Package leaflet: Information for the user

Flucloxacillin 250 mg powder for solution for injection/infusion
Flucloxacillin 500 mg powder for solution for injection/infusion
Flucloxacillin 1000 mg powder for solution for injection/infusion
Flucloxacillin 2000 mg powder for solution for injection/infusion
Flucloxacillin

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.
- This medicine has been prescribed for you. 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT FLUCLOXACILLIN IS AND WHAT IT IS USED FOR

Flucloxacillin powder for solution for injection/infusion contains the active substance flucloxacillin.

Flucloxacillin is an antibiotic belonging to a class of antibiotics called beta-lactamase resistant penicillins. Flucloxacillin works by killing bacteria that cause infections. It only works on specific types of bacteria.

Flucloxacillin is used to treat infections such as:
- Skin and soft tissue infections: abscesses, cellulites (inflammation of tissue below the skin)
- Respiratory tract infections: pneumonia, lung abscess, bronchopneumonia
- Bone and joint infections: bone and bone marrow infections (osteomyelitis), arthritis
- Inflammation of the lining of the heart and its valves (endocarditis)

Flucloxacillin is also indicated for prophylaxis in cardiovascular surgery (valve prostheses, artery prostheses) and in orthopedic surgery (arthroplasty, osteosynthesis and arthrotomy) because of the dominant pathogenic potential of staphylococci during such surgical procedures.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE FLUCLOXACILLIN

Do not take Flucloxacillin
- if you are allergic to Flucloxacillin or other beta-lactam antibiotics (e.g. penicillins, cephalosporins)
- if you have a previous history of jaundice/hepatic dysfunction after using Flucloxacillin
- for ocular or subconjunctival administration

Warnings and precautions
Talk to your doctor or pharmacist before taking Flucloxacillin:

- if you are taking or will be taking paracetamol. There is a risk of blood and fluid abnormality (high anion gap metabolic acidosis) which occurs when there is an increase in plasma acidity when flucloxacillin is used concomitantly with paracetamol, particularly in certain groups of patients at risk, e.g. patients with severe renal impairment, sepsis or malnutrition, especially if the maximum daily doses of paracetamol are used. High anion gap metabolic acidosis is a serious disease that must have urgent treatment.

The use of flucloxacillin, especially in high doses, may reduce the potassium levels in the blood (hypokalaemia). Your doctor may measure your potassium levels regularly during therapy with higher doses of flucloxacillin.

Tell your doctor if you have:
- kidney problems
- liver problems

Other medicines and Flucloxacillin
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, particularly the following:
- Probenecid (used in the treatment of gout) as this may interfere with how the body removes Flucloxacillin
- Bacteriostatic medicinal products such as chloramphenicol, erythromycin, sulphonamides, and tetracyclines (used to treat some infections) may interfere with the bactericidal action of Flucloxacillin
- Methotrexate (used to treat some autoimmunitary disorders) can reduce the elimination of Flucloxacillin
- There are case reports describing an altered (usually decreased) INR (International Normalised Ratio, laboratory test for blood clotting) in patients taking warfarin (drug used to inhibit blood clotting) and flucloxacillin concomitantly. Therefore, as a precaution, it is recommended to monitor prothrombin time or INR in patients taking warfarin regularly at the beginning, during and after discontinuation of flucloxacillin treatment.
- Voriconazole (used against fungal infections)

Flucloxacillin may also affect the results of some blood tests (Guthrie-test).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

Flucloxacillin should only be used by pregnant women if considered essential by the doctor. Flucloxacillin passes into breast milk, so ask your doctor for advice before you receive Flucloxacillin.

Driving and using machines
Flucloxacillin is not known to have any affect on your ability to drive or operate machinery.

Flucloxacillin contains sodium
Flucloxacillin 250 mg contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially ‘sodium- free’.

Flucloxacillin 500 mg contains 25 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.25% of the recommended maximum daily dietary intake of sodium for an adult. To be taken into consideration by patients on a controlled sodium diet.

Flucloxacillin 1000 mg contains 51 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.55% of the recommended maximum daily dietary intake of sodium for an adult. To be taken into consideration by patients on a controlled sodium diet.

Flucloxacillin 2000 mg contains 101 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 5.05% of the recommended maximum daily dietary intake of sodium for an adult. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE FLUCLOXACILLIN

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure. Your doctor or nurse will prepare your injection. This medicine will normally be given by an injection of a solution into a vein or a muscle or by infusion into a vein.

The recommended dose is
Adults and adolescents over 12 years of age
The usual dose is 1 g –4 g a day in three to four divided doses, given by intravenous or intramuscular injection.
For severe infections: up to 8 g daily can be given, administered in 4 infusions (over 20-30 min).

The maximum dose of 12 g per day should not be exceeded.

Methicillin-susceptible *Staphylococcus aureus.* Endocarditis: 2 g of Flucloxacillin every 6 h, increasing to 2 g every 4 h in patients weighing >85 kg.
To prevent infections after an operation the usual dose is 2 g intravenous (bolus or infusion)) before the operation when you are given your anaesthetic.. This is then followed by 2 g every 6 hours for 24 hours in cases of vascular and orthopaedic surgery, and for 48 h in cases of cardiac or coronary surgery.

No single dose, by injection or infusion should exceed 2 g.

Patients with severe kidney disorders
You may be given a lower dose, two or three times a day depending on how well your kidneys are working.

Children under 12 years of age
In mild to moderate infection: 25 to 50 mg Flucloxacillin per kg of bodyweight in 24 hours, given in three to four equally divided doses by intravenous or intramuscular injection.
For severe infections, up to 100 mg/kg a day may be given in three to four divided doses.

Methicillin-susceptible *Staphylococcus aureus*. Endocarditis: 200 mg/kg/24 hours of Flucloxacillin in three to four divided doses.
No single dose, by injection or infusion should exceed 33 mg per kg body weight.

Premature infants, neonates, sucklings and infants
Flucloxacillin should be administered to premature infants and neonates only after strict risk-benefit assessment because of the possible triggering of kernicterus (rare brain damage).
Neonates and premature babies and infants generally receive 25 to 50 mg/kg body weight daily, divided into three to four equal doses. An increase in the daily dose to a maximum of 100 mg/kg body weight may be possible.

If you use more Flucloxacillin than you should
As this medicine will normally be given to you by a nurse or a doctor. It is unlikely you will be given too much. If you think you have been given too much Flucloxacillin, tell your doctor or nurse immediately. If you have been given too much, you may feel sick, vomit, and/or have diarrhoea.

If you forget to use Flucloxacillin
As this medicine will normally be given to you by a nurse or a doctor, it is unlikely you will miss a dose. If you have any concerns, discuss this with your doctor or nurse.

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.

Tell your doctor immediately if you get any of the following side effects:
- Severe prolonged diarrhoea, which may have blood or mucus in it, accompanied by stomach pain and fever. This could be a condition called "pseudomembranous colitis"
- Sudden wheezing, swelling of your lips, tongue and throat or body, rash, fainting or difficulties to swallow. These are signs of a severe allergic reaction
- Reddening of the skin with blisters or peeling. There may also be severe blisters and bleeding in the lips, eyes, mouth, nose and genitals. This could be "Stevens-Johnson syndrome" or "toxic epidermal necrolysis"

These effects are very rare, affecting less than 1 in 10,000 people.

Other side effects include:

Common side effects (may affect up to 1 in 10 people)
- Minor gastrointestinal effects such as an upset stomach

Uncommon side effects (may affect up to 1 in 100 people)
- Skin rash
- Itchy skin

Very rare side effects (may affect up to 1 in 10,000 people)
- Abnormal decrease in some types of white blood cells in your blood (neutropenia) which can make you more likely to get infections
- Unusual bleeding or bruising caused by a reduction in the number of platelets in the blood (thrombocytopenia)
- Abnormal increase in a certain type of white blood cells in your blood (eosinophilia). Symptoms include weight loss, night sweats and fever
- Abnormal breakdown of red blood cells (haemolytic anaemia). Symtoms include tiredness, paleness, yellowing of skin, weakness, dizziness, shortness of breath and fast heart beat
- Convulsions (fits) with very high doses of Flucloxacillin in patients with kidney failure
- Skin rash, which may blister, and looks like small targets with central dark spots surrounded by a paler area, with dark ring around the edge (Erythema multiforme)
- Inflammation of the liver (hepatitis)
- Jaundice (cholestatic jaundice)
- Changes to the results of liver function tests
- Joint pain and muscular pain
- Swelling of tubes in the kidney
- Fever
- Cases of blood and fluid abnormality (high anion gap metabolic acidosis) which occurs when there is an increase in plasma acidity, when flucloxacillin is used concomitantly with paracetamol, generally in the presence of risk factors (see section 2)

Not known (cannot be estimated from the available data)
- Serious skin reactions
- A red, scaly rash with bumps under the skin and blisters (exanthematous pustulosis)
- Low potassium levels in the blood (hypokalaemia), which can cause muscle weakness, twitching or abnormal heart rhythm

Contact a doctor immediately if you get any of these symptoms.

Reporting of side effects
If you get any side effects, talk to your doctor 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 FLUCLOXACILLIN

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

This medicine does not require any special storage conditions.

Reconstituted/diluted solution: Chemical and physical in-use stability has been demonstrated for 1 hour at 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.

Do not use this medicine if you notice visible particles.

For single use only. Any unused solution should be discarded.

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 Flucloxacillin contains
- The active substance is flucloxacillin
  Each vial contains 250 mg, 500 mg, 1000 mg or 2000 mg Flucloxacillin (as Flucloxacillin sodium monohydrate).

There are no other ingredients.

What Flucloxacillin looks like and contents of the pack
Flucloxacillin is a white to off-white powder.

The cartons contain 1, 5, 10, 20 and 50 vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Ibigen S.r.l.
Via Fossignano 2
04011 Aprilia (LT)
Italy

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:

DE Flucloxacillin Ibisqus 250 mg Pulver zur Herstellung einer Injektions-/Infusionslösung
Flucloxacillin Ibisqus 500 mg Pulver zur Herstellung einer Injektions-/Infusionslösung
Flucloxacillin Ibisqus 1000 mg Pulver zur Herstellung einer Injektions-/Infusionslösung
Flucloxacillin Ibisqus 2000 mg Pulver zur Herstellung einer Injektions-/Infusionslösung

IE Flucloxacillin 250 mg Powder for solution for injection or infusion
Flucloxacillin 500 mg Powder for solution for injection or infusion
Flucloxacillin 1000 mg Powder for solution for injection or infusion
Flucloxacillin 2000 mg Powder for solution for injection or infusion

NL Flucloxacilline Ibisqus 250 mg Poeder voor oplossing voor injectie / infusie
Flucloxacilline Ibisqus 500 mg Poeder voor oplossing voor injectie / infusie
Flucloxacilline Ibisqus 1000 mg Poeder voor oplossing voor injectie / infusie
Flucloxacilline Ibisqus 2000 mg Poeder voor oplossing voor injectie / infusie

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This leaflet was last revised in

The following information is intended for healthcare professionals only:

For single use only. Any unused solution should be discarded.

Preparation of solution

Flucloxacillin may be added to the following infusion fluids:

- Water for injections
- Sodium chloride 9 mg/ml (0.9%) solution for injection
- Dextrose 50 mg/ml (5%) solution for injection
- Sodium chloride 1.8 mg/ml (0.18% with glucose) 40 mg/ml (4%) solution for injection

Intramuscular use

Add 1.5 ml Water for Injections to 250 mg vial contents.
Add 2.0 ml Water for Injections to 500 mg vial contents.
Add 3.0 ml Water for Injections to 1000 mg vial contents.
Add 4.0 ml water for injections to 2000 mg vial contents.

Intravenous use

Dissolve Flucloxacillin 250 mg in 5 ml Water for Injections.
Dissolve Flucloxacillin 500 mg in 10 ml Water for Injections.
Dissolve Flucloxacillin 1000 mg in 20 ml Water for Injections.
Dissolve Flucloxacillin 2000 mg in 40 ml Water for Injections.

Flucloxacillin reconstitution volumes

After reconstitution with water for injection, as above reported, the vials can be further added to 50, 100, 125, 200, 250 and 500 ml of the compatible infusion fluids.

The powder volume leads to a volume dilatation, according to the below table:

Strength	Reconstitution with water for injection	Final volume	Displacement value
Flucloxacillin 250 mg	5.0 ml	5.2 ml	0.2 ml
Flucloxacillin 500 mg	10.0 ml	10.3 ml	0.3 ml
Flucloxacillin 1000 mg	20.0 ml	20.6 ml	0.6 ml

Flucloxacillin 2000 mg	40.0 ml	41.2 ml	1.2 ml

Consequently, the final concentrations of the reconstituted solution are as calculated below:

Added volume	50 ml	100 ml	125 ml	200 ml	250 ml	500 ml
	Concentration (mg/ml)					
Flucloxacillin 250 mg	4.5	2.4	1.9	1.2	1.0	0.5
Flucloxacillin 500 mg	8.3	4.5	3.7	2.4	1.9	1.0
Flucloxacillin 1000 mg	14.2	8.3	6.9	4.5	3.7	1.9
Flucloxacillin 2000 mg	21.9	14.2	12.0	8.3	6.9	3.7

Administer by slow intravenous injection. Flucloxacillin may also be added slowly to infusion fluids or injected, suitably diluted, into the drip tube over a period of three to four minutes.

Appearance of the solution
Clear colourless or pale yellow particle free solution.
After reconstitution/dilution, the medicinal product should be visually inspected prior to use. Only clear solutions practically free from particles should be used.

Incompatibilities
Flucloxacillin should not be mixed with blood products or other proteinaceous fluids (e.g. protein hydrolysates) or with intravenous lipid emulsions.

If Flucloxacillin is prescribed concurrently with an aminoglycoside, the two antibiotics should not be mixed in the same syringe, intravenous fluid container or giving set; precipitation may occur.
Ringer's solution is not compatible with Flucloxacillin for injection/infusion.