Package leaflet: Information for the user

Benzylpenicillin sodium 600 mg Powder for Solution for Injection/Infusion
Benzylpenicillin sodium 3000 mg Powder for Solution for Injection/Infusion
benzylpenicillin sodium

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

What is in this leaflet

1. What Benzylpenicillin sodium is and what it is used for

Benzylpenicillin sodium is a medicine used to treat infections caused by benzylpenicillin-sensitive bacteria. It is used to treat adults, adolescents, children, newborn infants and premature infants.

Benzylpenicillin sodium is used for the following bacterial infections:
- skin and wound infections
- diphtheria
- lung inflammation
- pus accumulation in body cavities
- infections of the superficial layer of the skin that shows up as a particularly delimited extensive reddening called St. Anthony's fire
- inflammation of the
  - inner lining of the heart
  - membrane which lines the abdomen cavity and covers the abdominal organs
  - meninges
  - bone marrow
- brain abscesses
- certain infections of the genital tract
- anthrax
- tetanus
- gas gangrene
- an infection mainly spread by spoiled or perished food called listeriosis
- pasteurellosis, an infection that can be caught via contact with affected animals as through cat bites or scratches
- rat bite fever
- fusospirochaetosis, a specific infection caused by ulceration of the skin and mucous membranes
- actinomycosis also known as "lumpy jaw"
- complications of sexual transmitted infection called gonorrhoea and syphilis
- Lyme borreliosis, an infection caused by bacteria transmitted by tics.

2. What you need to know before you use Benzylpenicillin sodium

Do not use Benzylpenicillin sodium if you are/have

- allergic to benzylpenicillin
- had hypersensitivity reactions through treatment with penicillin, such as skin rash, itching, fever, shortness of breath, drop in blood pressure.
  Do not use Benzylpenicillin sodium, as there is a risk of life-threatening allergic shock.
- had a severe immediate hypersensitivity reaction to other medicines to treat bacterial infections called beta-lactam antibiotics, such as cephalosporin, carbapenem, monobactam.

Warnings and precautions

Talk to your doctor or pharmacist before you are given Benzylpenicillin sodium and during treatment if you are/have:

- ever experienced signs of intolerance after using other antibiotics, such as cephalosporins
  Your doctor will decide whether Benzylpenicillin sodium may be used and a hypersensitivity test is recommended before starting treatment.
- prone to allergic reactions (e.g. nettle-rash or hay fever) or asthma
  In such cases, there is an increased risk of hypersensitivity reactions.
- a heart condition or severe electrolyte disorders, such as of sodium, calcium, potassium, chloride
  Your doctor should monitor your intake of electrolytes, especially your potassium intake.
- reduced liver or kidney function
  Your doctor may have to adjust your dose or dosing interval of Benzylpenicillin sodium.
- epilepsy, accumulation of fluid in your brain or inflammation of meninges
  Your doctor will carefully monitor you, as you are at increased risk of seizures during therapy.
- a glandular fever, called mononucleosis
  There is an increased risk of skin reactions.
- a cancer of white blood cells, called acute lymphatic leukaemia
  There is an increased risk of skin reactions.
- a fungal skin disease
  You are at increased risk of developing allergy-like reactions.
- using medicines to inhibit blood coagulation
  Monitoring of blood coagulation is recommended and dose adjustment by the doctor of the orally-taking medicine to inhibit blood coagulation if necessary.
- diabetes
  The absorption of Benzylpenicillin sodium may be delayed in patients with diabetes if administered into the muscle.
- a sexually-transmitted disease and syphilis
  Your doctor will perform tests before starting and during treatment.
- being treated for Lyme borreliosis or complications of syphilis
  A temporary reaction called “Jarisch-Herxheimer reaction” may often occur due to the germ-killing effect of Benzylpenicillin sodium. Symptoms are sudden fever, chills, skin redness, headache, muscle and joint pain, tiredness and exhaustion. The symptoms may persist for several days. Contact your doctor for help relieving these symptoms.
- severe, persistent diarrhoea during treatment with Benzylpenicillin sodium
  This diarrhoea could be a result of a treatment-associated inflammation of the colon. Symptoms are bloody, mucous to watery diarrhoea; dull, diffuse to colicky abdominal pain; fever or, occasionally, a constant and painful need to pass stools. Your doctor should immediately stop using Benzylpenicillin sodium and initiate appropriate treatment.
- long-term treatment over several weeks
  Treatment with Benzylpenicillin sodium can cause overgrowth of certain non-sensitive bacteria or yeast-like fungi. Therefore, tell your doctor if you develop diarrhoea, itchy skin rash or growth of yeast-like fungi on mucous membranes. Furthermore, your doctor will regularly carry out certain blood tests during prolonged treatment of more than 5 days.
- to undergo a laboratory test
  Treatment with Benzylpenicillin sodium can influence the results. Therefore, inform your doctor before any laboratory test is performed about your treatment with Benzylpenicillin sodium.

Severe local reactions may occur in infants upon administration into the muscle. Therefore, injection into a vein of this age group should be performed wherever possible.

Other medicines and Benzylpenicillin sodium
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

In particular, tell your doctor if you are using any of the following medicines:
- probenecid: to treat gout
- indomethacin, phenylbutazone, acetylsalicylic acid and similar medicines to reduce fever, inflammation, rheumatic disorders and pain
- other medicines to treat bacterial infections
  Benzylpenicillin only act on certain bacteria. Therefore, Benzylpenicillin sodium should only be combined with other medicines to treat bacterial infections as decided by the doctor.
- digoxin: to treat heart weakness
- methotrexate: to treat severe joint inflammation, cancer and the skin disease psoriasis
  Combined use of methotrexate and Benzylpenicillin sodium must be avoided wherever possible. If this cannot be avoided, reduction of methotrexate dose and monitoring of methotrexate blood level by the doctor is recommended. This includes monitoring for possible side effects of methotrexate.
- medicines taken orally to inhibit blood coagulation, such as acenocoumarol, warfarin
  If combined use is required, suitable blood-clotting parameters should be carefully monitored during and after stopping treatment with Benzylpenicillin sodium. A dose adjustment of the medicine to inhibit blood coagulation may be necessary.

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 or pharmacist for advice before using this medicine.

- **pregnancy**
  Use of Benzylpenicillin sodium is possible throughout pregnancy if the doctor assesses it is necessary. However, Benzylpenicillin sodium is not recommended during pregnancy to treat syphilis.
- **breast-feeding**
  Benzylpenicillin passes into breast milk in small amounts. Although no side effects have been reported in breast-fed infants to date, the possibility must be considered. Inform your doctor immediately if diarrhoea, candida yeast fungal infection or rash occur in the child.
  In infants also fed on baby food, mothers should express and discard breast milk during treatment with Benzylpenicillin sodium. Breast-feeding can be started again 24 hours after the end of treatment.

Driving and using machines
Generally, Benzylpenicillin sodium has no influence on the ability to concentrate and react. However, serious side effects, like severe allergic reactions, Benzylpenicillin sodium can reduce the ability to react. Avoid driving or using machines should such serious side effects occur.

Benzylpenicillin sodium contains sodium
Benzylpenicillin sodium 600 mg Powder for Solution for Injection/Infusion
This medicine contains 38.6 mg sodium per vial, equivalent to 1.9% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Benzylpenicillin sodium 3000 mg Powder for Solution for Injection/Infusion
This medicine contains 193 mg sodium per vial, equivalent to 9.7% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

3. How to use Benzylpenicillin sodium

Benzylpenicillin sodium is usually administered by a doctor, who determines the method of use, dose and the dosing interval. Check with your doctor if you are not sure.

The usual recommended dose is:

- **adults and adolescents from 12 years**
  The usual daily dose is 0.6-3 g/day (1 to 5 million IU (international units)) divided into 4 to 6 doses.
  In case of severe infection, the daily dose can be increased to 6-24 g/day (10 to 40 million IU).
- **children from 1 month up to their 12th birthday**
  The usual daily dose is 18-60 mg/kg/day (0.03 to 0.1 million IU) per kilogram body weight divided into 4 to 6 doses. In case of severe infection, the daily dose can be increased to 60-600 mg/kg/day (0.1 to 1 million IU) per kilogram body weight.
- **new-born babies from 2 weeks up to 1 month**
  The usual daily dose is 18-60 mg/kg/day (0.03 to 0.1 million IU) per kilogram body weight divided into 3 to 4 doses. In case of severe infection, the daily dose can be increased to 120-600 mg/kg/day (0.2 to 1 million IU) per kilogram body weight.
- **premature and new-born babies up to 2 weeks**
  The usual daily dose is 18-60 mg/kg/day (0.03 to 0.1 million IU) per kilogram body weight divided into 2 doses. In case of severe infection, the daily dose can be increased to 120-600 mg/kg/day (0.2 to 1 million IU) per kilogram body weight.

Patients over 65 years and patients with reduced kidney or liver function
The doctor will check the kidney and liver function before and regularly during treatment. Based on the results, the doctor adjusts the dose and dosing interval as needed.

Duration of use
The duration of use is decided by the doctor. It depends on the severity of the infection, the germ-killing effect and the patient's symptoms, which can last from a few days to several weeks.

Method of use
Benzylpenicillin sodium is usually administered by a doctor.

Benzylpenicillin sodium can be injected into a muscle or a vein. Administration into a vein can be given as an injection using a syringe or as a short infusion, generally lasting between 30 and 60 minutes.

If you are given more Benzylpenicillin sodium than you should
Inform your doctor if you think you have been given too much. Overdose symptoms are increased excitability of nerves and muscles or susceptibility to fits in the brain.

If you forget to use Benzylpenicillin sodium
Talk to your doctor immediately.

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.

Severe allergic reactions (anaphylactic reactions or angioedema) which may occur as:

- skin rash or itchy skin, difficulty in breathing or tightness of the chest, puffiness of the eyelids, face or lips, swelling or redness of the tongue, fever, joint pains, swollen lymph nodes.

Side effects may occur with following frequencies:
common: may affect up to 1 in 10 people

- effect on laboratory tests.

uncommon: may affect up to 1 in 100 people

- allergic reactions

- nettle-rash
- severe allergic reactions affecting the whole body or which causes difficulty in breathing, such as asthma, skin bleeding, stomach and bowel disorders
- severe skin reactions, such as:
  - skin rash with fever and blisters called erythema multiforme
  - large scaly skin inflammation called exfoliative dermatitis
- fever
- joint pain
- inflammation of the mouth lining
- tongue inflammation, black hairy tongue
- nausea, vomiting.

rare: may affect up to 1 in 1,000 people
- electrolyte disturbances due to rapid infusion of high doses
- nerve disorders
  Convulsive reactions may occur upon infusion of high doses. This should be particularly considered in patients with severely reduced kidney function, epilepsy, inflammation of meninges or accumulation of fluid in the brain. This also applies to patients where a machine temporarily takes over the function of the heart and lungs during surgery.
- diarrhoea
  If diarrhoea occurs, the possibility of colon inflammation should be considered. See section 2 "Warnings and precautions".
- kidney disease
- abnormal presence of the protein albumin or blood in the urine
- sediment in the urine called cylindruria
- reduced urine output or failure to excrete urine
  This mostly clears up within 48 hours after stopping treatment.
- severe local reactions during administration into a muscle in infants.

very rare: may affect up to 1 in 10,000 people
- increased number of the white blood cells known as eosinophils
- reduced number of white blood cells (such as neutrophilic granulocytes, granulocytes), haemolytic anaemia (reduced blood levels of red blood cells) or all of them
- blood-clotting disorders.

not known: frequency cannot be estimated from the available data
- AGEP – acute generalised exanthematous pustulosis with symptoms such as severe drug skin reactions with or without reddening of the skin, fever, pustules
- maculo-papular rash (flat and red area on the skin)
- rash morbilliform (rash that looks like measles)
- itching
- erythema (inflammatory reddening of the skin)
- angioedema (swelling of the skin and mucosa and subcutaneous tissue, generally located on the face, mouth, or tongue)
- prolongation of the bleeding time and average time required in tests for blood to clot
- thrombocytopenia (reduced blood levels of platelets)
- a hypersensitivity reaction to proteins in the blood, called. serum sickness, with symptoms of fever, lymph node swelling, local redness at the injection site, itching
- Jarisch-Herxheimer reaction, characterised by sudden fever, chills, skin redness, headache, muscle and joint pain, tiredness and/or exhaustion
- metabolic encephalopathy (neurological disorders with convulsions and loss of consciousness).
- liver inflammation
- reduced bile flow in the gallbladder
- skin disease with blisters called pemphigoid.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system: 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 Benzylpenicillin sodium

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

Do not store above 25°C.

Chemical and physical in-use stability of the reconstituted and diluted product is concentration and temperature dependent. The following in-use storage times have been demonstrated:

	2°C to 8°C	**below 25°C**
300-546 mg/ml (500,000 – 910,000 IU/ml) (this range includes the recommended concentration for injection into the muscle)	48 hours	8 hours
60 mg/ml (100,000 IU/ml) (the recommended concentration for injection/infusion into the vein)	24 hours	4 hours

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°C to 8°C.

6. Contents of the pack and other information

What Benzylpenicillin sodium contains
The active substance is benzylpenicillin as sodium salt.

Benzylpenicillin sodium 600 mg Powder for Solution for Injection/Infusion:
One vial contains 600 mg (equivalent to approximately 1 mega IU) benzylpenicillin as sodium salt.

Benzylpenicillin sodium 3000 mg Powder for Solution for Injection/Infusion:
One vial contains 3000 mg (equivalent to approximately 5 mega IU) benzylpenicillin as sodium salt.

What Benzylpenicillin sodium looks like and contents of the pack
White to off-white powder for solution for injection/infusion.

Vials (5 ml, 15 ml or 30 ml) of glass type III with halogenated butyl rubber stopper (infusion stoppers) with an aluminium bordered cap with crimp seal or alternatively with flip-off bordered cap.

Pack sizes:
Benzylpenicillin sodium 600 mg Powder for Solution for Injection/Infusion:
1, 10 and 100 vials (with nominal volume of 5 ml)

Benzylpenicillin sodium 3000 mg Powder for Solution for Injection/Infusion:
1, 10, 25 and 50 vials (with nominal volume of 15 and 30 ml)

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder
Rowex Ltd., Bantry, Co. Cork, Ireland.

Manufacturer
Sandoz GmbH, Biochemiestraße 10, 6250 Kundl, Austria.

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

Austria	Penicillin G-Natrium Sandoz 500.000 IE – Trockenstechampulle Penicillin G-Natrium Sandoz 1 Mega IE – Trockenstechampulle Penicillin G-Natrium Sandoz 5 Mega IE – Trockenstechampulle Penicillin G-Natrium Sandoz 10 Mega IE – Trockenstechampulle
Denmark	Benzylpenicillinnatrium Sandoz
Germany	Penicillin G HEXAL 1 Million I.E. Pulver zur Herstellung einer Injektions-/Infusionslösung Penicillin G HEXAL 5 Millionen I.E. Pulver zur Herstellung einer Injektions-/Infusionslösung Penicillin G HEXAL 10 Millionen I.E. Pulver zur Herstellung einer Injektions-/Infusionslösung
Ireland	Benzylpenicillin sodium 600 mg Powder for Solution for Injection/Infusion Benzylpenicillin sodium 3000 mg Powder for Solution for Injection/Infusion
The Netherlands	Natriumbenzylpenicilline Sandoz 500.000 IE, poeder voor oplossing voor injectie Natriumbenzylpenicilline Sandoz 1.000.000 IE, poeder voor oplossing voor injectie Natriumbenzylpenicilline Sandoz 5.000.000 IE, poeder voor oplossing voor injectie Natriumbenzylpenicilline Sandoz 10.000.000 IE mega IE, poeder voor oplossing voor injectie
Norway	Benzylpenicillinnatrium Sandoz
United Kingdom	Benzylpenicillin sodium 600mg powder for solution for injection/infusion

This leaflet was last revised in 11/2021.

The following information is intended for healthcare professionals only:

Incompatibilities
The contents of the vial should only be used in a solution with water for injections, 5% glucose solution or 0.9% sodium chloride, in order to avoid incompatibilities.

In order to avoid undesirable chemical reactions or undesirable effects, the already dissolved vials should not be mixed with other mixed injections or infusions (e.g. Ringer's lactate solution).
Oxidising and reducing substances, alcohol, glycerol, macrogols and other hydroxy compounds can inactivate benzylpenicillin.

Benzylpenicillin solutions are most stable in the pH range 6 – 7 (optimum pH 6.8).

Benzylpenicillin is incompatible in solution with the following:
- cimetidine
- cytarabine

- chlorpromazine hydrochloride
- dopamine hydrochloride
- heparin
- hydroxyzine hydrochloride
- lactate
- lincomycin hydrochloride
- metaraminol
- sodium hydrogen carbonate
- oxytetracycline
- pentobarbital
- tetracycline hydrochloride
- thiopental sodium
- vancomycin.

Benzylpenicillin is not compatible with vitamin B complex and ascorbic acid in mixed solutions.

Special precautions for disposal and other handling
In order to avoid hypersensitivity reactions caused by degradation of product, it is recommended to use the injection or infusion solution immediately after preparation. The administration should at least take place within the maximum recommended in-use shelf life (see section 5).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Preparation of a solution for IV injection or infusion:
A solution for intravenous use can be prepared with the following solvents:
– water for injections (WFI)
– 5% glucose solution
– 0.9% sodium chloride solution.

The recommended concentration for intravenous use is 60 mg/ml (100,000 IU/ml).

An isotonic solution is obtained when using WFI as solvent (osmolarity of 60 mg/ml (100,000 IU/ml) in WFI is 337 mOsmol/l). It should be taken into account that more concentrated solutions and solutions in 5% glucose or 0.9% sodium chloride are hypertonic and that the use of 0.9% sodium chloride leads to an additional supply of electrolytes.

For Benzylpenicillin sodium **0.5 mega IU** powder for solution for injection / infusion a one-step reconstitution in the original vial suffices.

For Benzylpenicillin sodium **1 mega IU, 5 mega IU** and **10 mega IU** powder for solution for injection / infusion a two-step preparation is required, i.e. reconstitution in the original vial followed by dilution of the concentrated solution in another container.

The reconstitution and dilution instructions in the table underneath result in an IV injection / infusion of 60 mg/ml (100,000 IU/ml).

Reconstitution and dilution instructions for intravenous injection/infusion				
	Reconstitution step		**Dilution step**	
1 vial	*Recommended volume of solvent to be added for reconstitution*	*Resulting (concentrate for) solution for IV injection/infusion*	*Dilution until 60 mg/ml (100,000 IU/ml)*	*Resulting solution for injection/infusion*
Benzylpenicillin sodium 600 mg (1 mega IU) **powder for solution for injection / infusion** *(contains ± 0.6 gram powder)*	4.6 ml	**concentrate to be diluted before use** 5 ml = 600 mg (120 mg/ml) (5 ml = 1 mega IU) (200,000 IU/ml)	1 volume concentrate + 1 volume diluent e.g. add 5 ml concentrate to 5 ml diluent	**ready for use** 10 ml = 600 mg (60 mg/ml) (10 ml = 1 mega IU) (100,000 IU/ml)
Benzylpenicillin sodium 3000 mg (5 mega IU) **powder for solution for injection / infusion** *(contains ± 3 gram powder)*	7.9 ml	**concentrate to be diluted before use** 10 ml = 3000 mg (300 mg/ml) (10 ml = 5 mega IU) (0.5 mega IU/ml)	1 volume concentrate + 4 volumes diluent e.g. add 10 ml concentrate to 40 ml diluent	**ready for use** 50 ml = 3000 mg (60 mg/ml) (50 ml = 5 mega IU) (100,000 IU/ml)

Preparation of a solution for IM injection:
A solution for intramuscular use can be prepared with the following solvent:
- water for injections (WFI)

Due to the concentrated nature of a solution for intramuscular injection the recommended solvent is WFI in order to keep to tonicity as low as possible (any solution exceeding 60 mg/ml (100,000 IU/ml) is hypertonic).

The maximum volume for intramuscular administration is 5 ml per injection site and the maximum intramuscular dose is 6 g (10 mega IU). Higher doses can be given as intravenous infusion (see section 3).

Instructions for the one-step reconstitution in the original vial in the minimum amounts of solvent is described in the table underneath. Further dilution is possible, but depends on the combination of intended dose and maximum injection volume of 5 ml per injection site.

Reconstitution instructions for intramuscular injection		
1 vial	Recommended volume of solvent to be added for reconstitution	Resulting solution for intramuscular injection **(maximum 5 ml per injection site)**
Benzylpenicillin sodium 600 mg (1 mega IU) **powder for solution for injection / infusion** *(contains ± 0.6 gram powder)*	0.6 - 1 ml	
	e.g. 0.6 ml	1.1 ml = 600 mg (1 mega IU) (545 mg/ml (909,090 IU/ml))
	e.g. 1 ml	1.5 ml = 600 mg (1 mega IU) (400 mg/ml (666,667 IU/ml))
Benzylpenicillin sodium 3000 mg (5 mega IU) **powder for solution for injection / infusion** *(contains ± 3 gram powder)*	3 - 5 ml	
	e.g. 3 ml	5.5 ml = 3000 mg/ml (5 mega IU) (545 mg/ml (909,090 IU/ml))
	e.g. 5 ml	7.5 ml = 3000 mg (5 mega IU) (400 mg/ml (666,667 IU/ml))

Notes on intramuscular injection:

Up to a maximum of 10 mega IU Benzylpenicillin sodium, dissolved in 6 to 10 ml water for injection, is administered up to twice daily as a deep intramuscular injection into the upper, outer quadrant of the gluteus maximus or Hochstetter's ventrogluteal field.
5 ml per injection site should be regarded as the upper limit of tolerability. Repeated injections should be given on alternate sides. Higher doses can be given as an intravenous infusion.
Severe local reactions may occur with intramuscular administration, especially in infants. If possible, intravenous therapy should be performed.

Caution: Cerebral seizures may occur if the infusion is too rapid.