

Applicant: **Ando Pharma (Pty) Ltd**
Product Name: BENPEN 1 MU & 5 MU
Dosage form: Powder for solution for injection
Strength: Each vial contains 1 MU or 5 MU
Benzylpenicillin Sodium respectively

1.3.2 Proposed Clean PIL
eCTD 0002: pre-reg-cl
Date of submission: 30 May 2024

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

BENPEN 1 MU, 1 000 000 IU, Powder for solution for injection

BENPEN 5 MU, 5 000 000 IU, Powder for solution for injection

Benzylpenicillin sodium

Sugar free

Read all of this leaflet carefully before you are given BENPEN

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet

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

1. What BENPEN is and what it is used for

This medicine contains benzylpenicillin sodium, which is part of a group of medicine known as penicillins (“antibiotics”). Penicillins are used to kill certain type of bacteria (germs) which cause infections.

BENPEN is used for:

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- treating infections that are caused by bacteria that is sensitive to benzylpenicillin
- the prevention of the return of rheumatic fever (a disease caused by a streptococci bacterium that can affect the heart, joints, brain and skin)
- the prevention of infection of the heart if you undergo a surgery and suffer from a heart disease that affects your heart valves.

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

BENPEN should not be administered:

- if you are hypersensitive (allergic) to **penicillin or cephalosporins**.
- to babies, born to mothers who are allergic to penicillin during the neonatal period.

Warnings and precautions

Tell your doctor or healthcare provider before being given the injection:

Special care should be taken with BENPEN:

- if you have a penicillin allergy, you may develop anaphylactic shock (e.g., skin rash, itching, swelling, difficulty to breath) and need to be treated immediately.
- if you experience chest pain in the context of allergic reactions, which may be a symptom of allergy triggered heart attack (Kounis syndrome) (see section 4 ‘Possible side effects’).
- high doses of BENPEN will increase your daily amount of salt intake, inform your doctor if you are on a low salt diet.
- if you have a history of being allergic, especially to medicine.
- if you have kidney problems.
- if you have any heart problems.
- if you are treated for syphilis, a reaction to the bacterial toxins may occur, which lasts up to several days (Jarisch-Herxheimer reaction, see section 4). Typical symptoms are sudden fever (sometimes with chills),

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pale skin; followed by skin redness, headache, painful muscles and joints or tiredness. To suppress or alleviate a Jarisch-Herxheimer reaction, your doctor will start appropriate therapy.

- if you are treated with high doses of BENPEN, you can develop electrolyte imbalance (too low potassium and high levels of salt).
- if you are a diabetic patient, it may take longer for the intramuscular injection to be absorbed.
- if you are using BENPEN for long periods, you can develop superinfections such as severe and persistent diarrhoea. BENPEN should be discontinued, and appropriate treatment should be given.
- severe skin reactions have been reported with the use of BENPEN. Treatment should be stopped, and appropriate measures must be taken.
- if you have a history of hypersensitivity to other beta-lactam antibiotics (e.g., cephalosporins and carbapenems) see section 2.
- BENPEN can interfere with the results of certain urine and blood tests.

Other medicines and BENPEN

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Caution should be exercised when administering BENPEN at the same time as the following medicines:

- methotrexate (a medicine used in chemotherapy)
- probenecid (a medicine used to treat gout)

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before receiving BENPEN.

Driving and using machines

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It is not always possible to predict to what extent BENPEN may interfere with your daily activities. You should ensure that you do not engage in driving or operating machinery until you are aware of the measure to which BENPEN affects you.

3. How to use BENPEN

Your doctor will tell you how long your treatment with BENPEN will last.

You will not be expected to give yourself BENPEN. It will be given to you by a person who is qualified to do so.

If you have the impression that the effect of BENPEN is too strong or too weak, tell your doctor or pharmacist.

Your doctor will mix the BENPEN powder with water for injection.

BENPEN is given either as an injection in the veins (intravenous) or by a deep injection into a muscle (intramuscular).

The usual dose is:

Adults: *prevention:*

For prevention or recurrence of rheumatic fever: 200 000 units intramuscularly twice daily.

Patients with valvular heart disease undergoing surgery: 2 million units intravenously or intramuscularly 30 to 60 minutes preoperatively and 1 million units six hours later.

Adults: *treating infections:*

500 000 – 20 million units daily preferably in divided doses.

For severe infections such as meningitis, endocarditis and peritonitis, 20 million units per day may be used.

Children

The dose for babies and children is based on their weight.

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Prevention: Patients with valvular heart disease undergoing surgery: 50 000 units per kg body mass 30 to 60 minutes preoperatively and 25 000 units per kg body mass six hours later.

Treatment: 10 000 – 50 000 units per kg body mass per 24-hour period, divided in 4 doses.

Severe infections: 300 000 – 400 000 units/kg/day.

Neonates

Treatment: 50 000 units per kg body mass per day in divided doses.

Severe infections: 50 000 – 200 000 units/kg/day.

Your doctor will administer the therapeutic dose for at least 10 days when treating beta-haemolytic streptococcal infections.

If more BENPEN is being administered than should

Since a healthcare provider will administer BENPEN, he /she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

Irritation of the brain and shaking fits (convulsion) have been seen in patients when very high doses of BENPEN have been given by mistake, in particular to patients with poor kidney function.

If you forget to use BENPEN

Since a healthcare provider will administer BENPEN, it is unlikely that the dose will be missed.

4. Possible side effects

BENPEN can have side effects.

Not all side effects reported for BENPEN are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving BENPEN, please consult your healthcare provider for advice.

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If any of the following happens, stop using BENPEN and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting,
- chest pain in the context of allergic reactions, which may be a symptom of allergy triggered cardiac infarction (Kounis syndrome).

These are all very serious side effects. If you have them, you may have had a serious reaction to BENPEN. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- skin irritation, fever, headache, sore throat, sore muscles and fast heartbeat particularly in patients being treated for syphilis (a sexually transmitted disease)
- serum sickness (fever, general ill feeling, hives, itching, joint pain, swollen lymph nodes).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Less frequent side effects

- low levels of white blood cells which will make you vulnerable to infection
- using BENPEN can cause the bacterium *Clostridium difficile* to grow and infect the lining of the intestine, which can result in frequent watery diarrhoea
- fits (convulsions), especially large doses

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- inflammation of the kidney

Side effects with unknown frequency

- diarrhoea, nausea, heartburn
- thrombocytopenia (reduced blood levels of platelets)
- reduction in blood cell count and anaemias which might make you feel tired or dizzy
- bleeding disorders such as low red blood cells and low blood platelet count which causes prolongation of bleeding time
- swelling underneath the skin (angioedema)
- extreme redness of the skin, scaling, itching, swollen lymph nodes and inflammation of the blood vessels.
- a generalised sensitivity reaction with a raised, itchy rash, joint pains and an increased number of white blood cells, can develop within a few hours to several weeks after starting treatment
- metabolic encephalopathy (neurological disorders with convulsions and loss of consciousness)
- AGEP – Acute Generalized 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)
- erythema (inflammatory reddening of the skin)
- severe cutaneous adverse reaction (SCAR) is life-threatening. It consists of Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), drug reaction with eosinophilia and systemic symptoms (DRESS)
- superinfection by resistant organisms
- sore throat or tongue and a black hairy tongue
- thrush or infections with other germs
- increase in liver enzymes

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- rash with blisters arranged in a circle with central crusting or like a string of pearls (linear IgA disease)

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of BENPEN.

5. How to store BENPEN

Store all medicines out of reach of children.

Store at or below 30 °C (dry powder).

Once the content of the vial has been mixed with an injection solution, it should be used immediately.

BENPEN should not be administered after the expiry date printed on the pack or if the packaging is torn or shows signs of tampering.

Any BENPEN which is left over, not used or has passed its expiry date will be disposed of by hospital staff.

Do not dispose of unused medicine in drains and sewerage systems (e.g., toilets)

6. Contents of the pack and other information

What BENPEN contains

- The active substance in each BENPEN 1 MU vial is benzylpenicillin sodium equivalent to benzylpenicillin 1 000 000 IU.
- The active substance in each BENPEN 5 MU vial is benzylpenicillin sodium equivalent to benzylpenicillin 5 000 000 IU.

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What BENPEN looks like and contents of the pack

The powder for solution for injection is a white or almost white, crystalline powder.

BENPEN 1 MU: 7 mL mould vial, closed with butyl rubber stoppers, flip-off cap and adhesive vials label.

Pack size: 50 vials/tray/box, 20 boxes per carton.

BENPEN 5 MU: 20 mL mould vial, closed with butyl rubber stoppers, flip-off cap and adhesive vials label.

Pack size: 50 vials/tray/box, 12 boxes per carton.

Holder of Certificate of Registration

Ando Pharma (Pty) Ltd.

73 Keurboom Crescent

Platteklouf

Cape Town

7500

+ 27 21 911 4003

This leaflet was last revised in

To be allocated

Registration number

To be allocated upon SAHPRA's approval.