) should be further diluted immediately.

Reconstituted and diluted solution (for intravenous infusion)
Chemical and physical in-use stability has been demonstrated after reconstitution and further dilution to 100 mL as shown in the following table:

Infusion Fluid	**Hours (25° C)**
Water for injections	1
Sodium chloride 9 mg/ml (0.9%) solution for infusion	1
Ringer Solution	1
Hartmann's Solution; Ringer-Lactate Solution	1

Potassium Chloride 0.3% - Sodium Chloride 0.9% solution for infusion	1

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 are the responsibility of the user and would not be longer than the times stated above for the chemical and physical in-use stability.

Do not use this medicine if you notice particulates and/or discolouration. The solution should only be used if it is clear and free of particles.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Co-amoxiclav contains
The active substances are amoxicillin and clavulanic acid.

Each vial contains 2000 mg amoxicillin (as amoxicillin sodium) and 200 mg clavulanic acid (as potassium clavulanate).

The medicinal product contains no other ingredients.

What Co-amoxiclav looks like and contents of the pack
The medicinal product is a white powder for solution for infusion and is supplied in a clear glass vial.
Each carton contains 1or 10 vials.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Istituto Biochimico Italiano G. Lorenzini S.p.A.
Via Fossignano, 2
04011 Aprilia (LT)
Italy

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

Germany:	AMOXICLAV IBISQUS 2000 mg/200 mg Pulver zur Herstellung einer Infusionslösung
Ireland:	Co-amoxiclav 2000 mg/200 mg powder for solution for infusion
Austria:	Amoxicillin/Clavulansäure IBISQUS 2000 mg/200 mg Pulver zur Herstellung einer Infusionslösung
Belgium:	Amoxiclav IBI 2000 mg/200 mg poudre pour solution pour perfusion
Netherlands:	Amoxicilline/Clavulaanzuur IBISQUS 2000 mg/200 mg Poeder voor oplossing voor infusie
Malta:	Co-amoxiclav Ibisqus 2000 mg/200 mg Powder for solution for infusion

This leaflet was last revised in 05/2023.

The following information is intended for medical or healthcare professionals only

INFORMATION FOR THE HEALTHCARE PROFESSIONAL
Please refer to the Summary of Product Characteristics for further information

Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned below.
Co-amoxiclav should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates or with intravenous lipid emulsions.

If Co-amoxiclav is prescribed concomitantly 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. Amoxicillin/clavulanic acid solutions should not be mixed with infusion solutions containing glucose, dextran or bicarbonate.

Administration
Co-amoxiclav may be administered by intravenous infusion over 30 to 40 min. It is not suitable for intramuscular administration.

Reconstitution with Water for Injections Ph. Eur.

Co-amoxiclav	Amount of WFI to be added	Final volume
2000 mg/200 mg	20 ml	21.4 ml

A clear, colourless or pale straw coloured solution is produced. A transient pink colouration may or may not develop during reconstitution. Reconstituted solutions are normally colourless to yellow in colour. The reconstitution/dilution is to be made under aseptic conditions.

Dilution for infusion
The reconstituted solution should be diluted without delay to at least 100 ml of infusion fluid using a minibag or in-line burette.

Stability of prepared solutions
Reconstituted vials (before dilution for infusion)
The reconstituted solution (1 vial of 20 ml of water for injection) should be further diluted immediately.

Reconstituted and diluted solution (for intravenous infusion)
Chemical and physical in-use stability has been demonstrated after reconstitution and further dilution to 100 mL as shown in the following table:

Infusion Fluid	Hours
Water for Injection	1
Sodium Chloride Intravenous Infusion 0.9%	1
Ringer Solution	1
Hartmann's Solution; Ringer-Lactate Solution	1
Potassium Chloride 0.3% - Sodium Chloride 0.9% solution for infusion	1

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 are the responsibility of the user and would not be longer than the times stated above for the chemical and physical in-use stability.

The stability of Amoxicillin/clavulanic acid solutions for intravenous use is concentration-dependent. If more concentrated solutions are required, the stability periods should be adjusted accordingly.

Unused antibiotic solution should be discarded

Dosage

Adults and children ≥ 40 kg
For treatment of infections
Standard dose: 1000/100 mg every 8 to 12 hours.
Higher dose: 1000 mg/100 mg every 8 hours or 2000 mg/200 mg every 12 hours.

For very severe infections, the dose can be increased to a maximum of 2000 mg/200 mg every 8 hour.

For surgical prophylaxis.
For procedures less than 1 hour in duration, the recommended dose of Amoxicillin/clavulanic acid is 1000/100 mg to 2000/200 mg given at induction of anaesthesia. For procedures greater than 1 hour in duration, the recommended dose is 1000/100 mg to 2000/200mg given at induction of anaesthesia, with up to 3 doses of 1000/100 mg in 24 hours. Clear clinical signs of infection at operation will require a normal course of intravenous or oral therapy post-operatively.

Children < 40 kg
Children aged 3 months and over: 50 mg/5 mg per kg every 8 hours
Children aged less than 3 months or weighing less than 4 kg: 50 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.

Co-amoxiclav 2000 mg/200 mg should only be used in patients with a creatinine clearance (CrCl) of less than 30 ml / min for surgical prophylaxis when used in one infusion.

Hepatic impairment
Dose with caution and monitor hepatic function at regular intervals.