**SUMMARY OF PRODUCT CHARACTERISTICS**

# PENIBRIN® 500 mg
# PENIBRIN® 1 g
# PENIBRIN® 2 g

**Powder for Solution for Injection/Infusion**
**For I.M. or I.V. Injection**

## 1. NAME OF THE MEDICINAL PRODUCT

PENIBRIN® 500 mg
PENIBRIN® 1 g
PENIBRIN® 2 g

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Penibrin 500 mg:**
One vial contains 531.4 mg of ampicillin sodium (equivalent to 500 mg ampicillin).
**Penibrin 1 g:**
One vial contains 1063 mg of ampicillin sodium (equivalent to 1000 mg ampicillin).
**Penibrin 2 g:**
One vial contains 2126 mg of ampicillin sodium (equivalent to 2000 mg ampicillin).

Excipient with known effect:
**Penibrin 500 mg:** Each vial contains approximately 33 mg sodium.
**Penibrin 1 g:** Each vial contains approximately 66 mg sodium.
**Penibrin 2 g:** Each vial contains approximately 132 mg sodium.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder for solution for injection/infusion.
White to off-white powder.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Penibrin injection is recommended in serious infections when prompt, effective levels of the antibiotic must reach the site of infection. Such infections include meningitis, subacute bacterial endocarditis, peritonitis, septicemia, severe forms of chronic bronchitis, osteomyelitis, pneumonia and pyelonephritis due to susceptible organisms.

### 4.2 Posology and method of administration

*Parenteral drug products should be inspected visually for particulate matter and discoloration, prior to administration, whenever solution and container permit.*

The recommended dosages are given below:
In stubborn, severe infections, a higher dosage may be administered.

*Adults*
250-500 mg every 6 hours, by intramuscular or intravenous injection.

*Gonorrhea*
2 doses of 500 mg spaced 12 hours apart. Treatment may be repeated if necessary.

*Children*
12.5 mg/kg body weight every 6 hours, by intramuscular or intravenous injection.

***Note:*** Larger doses may be required for stubborn or severe infections. The children's dosage is intended for individuals whose weight will not cause a dosage to be calculated greater than that recommended for adults.

*Septicemia*
*Adults:*
A daily dosage of 8-14 g is recommended, starting with I.V. administration for at least 3 days and continuing with the I.M. route every 3-4 hours.

*Children*
A daily dosage of 150-200 mg/kg body weight is recommended, starting with I.V. administration for at least 3 days and continuing with the I.M. route every 3-4 hours.

*Bacterial meningitis caused by N. meningitidis or H. influenzae*
*Adults*
A few adults have been treated with doses ranging from 8-14 g daily. Treatment was initiated with intravenous drip therapy for at least 3 days, and continued with frequent (every 3-4 hours) I.M. therapy.

*Children*
Children have been treated with doses of 150-200 mg/kg body weight/day. Treatment was initiated with intravenous drip therapy for at least 3 days, and continued with frequent (every 3-4 hours) I.M. therapy.

**Special precautions for disposal and other handling**
Make sure that dispersal is complete. **Use only clear solutions prepared immediately before application. Any unused solution remaining after reconstitution must be discarded.**

For single use only.

**Intramuscular Use**
Use water for injections for reconstitution to provide a solution with a concentration of 250 mg/ml, as follows:
- 1.8 ml for the 500 mg vial.
- 3.5 ml for the 1 g vial.
- 6.8 ml for the 2 g vial.

**Intravenous Use**
**Penibrin 500 mg**
- Solution for I.V. administration:
  Dissolve the contents of the 500 mg vial in 5 ml solvent (water for injections).
- Solution for I.V. infusion:
  Dissolve the contents of the 500 mg vial in 5 ml solvent (water for injections). The prepared solution can be mixed with any amount of isotonic NaCl 0.9% solution.

**Penibrin 1 g**
- Solution for I.V. administration:
  Dissolve the contents of the 1 g vial in 5 ml solvent (water for injections).
- Solution for I.V. infusion:
  Dissolve the contents of the 1 g vial in 5 ml solvent (water for injections). The prepared solution can be mixed with any amount of isotonic NaCl 0.9% solution.

**Penibrin 2 g**
- Solution for I.V. administration:
  Dissolve the contents of the 2 g vial in 10 ml solvent (water for injections).
- Solution for I.V. infusion:
  Dissolve the contents of the 2 g vial in 10 ml solvent (water for injections). The prepared solution can be mixed with any amount of isotonic NaCl 0.9% solution.

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

***Caution:*** For direct intravenous administration, the solution should be injected slowly over a period of 3-5 minutes for doses up to 500 mg and over a period of 10-15 minutes for larger doses. More rapid administration may result in convulsive seizures. The infusion should last between 15 and 20 minutes.

*Intravenous Drip Infusion*
Isotonic 0.9% Sodium Chloride Injection appears to be a suitable diluent for the intravenous infusion. Reconstitute as directed above prior to diluting with any amount of isotonic 0.9% Sodium Chloride Injection and infuse over 15 to 20 minutes.

### 4.3 Contraindications

- Hypersensitivity to the active substance, to any other penicillin or to any of the excipients listed in section 6.1.
- History of a severe immediate hypersensitivity reaction (e.g., anaphylaxis) to another beta-lactam agent (e.g., a cephalosporin, carbapenem or monobactam) (see sections 4.4 and 4.8).
- History of jaundice/hepatic impairment due to ampicillin.

### 4.4 Special warnings and precautions for use

Before initiating therapy with ampicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents (see sections 4.3 and 4.8).
The possibility of fungal and bacterial superinfections should be taken into account during treatment. In such case, the medicinal product should be discontinued and replaced with another suitable treatment. Prolonged use may occasionally result in overgrowth of non-susceptible organisms.
Ampicillin has a limited spectrum of antibacterial activity. It is not suitable for use as a single agent for the treatment of some types of infections unless the pathogen is already documented and known to be susceptible or there is a very high suspicion that the most likely pathogen(s) would be suitable for treatment with ampicillin. This particularly applies when considering the treatment of patients with intraabdominal infections, female genital infections and endocarditis. Ampicillin should be used in the treatment of cystitis only when susceptibility is documented.
Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals.
Hypersensitivity and serum sickness-like reactions can be controlled with antihistamines and, if necessary, with systemic corticosteroids. If these types of reactions occur, ampicillin should be discontinued unless the doctor considers that the condition is life-threatening and can only be treated with ampicillin. Serious anaphylactic reactions require emergency treatment with adrenalin, oxygen and intravenous steroids.
Concomitant use of allopurinol during treatment with ampicillin can increase the likelihood of allergic skin reactions (see section 4.5).
Ampicillin should be avoided if infectious mononucleosis is suspected or the patient suffers from cytomegalovirus infection or lymphoid leukaemia since the occurrence of a morbilliform rash has been associated with this condition following the use of ampicillin.
Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.
In patients with renal impairment, the dose should be adjusted according to the degree of impairment.
Prolongation of prothrombin time has been reported rarely in patients receiving ampicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see sections 4.5 and 4.8).
During treatment with ampicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false-positive results may occur with non-enzymatic methods (see section 4.5).
Antibiotic-associated colitis (caused in most cases by *Clostridium difficile*) has been reported with nearly all antibacterial agents including ampicillin and may range in severity from mild to life-threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients presenting diarrhoea during or after the administration of any antibiotic (cases have been reported up to two months after the administration of antibacterial medicinal products). Should antibiotic-associated colitis occur, ampicillin should immediately be discontinued, a physician be consulted and an appropriate therapy initiated. Anti-peristaltic drugs are contra-indicated in this situation.

Excipients
Penibrin 500 mg contains approximately 33 mg sodium per vial, equivalent to 1.65% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
Penibrin 1 g contains approximately 66 mg sodium per vial, equivalent to 3.3% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
Penibrin 2 g contains approximately 132 mg sodium per vial, equivalent to 6.6% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

### 4.5 Interaction with other medicinal products and other forms of interaction

Bacteriostatic antibiotics
Antagonism in regard to bacteriostatic antibiotics such as, for example, chloramphenicol and tetracycline.

Probenecid
The coadministration of probenecid inhibits the tubular secretion of ampicillin and leads to higher and longer persisting ampicillin concentrations in serum and bile.

Allopurinol
The simultaneous use of allopurinol during treatment with ampicillin can promote the development of allergic skin reactions.

Anticoagulants
Coadministration of anticoagulants of the coumarin type can increase the tendency to bleeding.

Digoxin
An increase in the absorption of coadministered digoxin is possible during ampicillin therapy.

Methotrexate
Ampicillin can inhibit the excretion of methotrexate and thereby intensify undesirable effects of methotrexate. The methotrexate levels in the blood should be monitored.

Glucose tests
In the case of high urine concentrations of ampicillin, false-positive urine-glucose reactions may occur if the copper reduction method is used. It is therefore recommended that glucose tests are based on enzymatic glucose oxidase reactions (see section 4.4).

### 4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of ampicillin in pregnant women. These data do not suggest that ampicillin has any adverse effects on pregnancy or the health of the foetus/newborn. No other relevant epidemiological data are available to date.
Animal studies do not indicate direct or indirect harmful effects respect to reproductive toxicity (see section 5.3).
As a precautionary measure, it is preferable to avoid the use of ampicillin during pregnancy. The treating doctor should consider whether the benefits to the pregnant woman outweigh the potential risks to the foetus.

Breast-feeding
Ampicillin is excreted in human milk and effects have been shown in breastfed newborns/infants of treated women. Breastfed infants may therefore suffer from diarrhoea and mucosal yeast colonisation, which in some cases may necessitate the discontinuation of breast-feeding. The possibility of sensitisation should be considered. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from ampicillin therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
In animal studies, ampicillin had no effect on fertility (see section 5.3).

### 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g., allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

### 4.8 Undesirable effects

Summary of the safety profile
The most commonly reported undesirable effects are skin reactions (pruritis, rash, exanthema, itching), abdominal pain, meteorism, soft stools, diarrhoea, nausea and vomiting.
People who have previously experienced hypersensitivity to penicillin and people with allergy, asthma, hay fever or urticaria in their medical history have a greater risk of hypersensitivity reactions.

Tabulated list of adverse reactions
The undesirable effects derived from clinical studies and post-marketing surveillance, sorted by MedDRA System Organ Class are listed below.
The following terminologies have been used in order to classify the occurrence of undesirable effects:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (frequency cannot be estimated from the available data)

| System Organ Class | Preferred Term |
|---|---|
| Infections and infestations | |
| Uncommon | Infection with fungi or resistant bacteria especially during prolonged and/or repeated use. |
| Blood and lymphatic system disorders | |
| Uncommon | Thrombocytopenia, anaemia, agranulocytosis, leukopenia, eosinophilia, thrombocytopenic purpura, haemolytic anaemia. |
| Very rare | Granulocytopenia, pancytopenia, prolongation of bleeding and prothrombin time[1]. |
| Immune system disorders [2,8] | |
| Uncommon | Serious allergic reactions such as serum sickness, allergic nephritis. |
| Rare | Life-threatening anaphylactic shock[6]. |
| Not known | Hypersensitivity (see section 4.4). |
| Nervous system disorders[9] | |
| Rare | Dizziness, headache, myoclonus and seizures (in renal insufficiency or at very high intravenous doses). |
| Respiratory, thoracic and mediastinal disorders | |
| Uncommon | Laryngeal oedema. |
| Gastrointestinal disorders | |
| Very common | Abdominal pain, nausea, vomiting, meteorism, soft stools, diarrhoea[7]. |
| Uncommon | Enterocolitis, stomatitis, glossitis, pseudomembranous colitis[8] (in most cases caused by *Clostridium difficile*). |

| | |
|---|---|
| Not known | Black hairy tongue. |
| Skin and subcutaneous tissue disorders | |
| Very common | Pruritus, rash, exanthema, itching[3]. |
| Common | Morbilliform rash[4], exanthema and enanthem in the oral region[5]. |
| Uncommon | Angioneurotic oedema, allergic vasculitis, exfoliative dermatitis, exudative erythema multiforme, urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis. |
| Hepatobiliary disorders | |
| Uncommon | Transaminase elevation. |
| Musculoskeletal and connective tissue disorders | |
| Not known | Arthralgia. |
| Renal and urinary disorders | |
| Uncommon | Crystalluria on high-dose intravenous administration, acute interstitial nephritis. |
| Very Rare | Acute renal failure with excretion of urine crystals. |
| General disorders and administration site conditions | |
| Common | Swelling and pain, localised phlebitis. |
| Uncommon | Drug fever. |
| Not known | Fever. |

[1] See section 4.4.
[2] See sections 4.3 and 4.4.
[3] An immediate-type urticarial reaction generally suggests a true penicillin allergy and necessitates the interruption of treatment and institution of suitable medical measures. Medical advice should be sought regarding the future use of beta-lactam antibiotics.
[4] The typical, measles-like rash develops several (5 to 11) days after the start of treatment.
[5] The incidence of exanthem is higher in patients with infectious mononucleosis or lymphatic leukaemia.
[6] Allergic reactions are more likely to occur in patients with a tendency to allergies.
[7] These undesirable effects are usually mild in nature and frequently subside during, or otherwise after discontinuing the treatment.
[8] If there are signs of pseudomembranous colitis or severe hypersensitivity reactions, the treatment should be discontinued and medical treatment (see section 4.4) provided.
[9] If central nervous excitation, myoclonus or seizures occur, ampicillin should be discontinued and suitable treatment instituted.

Description of selected adverse reactions

Anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia and agranulocytosis have been reported during treatment with penicillins. These reactions are generally reversible after discontinuing treatment and are believed to be sensitisation phenomena.

A moderate rise in serum concentration of aspartate aminotransferase (ASAT) has been observed, particularly in infants; however, the significance of these findings is unknown. Mild, temporary rises in ASAT have been observed in people who receive larger (two to four times) and more frequent intramuscular injections than usual. Information indicates that ASAT is released at the administration site of the intramuscular injection of ampicillin sodium and that the presence of an increased amount of this enzyme in the blood is not necessarily a sign that the liver is affected.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:
https://sideeffects.health.gov.il.

### 4.9 Overdose

Symptoms

Typical signs of intoxication following the administration of larger amounts of ampicillin have not been observed to date. Long-term therapy is also not associated with specific toxic adverse reactions.

Toxic reactions can include nausea, vomiting, diarrhoea, electrolyte disorders, altered consciousness, coma, haemolytic reactions and acidosis.

The single administration of a larger amount of ampicillin is not acutely poisonous (toxic). The administration of very high doses can lead to oliguric renal failure and may have effects on nerve cells, for example in the form of central nervous excitation, impairments of muscular function and seizures. The risk of these undesirable effects is increased in patients with severely impaired renal function.

In individual cases, however, these effects were only observed after intravenous administration.

Management

In the event of an overdose, the treatment should be discontinued.

There is no specific antidote in the event of overdose. Treatment comprises symptomatic measures with particular attention to maintaining the water/electrolyte balance.

Ampicillin can be removed from the body by haemodialysis but not via peritoneal dialysis.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group:** Antibacterials for systemic use, penicillins with extended spectrum.
**ATC code:** J01CA01.

Mechanism of action

The mechanism of action of ampicillin is based on inhibition of bacterial wall synthesis (in the growth phase) via blockade of the penicillin-binding proteins (PBPs) such as the transpeptidases. This results in a bactericidal action.

PK/PD relationship

The efficacy depends mainly on the time period for which the active substance level of ampicillin remains above the minimal inhibitory concentration (MIC) of the microorganism.

Mechanisms of resistance

Resistance to ampicillin can be due to the following mechanisms:

- Inactivation by beta-lactamases: ampicillin has only low beta-lactamase stability and is therefore not active against beta-lactamase forming bacteria. Almost all strains of some bacterial species form beta-lactamases. These species are therefore naturally resistant to ampicillin (e.g., *Enterobacter cloacae, Klebsiella pneumoniae*).
- Reduced affinity of PBPs for ampicillin: the acquired resistance of pneumococci and other streptococci is due to the modification of existing PBPs as the result of a mutation. Methicillin (oxacillin)-resistant staphylococci, however, are resistant due to the formation of an additional PBP with reduced affinity for ampicillin.
- Insufficient penetration of ampicillin through the outer cell wall of gram-negative bacteria can result in inadequate inhibition of the PBPs.
- Ampicillin can be actively extruded from the cell by efflux pumps.

Partial or complete cross-resistance of ampicilllin exists with amoxicillin and to some extent with other penicillins and cephalosporins.

Breakpoints

MIC breakpoints for ampicillin are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

| Microorganism | Susceptible ≤ | Resistant ≥ |
|---|---|---|
| *Enterobacteriaceae* | ≤ 8 mg/l | ≥ 8 mg/l |
| *Enterococcus spp.*[1] | ≤ 4 mg/l | ≥ 8 mg/l |
| *Haemophilus influenzae* | ≤ 1 mg/l | ≥ 1 mg/l |
| *Staphlococcus spp.*[2] | ≤ 0.12 mg/l | ≥ 0.12 mg/l |
| *Streptococcus* A, B, C, G[2] | ≤ 0.25 mg/l | ≥ 0.25 mg/l |
| *Streptococcus pneumoniae* | ≤ 0.5 mg/l | ≥ 2 mg/l |
| Other *streptococci*[1] | ≤ 0.5 mg/l | ≥ 2 mg/l |
| *Neisseria meningitidis* | ≤ 0.12 mg/l | ≥ 1 mg/l |
| Gram-negative anaerobes | ≤ 0.5 mg/l | ≥ 2 mg/l |
| Gram-positive anaerobes | ≤ 4 mg/l | ≥ 8 mg/l |
| Non-species-specific limit values | ≤ 2 mg/l | ≥ 8 mg/l |
| *Listeria monocytogenes* | ≤ 1 mg/l | ≥ 1 mg/l |

[1] In endocarditis, refer to national or international endocarditis guidelines for breakpoints.
[2] Breakpoints values are based on benzylpenicillin breakpoints.

Susceptibility

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infection is questionable.

**Commonly susceptible species**

***Aerobic gram-positive microorganisms***
*Enterococcus faecalis*
*Staphylococcus aureus (methicillin-sensitive)*
*Streptococcus agalactiae*
*Streptococcus pneumoniae (incl. penicillin-intermediate strains)*
*Streptococcus pyogenes*
*Streptococci of the Viridans group* ^

***Anaerobic microorganisms***
*Bacteroides fragilis*°
*Fusobacterium nucleatum* °

***Other microorganisms***
*Gardnerella vaginalis*°

**Species for which acquired resistance may be a problem**

***Aerobic gram-positive microorganisms***
*Enterococcus faecium*+
*Staphylococcus aureus*[3]
*Staphylococcus epidermidis*+
*Staphylococcus haemolyticus*+
*Staphylococcus hominis*+

***Aerobic gram-negative microorganisms***
*Escherichia coli*
*Haemophilus influenzae*
*Klebsiella oxytoca*
*Moraxella catarrhalis*∞
*Neisseria gonorrhoeae*
*Proteus mirabilis*
*Proteus vulgaris*

***Anaerobic microorganisms***
*Prevotella spp.*

**Inherently resistant organisms**

***Aerobic gram-positive microorganisms***
*Staphylococcus aureus (methicillin-resistant)*

***Aerobic gram-negative microorganisms***
*Acinetobacter baumannii*
*Citrobacter freundii*
*Enterobacter cloacae*
*Klebsiella pneumoniae*
*Morganella morganii*
*Pseudomonas aeruginosa*
*Serratia marcescens*
*Stenotrophomonas maltophilia*

***Anaerobic microorganisms***
*Bacteroides spp.*

***Other microorganisms***
*Chlamydia spp.*
*Chlamydophila spp.*
*Legionella pneumophila*
*Mycoplasma spp.*
*Ureaplasma urealyticum*

° No current data were available when the table was published. Sensitivity is assumed in the primary literature, standard works and therapy recommendations.
+ The resistance rate is above 50% in at least one region.
^ Collective name for a heterogeneous group of *Streptococcus* species. Resistance rate can vary depending on the *Streptococcus* species concerned.
∞ No recent data available; in studies (older than 5 years) the proportion of resistant strains is reported as ≥10%.
[3] The resistance rate is <10% in the outpatient setting.

### 5.2 Pharmacokinetic properties

Distribution

Ampicillin is extensively distributed to tissues, crosses the placental barrier and diffuses into breast milk. Only 5% of the ampicillin concentration in plasma diffuses into cerebrospinal fluid (CSF) with intact meninges. With inflamed meninges, the ampicillin concentration in CSF can increase to 50% of the ampicillin concentration in plasma.

The serum protein binding is 17-20%. The apparent volume of distribution is about 15 L.

Higher concentrations of the active form are observed in bile than in serum.

Serum level

After oral administration of 1000 mg ampicillin, peak plasma levels of about 5 mg/l are reached after 90 to 120 min. After intramuscular injection, peak plasma levels are reached after 30 to 60 min.

Biotransformation

Ampicillin is partly metabolised to microbiologically inactive penicilloates.

Elimination

Ampicillin is eliminated intact mainly by the renal route, but also through bile and faeces. After oral administration, about 40% of a dose is recovered unchanged in the urine. After parenteral administration, about 73 +/- 10% of an administered dose is excreted as unchanged substance in the 0- to 12-hour urine. Up to 10% of a dose is eliminated in the form of biotransformation products. The elimination half-life is about 50 to 60 min. In oliguria, the half-life may be prolonged to 8 to 20 hours. The half-life is also prolonged in newborns (2 to 4 hours). The renal clearance of ampicillin is about 194 ml/min after intravenous administration.

### 5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies repeated-dose toxicity and genotoxicity.

Following intravenous administration no teratogenic potential or pre-natal effects were observed in the rat or rabbit. Repeated administration for up to 13 weeks in the rat and dog (2 mg/kg/day) showed no histological effects on the ovary; however, reversible impairment of spermatogenesis was observed in the dog at 200 mg/day. In animal studies at doses higher than those used in humans, ampicillin did not have any adverse effects on fertility.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

None

### 6.2 Incompatibilities

Ampicillin solutions should always be administered separately, unless compatibility with other infusion solutions or medicines has been established.

This medicinal product must not be mixed with other solutions except those mentioned in section 4.2.

Ampicillin solutions should not be mixed with aminoglycosides, metronidazole and injectable tetracycline derivatives such as oxytetracycline, rolitetracycline and doxycycline. Visual signs of incompatibility are precipitation, clouding and discoloration.

### 6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

*Shelf-life after preparation of the ready-to-use solution*

Use only clear solutions prepared immediately before application.

Any unused solution remaining after reconstitution must be discarded.

### 6.4 Special precautions for storage

Store below 25°C.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

### 6.5 Nature and contents of container

Glass vial with halogenated butyl rubber stopper.

Pack sizes: 1 vial, 10 vials or 25 vials.

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal

The solutions should always be prepared freshly before use and checked for clarity. Use only clear solutions for injection or infusion! Do not use solutions with cloudiness or precipitation.

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

## 7. LICENCE HOLDER AND MANUFACTURER

**Licence holder:**
Abic Marketing Ltd. (Teva Group),
P.O. Box 8077, Netanya.

**Manufacturer:**
Sandoz GmbH,
Kundl, Austria.

## 8. REGISTRATION NUMBERS:

**Penibrin 500:** 115.63.22419
**Penibrin 1 g:** 032.41.22422
**Penibrin 2 g:** 102.72.27337

**The leaflet was revised in February 2021 according to MoH guidelines.**