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

Active substance: 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 or pharmacist.
- 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 germ-killing medicine (antibiotic), which is used to treat certain infectious diseases. In this regard, Benzylpenicillin sodium is suitable for treating adults, adolescents, children, newborn infants and premature infants.

Benzylpenicillin sodium is used for the following infections:

- blood poisoning (septicaemia)
- skin and wound infections
- diphtheria (an acute infectious disease of the upper airways)
- pneumonia
- pus accumulation in body cavities (empyema)
- erysipelas (St. Anthony’s fire)
- inflammation of the inner lining of the heart (bacterial endocarditis)
- peritonitis
- meningitis
- brain abscesses
- inflammation of the bone marrow (osteomyelitis)
- certain infections of the genital tract.

Benzylpenicillin sodium is also effective in the following specific infections:
- anthrax
- lockjaw (tetanus)
- gas gangrene
- listeriosis (an infection mainly spread by spoiled or perished food)
- pasteurellosis (an infection that can be caught via contact with affected animals, or which is also caused by cat bites or scratches)
- rat bite fever
- fusospirochaetosis (a specific infection caused by ulceration of the skin and mucous membranes)
- actinomycosis (“lumpy jaw”)

- complications in gonorrhoea and syphilis
- Lyme borreliosis (an infectious disease transmitted by tics), from the second stage of the disease onwards.

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

Do not use Benzylpenicillin sodium
- if you are allergic to benzylpenicillin.
- if you have ever been treated with a penicillin before and hypersensitivity reactions occurred (e.g. skin rash, itching, fever, shortness of breath, drop in blood pressure). In this case, as there is a risk of life-threatening anaphylactic shock, Benzylpenicillin sodium must not be used.
- if you have a history of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. cephalosporin, carbapenem or monobactam).

Warnings and precautions
Please talk to your doctor or pharmacist before you are given Benzylpenicillin sodium
- if, before treatment with penicillin, you have ever experienced signs of intolerance after using other antibiotics (e.g. cephalosporins). In this case, your doctor will decide whether Benzylpenicillin sodium may be used. Before the start of treatment, a hypersensitivity test should therefore be carried out.
- if you are prone to allergic reactions (e.g. nettle rash or hay fever) or asthma. In such cases, there is an increased risk of hypersensitivity reactions.
- if you suffer from a heart condition or severe electrolyte disorders (e.g. sodium, calcium, potassium, chloride): Your doctor should monitor your intake of electrolytes, especially your potassium intake.
- if your liver or kidney function is impaired. In such cases, your doctor may have to individually adjust your dosage or dosing interval of Benzylpenicillin sodium (see section 3. “How to use Benzylpenicillin sodium”).
- if you suffer from epilepsy or if you have brain oedema or meningitis. Your doctor will carefully monitor you, as you are at increased risk of seizures during therapy.
- if you have glandular fever (mononucleosis). There is an increased risk of skin reactions.
- if you are suffering from acute lymphatic leukaemia (a type of blood cancer). There is an increased risk of skin reactions.
- if you are currently suffering from any fungal skin disease (dermatomycoses). You are at increased risk of developing allergy-like reactions.
- if you are also receiving so-called anticoagulants. In rare cases, prolongation of the prothrombin time has been reported in patients receiving penicillins. Appropriate monitoring should be performed. Adjustment of the oral anticoagulant dose may be necessary to obtain the desired degree of anticoagulation (see “Other medicines and Benzylpenicillin sodium”).
- if you have diabetes. In the event of intramuscular administration, the absorption of Benzylpenicillin sodium may be delayed.
- In patients with existing sexually-transmitted diseases, concurrent syphilis should be ruled out before the start of therapy.
- In patients being treated for Lyme borreliosis or complications of syphilis, a temporary reaction (known as a “Jarisch-Herxheimer reaction”) may often occur due to the germicidal effect of Benzylpenicillin sodium on the pathogens within these patients. This reaction may be characterised by sudden fever, chills, skin redness, headache, muscle and joint pain, tiredness and/or exhaustion. The symptoms may persist for several days. Tell your doctor who can help you to relieve these temporary symptoms.
- if you experience severe, persistent diarrhoea during treatment with Benzylpenicillin sodium, this could be a result of antibiotic-associated colitis (inflammation of the colon). Symptoms of this are bloody/mucous, watery diarrhoea; dull, diffuse to colicky abdominal pain; fever or, occasionally, a constant and painful need to pass stools. Benzylpenicillin sodium should be stopped immediately and a doctor will initiate appropriate treatment immediately.
- during long-term treatment (several weeks), any antibiotic therapy can cause overgrowth of certain non-sensitive germs (bacteria or yeast-like fungi). For this reason, tell your doctor if you develop diarrhoea, itchy skin rash or colonisation of the mucous membranes by yeast-like fungi. Furthermore, your doctor will carry out regular checks on certain blood tests (electrolytes, kidney function tests, blood count monitoring, etc.) during prolonged treatment (more than 5 days).
- Severe local reactions may occur in infants upon intramuscular administration. Wherever possible, intravenous therapy should be performed.

- When intravenously administering very high doses (above 10 mega IU/day), the administration site should be alternated every other day to avoid superinfections and thrombophlebitis.
- Due to possible electrolyte disturbances, Benzylpenicillin sodium should be administered slowly with infusions of more than 10 mega IU and, due to the possibility of seizure reactions, when administering more than 20 mega IU (see section "Possible side effects").

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

In particular, tell your doctor if you are taking medicines with the following active substances:
- probenecid (medicine used to treat gout)
- indomethacin, phenylbutazone, acetic acid, salicylates (medicines used to reduce fever and inflammation, as well as for rheumatism and other pain)

These active substances can lead to increased concentrations of Benzylpenicillin sodium and increase the time that it remains within the body.

Other antibiotics
As penicillins only act on certain germs, Benzylpenicillin sodium should only be combined with certain antibiotics. Your doctor will decide which combinations are effective.

Digoxin (heart medication)
If given at the same time as Benzylpenicillin sodium, the heartbeat may become slower (bradycardia).

Methotrexate (chemotherapy agent used in cancer treatment)
If combined with Benzylpenicillin sodium treatment, the excretion of methotrexate will be reduced. Combined use of methotrexate and penicillin must be avoided wherever possible. If combined use cannot be avoided, a reduction in the methotrexate dose should be considered and methotrexate serum levels should be monitored. The patient should be monitored for possible additional side effects of methotrexate, including leukopenia, thrombocytopenia and pus accumulation under the skin.

Oral anticoagulants
Oral anticoagulants and penicillin antibiotics have been used extensively in practice without interactions. However, in the literature, there have been reports of an increased number of patients who were prescribed acenocoumarol or warfarin at the same time as penicillin. If combined use is required, the prothrombin time or other suitable blood-clotting parameters should be carefully monitored when co-administering or discontinuing penicillin. Furthermore, an adjustment of the oral anticoagulant dose may be necessary.

Effect on technical laboratory procedures
Tell your doctor before any laboratory tests are performed. The outcome of these tests may produce false results during treatment with Benzylpenicillin sodium (see section "Possible side effects").

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
Benzylpenicillin crosses the placenta and enters the blood circulation of the embryo or foetus. Experience to date with pregnant women and animal studies do not indicate any damage to the embryo or foetus. Use of Benzylpenicillin sodium is possible throughout the entire pregnancy if the doctor thinks there is an indication for its use.

Benzylpenicillin sodium is not indicated during pregnancy for the treatment of syphilis.

Breast-feeding
Penicillins pass into breast milk in small amounts.

Although no side effects have been reported in breast-fed infants to date, the possibility of sensitisation or an adverse effect on the intestinal flora in the infant must nevertheless be considered. In the case of occurrence of diarrhoea, candidosis or rash in the child, ask your doctor immediately who will give you advice, because these disorders in the child could be due to Benzylpenicillin sodium.
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
No effects on the ability to drive or use machines have been observed. Due to the occurrence of possible serious side effects (e.g. anaphylactic shock with collapse and anaphylactoid reactions, see section 4), Benzylpenicillin sodium can have an influence on the ability to drive and use machines.

Benzylpenicillin sodium contains sodium
1 mega IU (= approximately 0.6 g) Benzylpenicillin sodium contains 1.68 mmol sodium; 10 mega IUs are therefore equivalent to a sodium exposure of 100 mL isotonic saline solution.

3. How to use Benzylpenicillin sodium

Benzylpenicillin sodium is usually administered by a doctor.

Benzylpenicillin sodium has a wide dosage margin; your doctor will determine the method of administration, dosage level and the dosing interval.

In general, the following dosage guidelines apply:

Age group	***Dosage***		***Dosing interval***
Adults and adolescents (aged 12 years or over)	high (IV)	10 - 40 mega IU/day	divided into 4 - 6 doses
	normal (IM, IV)	1 - 5 mega IU/day	divided into 4 - 6 doses
Children (from 1 month old up until their 12th birthday)	high (IV)	0.1 - 0.5 (-1.0) mega IU/kg/day	divided into 4 - 6 doses
	normal (IM, IV)	0.03 - 0.1 mega IU/kg/day	divided into 4 - 6 doses
Newborn infants (aged 2 to 4 weeks)	high (IV)	0.2 - 0.5 (-1.0) mega IU/kg/day	in 3 - 4 single doses
	normal (IM, IV)	0.03 - 0.1 mega IU/kg/day	in 3 - 4 single doses
Premature and newborn infants (up to 2 weeks of age)	high (IV)	0.2 - 0.5 (-1.0) mega IU/kg/day	in 2 single doses
	normal (IM, IV)	0.03 - 0.1 mega IU/kg/day	in 2 single doses

Special patient groups:
- Elderly patients (over 65 years of age)
- Patients with impaired kidney function
- Patients with impaired liver function

In these patient groups, the doctor will check the kidney and liver function before the start of therapy and regularly during treatment, and will individually adjust the dose and dosing interval.

Special dosage instructions apply for the following diseases:
- Bacterial endocarditis*:* Adults are given 10 - 80 mega IU/day intravenously in combination with aminoglycosides.
- Meningitis*:* Due to increased seizure susceptibility and Jarisch-Herxheimer reactions, no more than 20 - 30 mega IU/day should be administered in adults and no more than 12 mega IU/day in children. Administration of the first dose should be protracted for very severe clinical forms - initially 1/4 of the individual single dose - and given slowly under very strict surveillance.

- Lyme borreliosis*:* In adults, 20 - 30 mega IU/day intravenously in 2 - 3 doses over 14 days and in children, 0.5 mega IU/kg/day intravenously in 2 - 3 doses over 14 days.

Duration of treatment
The duration of treatment is decided by the doctor. The usual duration of treatment is 10 to 14 days for most therapeutic indications. It depends on the severity of the infection, the pathogen response and the patient's clinical symptoms and can last for a few days to up to several weeks. Treatment with Benzylpenicillin sodium must be continued for at least 2 - 3 days after clinical symptoms have worn off.

According to WHO recommendations, a treatment period of at least 10 days should be observed for streptococcal diseases.

Method of administration

Benzylpenicillin sodium is usually administered by a doctor.

Benzylpenicillin sodium can be injected into a muscle (intramuscularly) or into a vein (intravenously). Intravenous administration can be given as an injection (using a syringe) or as a short infusion (if using 10 mega IU/100 mL: as a slower injection, generally lasting between 30 and 60 minutes).
Notes for the doctor on intramuscular injection:
Up to a maximum of 10 mega IU (= approximately 6 g) Benzylpenicillin sodium, dissolved in 6 - 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 IV 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.

In specific clinical situations, Benzylpenicillin sodium can also be given via the intrapleural route (into the space between the lung and chest), intra-articular route (directly into a joint) or intralumbar route (into the spinal canal).
In this event, the following information applies:
- Intrapleural instillation: up to 0.2 mega IU (5,000 IU/mL)
- Intra-articular injection: up to 0.1 mega IU (25,000 IU/mL)
- Intralumbar administration:
  Adults, adolescents (aged 12 years or over): 10,000 up to a maximum of 20,000 IU
  Children (aged 6 - 12 years): 8,000 IU
  Infants (aged 1 - 6 years): 5,000 IU
  Babies (aged 1 - 23 months): 2,500 IU.
  After withdrawing a corresponding amount of cerebrospinal fluid, the sterile solution (no more than 1,000 IU/mL) must be injected slowly (1 mL/min) at body temperature. Local therapy should always be given only as a supplement to systemic treatment. For intralumbar instillations, the dosage for systemic treatment (IV, IM) must be reduced accordingly.

Note for the doctor: You will find information on incompatibilities and other instructions for handling at the end of this package leaflet.

If you are given more Benzylpenicillin sodium than you should
In the event of an overdose, increased neuromuscular hyperexcitability or susceptibility to cerebral seizures can be expected. Countermeasures by the doctor: discontinue the medicine, clinical surveillance and symptomatic treatment, if required. Benzylpenicillin sodium is dialysable.

If you forget to use Benzylpenicillin sodium
If you think you have missed a dose, 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.

Usually, the following frequencies are used for evaluating side effects:

Very common	(may affect more than 1 in 10 patients treated)
Common	(may affect up to 1 in 10 patients treated)
Uncommon	(may affect up to 1 to 100 patients treated)
Rare	(may affect up to 1 to 1,000 patients treated)
Very rare	(may affect up to 1 in 10,000 patients treated)
Not known	(cannot be estimated from the available data)

Blood and lymphatic system disorders

Very rare: effects on blood and blood components (eosinophilia, leucopenia, neutropenia, granulocytopenia, thrombocytopenia, agranulocytosis, pancytopenia), haemolytic anaemia (a specific type of anaemia), blood-clotting disorders

Not known: prolongation of the bleeding time and prothrombin time (see section "Warnings and precautions")

Immune system disorders

Uncommon: allergic reactions: nettle rash with or without itching (urticaria); swelling of the skin and mucous membranes, especially in the facial region, mouth, throat and larynx (angioedema); severe skin reactions (erythema multiforme, exfoliative dermatitis); fever; joint pain; severe hypersensitivity reactions (asthma, skin bleeding, gastrointestinal disorders)

Not known: serum sickness (hypersensitivity reactions such as 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)

Metabolism and nutrition disorders

Rare: Electrolyte disturbances may occur upon rapid infusion of high doses.

Nervous system disorders

Rare: nerve disorders. Convulsive reactions may occur upon infusion of high doses (in adults, more than 20 mega IU); this should be particularly borne in mind in patients with severely impaired renal function, epilepsy, meningitis, cerebral oedema or during cardiopulmonary bypass.

Gastrointestinal disorders

Uncommon: inflammation of the mouth lining (stomatitis), burning tongue (glossitis), black hairy tongue, nausea, vomiting

If diarrhoea occurs during therapy, the possibility of colon inflammation (pseudomembranous colitis) should be considered (see section "Warnings and precautions").

Hepatobiliary disorders

Not known: liver inflammation (hepatitis), bile congestion in the gallbladder (cholestasis).

Skin and subcutaneous tissue disorders

Not known: skin conditions with blistering (pemphigoid).

Renal and urinary disorders

Rare: kidney disease, excretion of protein or blood in the urine, sediment in the urine (cylindruria) reduced urine output or failure to excrete urine (mostly clears up within 48 hours after stopping treatment).

General disorders and administration site conditions
Rare: Severe local reactions can occur with intramuscular administration to infants.

Investigations
Common: Effect on the following technical laboratory methods:

- positive direct Coombs' test
- Folin-Ciocalteu-Lowry method, Biuret method to determine protein in the urine
- ninhydrin method to determine amino acids
- electrophoresis methods to determine albumin
- non-enzymatic urine glucose detection and urobilinogen detection
- Zimmermann reactions to determine steroids in the 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 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

Do not store above 25°C.

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.

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**
500,000 – 910,000 IU/ml (this range includes the recommended concentration for IM injection)	48 hours	8 hours
100,000 IU/ml (the recommended concentration for IV injection/infusion)	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.

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

Benzylpenicillin sodium 600 mg Powder for Solution for Injection/Infusion:
One vial contains 1,000,000 IU (equivalent to approximately 0.6 g) benzylpenicillin as sodium salt (= 1.68 mmol or 38.6 mg of sodium).

Benzylpenicillin sodium 3000 mg Powder for Solution for Injection/Infusion:
One vial contains 5,000,000 IU (equivalent to approximately 3 g) benzylpenicillin as sodium salt (= 8.42 mmol or 193 mg sodium).

What Benzylpenicillin sodium looks like and contents of the pack
White to off-white powder for solution for injection / infusion
pH - value after reconstitution: 5.5 - 7.5

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 02/2021.

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 etc.).
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 HCl
- dopamine HCl
- heparin
- hydroxyzine HCl
- lactate
- lincomycin HCl
- metaraminol
- sodium hydrogen carbonate
- oxytetracycline
- pentobarbital
- tetracycline HCl
- thiopental Na
- 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 products 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 100,000 IU/ml.

An isotonic solution is obtained when using WFI as solvent (osmolarity of 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 **500,000 IU** powder for solution for injection/infusion a one-step reconstitution in the original vial suffices.

For Benzylpenicillin sodium **1,000,000 IU, 5,000,000 IU** and **10,000,000 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 100,000 IU/ml.

Reconstitution and dilution instructions for IV 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 10 mega IU/100 ml or 100,000 IU/ml)*	*Resulting solution for IV injection/infusion*
Benzylpenicillin sodium 500,000 IU powder for solution for injection/ infusion *(contains ± 0.3 gram powder)*	4.8 ml	**ready for use** 5 ml = 500,000 IU (100,000 IU/ml)	not applicable	not applicable
Benzylpenicillin sodium 1,000,000 IU powder for solution for injection/ infusion *(contains ± 0.6 gram powder)*	4.6 ml	**concentrate to be diluted before use** 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 = 1 Mega IU (100,000 IU/ml)

Reconstitution and dilution instructions for IV 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 10 mega IU/100 ml or 100,000 IU/ml)*	*Resulting solution for IV injection/infusion*
Benzylpenicillin sodium 5,000,000 IU powder for solution for injection/ infusion *(contains ± 3 gram powder)*	7.9 ml	**concentrate to be diluted before use** 10 ml = 5 Mega IU (500,000 IU/ml)	1 volume concentrate + 4 volumes diluent e.g. add 10 ml concentrate to 40 ml diluent	**ready for use** 50 ml = 5 Mega IU (100,000 IU/ml)
Benzylpenicillin sodium 10,000,000 IU powder for solution for injection/ infusion *(contains ± 6 gram powder)*	15.8 ml	**concentrate to be diluted before use** 20 ml = 10 Mega IU (500,000 IU/ml)	1 volume concentrate + 4 volumes diluent e.g. add 20 ml concentrate to 80 ml diluent	**ready for use** 100 ml = 10 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 100,000 IU/ml is hypertonic).

The maximum volume for intramuscular administration is 5 ml per injection site and the maximum intramuscular dose is 10,000,000 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 IM injection		
1 vial	*Recommended volume of solvent to be added for reconstitution*	*Resulting solution for IM injection* **(maximum 5 ml per injection site)**
Benzylpenicillin sodium	0.3 - 0.6 ml	

5,000,000 IU powder for solution for injection/infusion *(contains ± 3 gram powder)*	e.g. 0.3 ml	0.55 ml = 0.5 Mega IU (909,090 IU/ml)
	e.g. 0.6 ml	0.75 ml = 0.5 Mega IU (666,667 IU/ml)
Benzylpenicillin sodium **1,000,000 IU** powder for solution for injection/infusion} *(contains ± 0.6 gram powder)*	0.6 - 1 ml	
	e.g. 0.6 ml	1.1 ml = 1 Mega IU (909,090 IU/ml)
	e.g. 1 ml	1.5 ml = 1 Mega IU (666,667 IU/ml)
Benzylpenicillin sodium **5,000,000 IU** powder for solution for injection/infusion} *(contains ± 3 gram powder)*	3 - 5 ml	
	e.g. 3 ml	5.5 ml = 5 Mega IU (909,090 IU/ml)
	e.g. 5 ml	7.5 ml = 5 Mega IU (666,667 IU/ml)
Benzylpenicillin sodium **10,000,000 IU** powder for solution for injection/infusion} *(contains ± 6 gram powder)*	6-10 ml	
	e.g. 6 ml	11 ml = 10 Mega IU (909,090 IU/ml)
	e.g. 10 ml	15 ml = 10 Mega IU (666,667 IU/ml)