PACKAGE LEAFLET

Package leaflet: Information for the user

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 are given 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 Flucloxacillin is and what it is used for

Flucloxacillin is an antibiotic belonging to a class of antibiotics called beta-lactamase resistant penicillins. The active substance is flucloxacillin. Flucloxacillin works by killing bacteria that cause infection. It only works with specific strains of bacteria.

Flucloxacillin is used in all age groups to treat infections such as:
• Skin and soft tissue infections, like abscesses, cellulitis (inflammation of tissue below the skin), infected burns, pustular dermatitis (impetigo)
• Upper respiratory tract infections, like sore throat (pharyngitis, tonsillitis), inflammation of the sinuses (sinusitis)
• Lower respiratory tract infections, like pneumonia, lung abscess, bronchopneumonia
• Bone and joint infections, like bone and bone marrow infections (osteomyelitis), arthritis
• Inflammation of the lining of the heart and its valves (endocarditis)

Flucloxacillin is also used to prevent infections that occur during heart and lung surgery (valve prostheses, artery prostheses) and in bone, joint and muscle surgery (orthopaedic surgery) because of the dominant pathogenic potential of staphylococci during such surgical procedures.

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

Flucloxacillin must not be given
- if you are allergic to flucloxacillin sodium monohydrate or other betalactam antibiotics (e.g. penicillins, cephalosporins),
- if you have previous history of liver problems from taking flucloxacillin
- for ocular or subconjunctival (eye) administration
- into the spinal canal containing the spinal cord

Warnings and precautions
Talk to your doctor or pharmacist before you are given Flucloxacillin:
• if you have kidney problems
• if you have liver problems
• if you are taking or will be taking paracetamol
• if you have ever had a skin rash or swelling of the face or neck when taking an antibiotic
• if you are on a low sodium diet
• if the skin of your newborn baby appears yellow (jaundice)
• if you have stomach pain and diarrhoea, which may contain blood and mucus
• if you are 50 years of age or older
• if you have any serious health conditions

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 together with paracetamol, particularly in certain groups of patients at risk, e.g. patients with severe kidney 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 the therapy with higher doses of flucloxacillin.

Other medicines and Flucloxacillin
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines, including medicines obtained without a prescription.
Especially:
• methotrexate (used to treat some autoimmune disorders) can reduce the elimination of flucloxacillin (increased risk of toxicity)
• probenecid and sulfinpyrazone (used in the treatment of gout), phenylbutazone, oxyphenbutazone and indometacin (antirheumatic agents) and acetyl salicylic acid (an analgesic) as these may interfere with how the body removes flucloxacillin
• voriconazole (used against fungal infections).
• Medicines to prevent blood clots (e.g. warfarin), as an altered (usually reduced) INR (International Normalised Ratio) has been described in rare cases in patients receiving warfarin and flucloxacillin concomitantly.

Other antibiotics such as chloramphenicol, erythromycin, and tetracyclines (used to treat some infections) as it may affect the action of Flucloxacillin.

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.
Flucloxacillin should be used during pregnancy only if your doctor believes it is essential.
Flucloxacillin is excreted in human milk. There is a risk of hypersensitivity reactions in newborn babies who are breast-fed or of acute changes in their gut flora, resulting in diarrhoea or candidiasis. Ask your doctor for advice before being administered Flucloxacillin.
There are no data available on fertility in humans.

Driving and using machines
Not applicable.

Flucloxacillin contains sodium
Flucloxacillin 500 mg powder for solution for injection/infusion: This medicine contains 25.32 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to

1.2 % of the recommended maximum daily dietary intake sodium for an adult.

Flucloxacillin 1000 mg powder for solution for injection/infusion:
This medicine contains 50.64 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 2.5 % of the recommended maximum daily dietary intake sodium for an adult.

Flucloxacillin 2000 mg powder for solution for injection/infusion:This medicine contains 101.23 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 5 % of the recommended maximum daily dietary intake sodium for an adult.

Talk to your pharmacist or doctor if you need Flucloxacillin on a daily basis for a prolonged period of time, especially if you have been advised to have a low salt diet.

The maximum recommended daily dose of this medicinal product contains 607.68 mg sodium (found in table salt). This is equivalent to 30.38 % of the adult recommended maximum daily dietary intake for sodium.

3. How Flucloxacillin is given

Your doctor will decide on the dose and the duration of treatment. This will depend on the severity and type of infection you have.

Your doctor or nurse will give you this medicine by injection into a muscle (intramuscular) or injection/infusion into a vein (intravenous). Flucloxacillin should not be administered into the eye.

Flucloxacillin 500 mg powder for solution for injection/infusion can also be given to you by injection into a joint (intraarticular) or injection into the lining of the lung (intrapleural).

Injection into a muscle (intramuscular) or injection into a vein (intravenous)

Adults and adolescents at and over 12 years:
1000 mg – 4000 mg/day given in three to four divided doses.
For severe infections: up to 8000 mg daily can be given, administered in 4 infusions (over 20-30 minutes).
No single dose, by injection or infusion should exceed 2000 mg.
Maximum daily dose: 12 000 mg.
For infection of the heart (endocarditis): 2000 mg of flucloxacillin every 6 hours, increasing to 2000 mg every 4 hours in patients weighing >85 kg.
To prevent infections after an operation the usual dose is 2000 mg before the operation when you are given your anaesthetic. This is then followed by 2000 mg every 6 hours for 24 hours in cases of vascular or orthopaedic surgery and for 48 hours in cases of cardiac or coronary surgery.

Children under 12 years of age:
In mild to moderate infections: 25-50 mg per kg body weight in 24 hours. This will be given in three or four divided doses.
For severe infections: Up to 100 mg per kg body weight in 24 hours. This will be given in three or four divided doses each day.
For infections of the heart (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 mg to 50 mg/kg/24 hours, divided into three to four equal doses. The daily dose may be increased to a maximum of 100 mg/kg/24 hours.

Patients with severe kidney problems
If you have kidney problems, you may be given a lower dose just twice or three times a day depending on your kidney function.
Flucloxacillin 500 mg powder for solution for injection/infusion may also be administered by other routes, together with systemic therapy:
- 250 mg to 500 mg by injection into the lining of the lung (intrapleural) and injection into a joint (intraarticular).

If you are given 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, but if you think you have been given too much Flucloxacillin tell your doctor or nurse immediately. Signs may be nausea, vomiting and diarrhoea.

If you forget to receive Flucloxacillin
As this medicine will normally be given to you by a nurse or a doctor it is unlikely you will miss a dose, but 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 or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
If you notice any of the following serious side effects, stop taking Flucloxacillin and contact a doctor immediately:
- Severe prolonged diarrhoea, which may have blood or mucus in it, accompanied with stomach pain and fever. This could be "pseudomembranous colitis".
- Sudden wheezing, swelling of your lips, tongue and throat or body, rash, fainting or difficulties to swallow (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 up to 1 in 10,000 people.

Other side effects are:

Common (may affect up to 1 in 10 people):
- Mild gastrointestinal disturbances.

Uncommon (may affect up to 1 in 100 people):
- Skin rash, itchy skin
- Red or purple spots on the skin caused by bleeding underneath the skin

Very rare (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). Symptoms include tiredness, paleness, yellowing of skin, weakness, dizziness, shortness of breath and fast heart beat.
- Convulsion (fits) with very high doses of flucloxacillin in patients with kidney failure
- Skin rash, which may blister, and look 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 (yellowing of the skin and whites of eye)
- Changes to the results of liver function tests
- Joint pain and muscular pain
- Kidney problems
- Fever
- Blood and fluid abnormality (high anion gap metabolic acidosis) which occurs when there is an increase in plasma acidity, when flucloxacillin is used together with paracetamol, generally in the presence of risk factors (see section 2).

Not known (frequency cannot be estimated from the available data)
- Serious skin reactions. A red, scaly rash with bumps under the skin and blisters (exanthematous pustulosis). Contact a doctor immediately if you get any of these symptoms.
- Inflammation of blood vessels (phlebitis).
- Low potassium levels in the blood (hypokalaemia), which can cause muscle weakness, twitching or abnormal heart rhythm.

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

This medicine does not require any special storage conditions.

Use immediately after first opening.

After reconstitution:
Intramuscular use
Chemical and physical in-use stability has been demonstrated for:
- 4 hours at 23-27°C in artificial light when reconstituted with water for injection and lidocaine solution 1 % w/v.
- 24 hours at 2-8°C protected from light when reconstituted with water for injection and lidocaine solution 1 % w/v.

Intravenous use
Chemical and physical in-use stability has been demonstrated for:

- 4 hours at 23-27°C in artificial light when reconstituted with water for injection and sodium chloride 9 mg/mL (0.9 %) solution.
- 24 hours at 2-8°C protected from light when reconstituted with water for injection and sodium chloride 9 mg/mL (0.9 %) solution.

Intravenous infusion
Chemical and physical in-use stability has been demonstrated for:
- 2 hours at 23-27°C in artificial light when reconstituted with water for injection, sodium chloride 9 mg/mL (0.9 %) solution, glucose 5 % w/v solution or sodium chloride 1.8 mg/mL (0.18 %) with glucose 4% w/v solution.
- 24 hours at 2-8°C protected from light when reconstituted with water for injection, sodium chloride 9 mg/mL (0.9 %) solution, glucose 5 % w/v solution or sodium chloride 1.8 mg/mL (0.18 %) with glucose 4 % w/v solution.

From a microbiological point of view, 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 normally not be longer than 24 hours at 2 to 8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Reconstitution using Hartmann solution:
- at 23-27°C: use immediately
- at 2-8°C: 2 hours protected from light.

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.
Flucloxacillin 500 mg powder for solution for injection/infusion
Each vial contains 500 mg flucloxacillin as flucloxacillin sodium monohydrate.
Flucloxacillin 1000 mg powder for solution for injection/infusion
Each vial contains 1000 mg flucloxacillin as flucloxacillin sodium monohydrate.
Flucloxacillin 2000 mg powder for solution for injection/infusion
Each vial contains 2000 mg flucloxacillin as flucloxacillin sodium monohydrate.

There are no other ingredients.

What Flucloxacillin looks like and contents of the pack

White or almost white, crystalline powder for solution for injection/infusion

Flucloxacillin 500 mg powder for solution for injection/infusion:
20 ml Type III clear glass vial sealed with chlorobutyl rubber stoppers and aluminum caps, with white plastic flip off cap.

Flucloxacillin 1000 mg powder for solution for injection/infusion:
50 ml Type III clear glass vial sealed with chlorobutyl rubber stoppers and aluminum caps, with red plastic flip off cap.

Flucloxacillin 2000 mg powder for solution for injection/infusion:

50 ml Type III clear glass vial sealed with chlorobutyl rubber stoppers and aluminum caps, with white plastic flip off cap.

Pack sizes: cartons of 1 or 10 vials.

Not all pack sizes may be marketed.

Marketing Authorization Holder
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This medicine is authorised in the Member States of the European Economic Area under the following names:

Germany	Flucloxacillin Noridem 500 mg Pulver zur Herstellung einer Injektions-/Infusionslösung Flucloxacillin Noridem 1000 mg Pulver zur Herstellung einer Injektions-/Infusionslösung Flucloxacillin Noridem 2000 mg Pulver zur Herstellung einer Injektions-/Infusionslösung
Austria	Flucloxacillin Noridem 500 mg Pulver zur Herstellung einer Injektions-/Infusionslösung Flucloxacillin Noridem 1000 mg Pulver zur Herstellung einer Injektions-/Infusionslösung Flucloxacillin Noridem 2000 mg Pulver zur Herstellung einer Injektions-/Infusionslösung
Netherlands	Flucloxacilline Noridem 500 mg Poeder voor oplossing voor injectie/infusie Flucloxacilline Noridem 1000 mg Poeder voor oplossing voor injectie/infusie Flucloxacillin Noridem 2000 mg Poeder voor oplossing voor injectie/infusie
Greece	SKOVOLEN SKOVOLEN SKOVOLEN
Ireland	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
Portugal	Flucloxacilina Noridem Flucloxacilina Noridem
Belgium	Flucloxacilline Noridem 500 mg Poudre pour solution injectable/pour perfusion / Poeder voor oplossing voor injectie/infusie / Pulver zur Herstellung einer Injektions-/Infusionslösung

	Flucloxacilline Noridem 1000 mg Poudre pour solution injectable/pour perfusion / Poeder voor oplossing voor injectie/infusie / Pulver zur Herstellung einer Injektions-/Infusionslösung Flucloxacilline Noridem 2000 mg Poudre pour solution injectable/pour perfusion / Poeder voor oplossing voor injectie/infusie / Pulver zur Herstellung einer Injektions-/Infusionslösung

This leaflet was last revised in {MM/YYYY}.

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The following information is intended for healthcare professionals only:

Overdose

Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident, which may lead to fluid and electrolyte disturbance and should be treated symptomatically.
In case of neurological disorders with convulsions, symptomatic treatment is essential (rehydration and diazepam).
Flucloxacillin is not removed from the circulation by haemodialysis.

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 administration set; precipitation may occur.
This medicinal product must not be mixed with other medicinal products except those mentioned in the following section “Instructions on reconstitution/dilution of the medicinal product” below.

Instructions on reconstitution/dilution of the medicinal product

Flucloxacillin can be added to the following solutions for infusion:
- Water for injection
- Sodium chloride 9 mg/mL (0.9 %) solution for injection
- Glucose 5% w/v solution
- Sodium chloride 1.8 mg/mL (0.18 %) solution for injection and glucose 4 % w/v solution
- Hartmann solution

Route of administration	**Solvent**		**Stability of the solution at room temperature**
	Volume to be added	**Type**	

Intramuscular use Flucloxacillin 500 mg Flucloxacillin 1000 mg Flucloxacillin 2000 mg	2 mL 3 mL 4 mL	Water for injection Lidocaine 1 % w/v solution	4 hours in artificial light (24 hours in the refrigerator)
Intravenous use as an injection Flucloxacillin 500 mg Flucloxacillin 1000 mg Flucloxacillin 2000 mg	10 mL 20 mL 40 mL	Water for injection Sodium chloride 9 mg/mL (0.9 %) solution for injection	4 hours in artificial light (24 hours in the refrigerator)
Intravenous use as an infusion Flucloxacillin 500 mg Flucloxacillin 1000 mg Flucloxacillin 2000 mg	Volume equivalent to a concentration of 1 % w/v	Water for injection Sodium chloride 9 mg/mL (0.9 %) solution for injection Glucose 5 % solution Sodium chloride 1.8 mg/mL (0.18 %) solution for injection and glucose 4 % w/v solution	2 hours in artificial light (24 hours in the refrigerator)
		Hartmann solution	Use immediately (2 hours in refrigerator)
Intrapleural use Flucloxacillin 500 mg	5 mL	Water for injections Sodium chloride 9 mg/mL (0.9 %) solution for injection	4 hours in artificial light (24 hours in the refrigerator)
	10 mL	Water for injections Sodium chloride 9 mg/mL (0.9 %) solution for injection	4 hours in artificial light (24 hours in the refrigerator)
Intraarticular use Flucloxacillin 500 mg	5 mL	Water for injections Sodium chloride 9 mg/mL (0.9 %) solution for injection	4 hours in artificial light (24 hours in the refrigerator)

Appearance of the solution
Clear, colourless or pale yellow, particle-free solution.

Only clear solutions practically free from particles should be used.
For single use only.
Any unused solution should be discarded.
Flucloxacillin may also be added to infusion fluids or injected, suitably diluted, into the drip tube.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.