SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

<Product Name> 250 mg powder for solution for injection/infusion
<Product Name> 500 mg powder for solution for injection/infusion
<Product Name> 1 g powder for solution for injection/infusion
<Product Name> 2 g powder for solution for injection/infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Product Name> 250 mg:
One vial contains 266 mg of ampicillin sodium (equivalent to 250 mg of ampicillin).

<Product Name> 500 mg:
One vial contains 531 mg of ampicillin sodium (equivalent to 500 mg ampicillin).

<Product Name> 1 g:
One vial contains 1063 mg of ampicillin sodium (equivalent to 1000 mg ampicillin).

<Product Name> 2 g:
One vial contains 2126 mg of ampicillin sodium (equivalent to 2000 mg ampicillin).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

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

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<Product Name> is indicated in the treatment of infections caused by ampicillin sensitive organisms (see sections 4.4 and 5.1). As needed, ampicillin should be administered after initial broad spectrum coverage with a third generation cephalosporin.
• Complicated acute bacterial sinusitis
• Endocarditis
• Pyelonephritis
• Cystitis (see section 4.4)
• Intra-abdominal infections
• Female genital infections
• Listeria Meningitis when used in conjunction with an aminoglycoside

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology
The dose level of ampicillin is dependent on the patient's age, weight and renal function, the severity and site of infection and the presumed or identified etiologic agents.

Adults and adolescents (over 12 years of age)

Intravenous or intra-muscular injection
500 mg every 4 to 6 hours (the daily dose can be increased to 6 g in case of severe infection).

Paediatric population (up to 12 years of age)
Intravenous injection or infusion

Child 1 month – 12 years
25 mg/kg (max 1g) every 6 hours (the dose can be doubled in case of severe infection to 50 mg/kg (max 2 g) every 6 hours).

Neonate 21 – 28 days
30 mg/kg every 6 hours (the dose can be doubled in case of severe infection).

Neonate 7 – 21 days
30 mg/kg every 8 hours (the dose can be doubled in case of severe infection).

Neonate under 7 days
30 mg/kg every 12 hours (the dose can be doubled in case of severe infection).

Special populations
Renal impairment
No dose adjustment is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.
For severely impaired renal function with a glomerular filtration rate of 30 ml/min and less, a reduction in the dose is recommended, since an accumulation of ampicillin is to be expected:
- at a creatinine clearance of 20 to 30 ml/min, the normal dose should be reduced to ⅔,
- at a creatinine clearance below 20 ml/min, the normal dose should be reduced to ⅓.

As a general rule, a dose of 1 g ampicillin in 8 hours should not be exceeded in patients with severe renal insufficiency.

Duration of treatment
The duration of use depends on the course of the disease. As a general rule, ampicillin is used for 7 to 10 days, but for at least another 2 to 3 days after the signs of disease have subsided.
For the treatment of infections with beta-haemolytic streptococci, for safety reasons it is recommended to extend the treatment to at least 10 days to prevent late complications (e.g. rheumatic fever, glomerulonephritis).

Method of administration
Intramuscular or intravenous injection, or as intermittent or slow infusion.
For intramuscular administration, the usual limit of the injection volume must be complied with.

Intravenous injections are given slowly over 5–10 minutes. Too rapid an injection can cause convulsions.

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

Treatment control
With long-term treatment, renal function, liver function and haematopoietic function should be checked periodically.

4.3 Contraindications

Hypersensitivity to the active substance, to any other penicillin or to any of the excipients listed in section 6.1.
Penicillin allergy and type 1 reaction to cephalosporins.

4.4 Special warnings and precautions for use

The possibility of superinfection with fungal organisms or bacteria should be borne in mind during treatment. In such cases, the medicinal product must be discontinued and an alternative, appropriate treatment introduced.

In the event of shock, absorption from intramuscular injections is reduced. Intravenous treatment should be considered for seriously ill patients.

A significant proportion (up to 90%) of patients with infectious mononucleosis or lymphocytic leukaemia who receive ampicillin get skin rashes. Normally, the rash begins 7 to 10 days after the start of treatment with oral ampicillin and continues for several days or a week after it is discontinued. In most patients, this is maculopapular, pruritic and generalised. The use of ampicillin in patients with mononucleosis is therefore not recommended. It is not known whether these patients are actually allergic to ampicillin.

Severe and occasionally fatal anaphylactic reactions in patients undergoing penicillin treatment have been reported. As with other penicillins, it can be expected that unforeseen reactions are mainly limited to hypersensitivity. Hypersensitivity reactions are more likely in persons that have previously reacted with hypersensitivity to penicillins and in persons with allergies, asthma, hay fever or urticaria in their anamnesis.

Patients with previous hypersensitivity reactions to penicillin can experience severe hypersensitivity reactions when using cephalosporins. Thorough investigation must be carried out concerning previous hypersensitivity reactions in regard to penicillins and cephalosporins. In the event of known allergies and previous anaphylactic reactions to other allergens, particular vigilance and contingency plans must be in place at the start of treatment. Severe anaphylactic reactions require immediate emergency treatment.

There have been reports of *Clostridioides difficile*-associated diarrhoea (CDAD) in connection with almost all antibacterial medicinal products, including ampicillin, that can vary in degree of severity from mild diarrhoea to fatal colitis. CDAD must be evaluated in all patients with diarrhoea during or after the use of antibiotics. CDAD has been reported as occurring from the first day of treatment and up to 10 weeks after the administration of antibacterial medicinal products. If there is suspected or confirmed CDAD, the triggering antibacterial medicinal products must be withdrawn and another form of treatment considered.

False positive reactions can occur in certain tests for glucosuria.

Dosage adjustment is recommended for patients with reduced kidney function (creatinine clearance < 50 mL/min) (see section 4.2).

<Product Name> 250 mg
This medicine contains less than 1 mmol sodium (23 mg) per vial of 2.5 ml, that is to say essentially ‘sodium-free’.

<Product Name> 500 mg
This medicinal product contains 32.9 mg sodium per vial of 5 ml, equivalent to 1.65% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

<Product Name> 1 g
This medicinal product contains 65.8 mg sodium per vial of 10 ml, equivalent to 3.29% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

<Product Name> 2 g
This medicinal product contains 131.6 mg sodium per vial of 20 ml, equivalent to 6.58% 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

Contraceptives (Combined Oral Contraceptive Pill-COCP)
On very rare occasions, penicillins can reduce the absorption and therefore the effect of COCP.

Probenecid
Concomitant administration of probenecid inhibits the tubular secretion of penicillin.

Allopurinol
Concomitant use of allopurinol can increase the risk of allergic skin reactions.

Methotrexate
The effect/toxicity of methotrexate may be increased if it is used concomitantly with penicillins as its excretion is reduced.

4.6 Fertility, pregnancy and lactation

Pregnancy
Long clinical experience indicates a low risk of adverse reactions on pregnancy, the foetus or newborn infants. However, there are no extensively controlled studies of pregnant women.

This medicinal product can be used during pregnancy if the treating physician considers that the potential benefits outweigh the potential risks for the mother as well as the child

Breast-feeding
The preparation passes into human milk to a minor extent. No therapeutic effect on any infection in the child can be expected Small amounts of the active substance in human milk can increase the risk of sensitisation.

4.7 Effects on ability to drive and use machines

The medicinal product is not thought to affect the ability to drive or use machines.

4.8 Undesirable effects

Approx. 5% of patients develop skin reactions.
The following adverse reactions have been reported in connection with the use of ampicillin:

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)

Frequency	Organ classification	Undesirable effects
Common (≥1/100 to <1/10)	*Gastrointestinal disorders*	Diarrhoea
	Skin and subcutaneous tissue disorders	Exanthema
Uncommon (≥1/1,000 to <1/100)	*Blood and lymphatic system disorders*	Anaemia, thrombocytopenia, eosinophilia, leukopenia, agranulocytosis[1].
	Gastrointestinal disorders	Glossitis, stomatitis, hairy tongue, nausea, vomiting, enterocolitis, pseudomembranous colitis.
	Skin and subcutaneous tissue disorders	Urticaria
Rare (≥1/10,000 to <1/1,000)	*Immune system disorders*	Anaphylaxis, exfoliative dermatitis and erythema multiforme.
Not known (cannot be estimated from the available data)	*Immune system disorders*	Steven-Johnson syndrome, toxic epidermal necrolysis

Local pain during intramuscular injections can occur.
[1]These reactions are normally reversible upon discontinuation of the treatment and are assumed to be a hypersensitivity phenomenon.
Urticaria and other types of skin rashes can be controlled by treating them symptomatically; however, discontinuation should be considered.
A moderate increase in serum glutamate oxaloacetate transaminase (SGOT) has been observed, particularly in infants; however, the significance of this is unknown. Slight, transient SGOT increases have been observed in individuals who received frequent intramuscular injections with larger-than-normal (two to four times) normal doses. It has been shown that intramuscular injections of ampicillin sodium lead to a release of GOT at the injection site, and an increase in serum levels of this enzyme is not necessarily a sign of liver damage.

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

High penicillin doses are usually well tolerated. Toxic reactions: Electrolyte disturbance, convulsions, reduced consciousness. Haemolytic reactions, renal failure, acidosis. Discontinue treatment in the event of an overdose. Treatment: Symptomatic treatment. In the event of kidney damage, ampicillin can be removed through haemodialysis, but not through 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.
Ampicillin is active against gram-positive cocci and rods gram-negative cocci and a large number of gram-negative rods, e.g. most strains of *Haemophilus influenzae, Escherichia coli, Salmonella* and *Proteus mirabilis* are sensitive.

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.

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 ampicillin exists with amoxicillin and to some extent with other penicillins and cephalosporins.

Pseudomonas aeruginosa, *Klebsiella*, indole-positive *Proteus* spp, *Bacteroides fragilis*, *Providencia* and penicillinase-producing staphylococci are resistant. Some strains of *Haemophilus influenzae* can be resistant – something that should be noted in cases of severe infections such as epiglottitis and meningitis. Selection of resistant bacteria may occur.
Resistance is often of the R-factor type.

Breakpoints
European Committee on Antimicrobial Susceptibility Testing (EUCAST), clinical breakpoints for MIC testing for ampicillin are presented below:

Microorganism	**Susceptible ≤ (mg/l)**	**Resistant > (mg/l)**	**Notes**
*Enterobacterales**	≤8	>8	Wild type *Enterobacterales* are categorised as susceptible to aminopenicillins. Some countries prefer to categorise wild-type isolates of *E. coli* and *P. mirabilis* as "Susceptible, increased

Microorganism	**Susceptible ≤ (mg/l)**	**Resistant > (mg/l)**	**Notes**
			exposure". When this is the case, MIC breakpoint S ≤ 0.5 mg/L is used.
Staphylococcus spp, *S. saprophyticus*	-	-	Most staphylococci are penicillinase producers which make them resistant to ampicillin. When staphylococci test as susceptible to benzylpenicillin and cefoxitin they can be reported as susceptible to Ampicillin. Ampicillin susceptible *S. saprophyticus* are mecA -negative (without or with a beta-lactamase inhibitor)
Enterococcus spp.	≤4	>8	Ampicillin resistance in *E. faecalis* is rare and should be confirmed with an MIC test.
Streptococcus groups A, B, C and G	-	-	The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility with the exception of phenoxymethylpenicillin and isoxazolylpenicillins for streptococcus group B
Streptococcus pneumoniae	≤0.5	>2	The oxacillin 1 unit disk screen test shall be used to exclude beta-lactam resistance mechanisms.
Viridans group streptococci	≤0.5	>2	
Haemophilus influenzae	≤1	>1	Beta-lactamase positive isolates can be reported resistant to ampicillin without inhibitors. Tests based on a chromogenic cephalosporin can be used to detect the beta-lactamase.
Moraxella catarrhalis	-	-	Most *M. catarrhalis* produce beta-lactamase, although beta-lactamase production is slow and may give weak results with in vitro tests. Beta-lactamase producers should be reported resistant to penicillins and aminopenicillins without inhibitors.
Neisseria gonorrhoeae	-	-	Always test for beta-lactamase. If positive, report resistant to ampicillin. Tests based on a chromogenic cephalosporin can be used to detect the beta-lactamase. The susceptibility of beta-lactamase negative isolates to ampicillin can be inferred from benzylpenicillin.
Neisseria meningitidis	≤0.125	>1	
Gram-positive anaerobes except *Clostridioides difficile*	≤4	>8	Susceptibility to ampicillin can be inferred from susceptibility to benzylpenicillin
Gram-negative anaerobes	≤0.5	>2	Susceptibility to ampicillin can be inferred from susceptibility to benzylpenicillin
Listeria monocytogenes	≤1	>1	
Pasteurella multocida	≤1	>1	
Aerococcus sanguinicola and urinae	≤0.25	>0.25	
Kingella kingae	≤0.06	>0.06	Susceptibility to ampicillin can be inferred from susceptibility to benzylpenicillin
PK-PD (Non-species related) breakpoints These breakpoints are used only when there are no species-specific breakpoints or other recommendations (a dash or a note).	≤2	>8	If the MIC is greater than the PK-PD resistant breakpoint, advise against use of the agent. If the MIC is less than or equal to the PK-PD susceptible breakpoint, suggest that the agent can be used with caution.

* Recent taxonomic studies have narrowed the definition of the family Enterobacteriaceae. Some previous members of this family are now included in other families within the Order *Enterobacterales*. Breakpoints in this table apply to all members of the Enterobacterales.

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** Streptococcus groups A, B, C and G *Enterococcus faecalis* *Listeria monocytogenes* *Staphylococcus saprophyticus* *Aerococcus sanguinicola* and *urinae* **Aerobic gram-negative microorganisms** *Neisseria meningitidis* *Pasteurella multocida*
Species for which acquired resistance may be a problem	**Aerobic gram-negative microorganisms** *Enterobacterales* *Haemophilus influenzae* *Neisseria gonorrhoeae* *Moraxella catarrhalis* **Anaerobic microorganisms** *Prevotella* spp. **Aerobic gram-positive microorganisms** *Staphylococcus aureus* *Enterococcus faecium* *Streptococcus pneumoniae*
Inherently resistant organisms	**Aerobic gram-negative microorganisms** *Pseudomonas aeruginosa* *Acinetobacter baumannii* *Citrobacter freundii* *Enterobacter cloacae* *Klebsiella pneumoniae* *Morganella morganii* *Aeromonas* spp. **Anaerobic microorganisms** *Clostridioides difficile* **Other microorganisms** *Mycobacterium tuberculosis*

5.2 Pharmacokinetic properties

Absorption
A maximum serum concentration of approx. 8 µg/mL occurs one hour after intramuscular injection of 500 mg ampicillin. A maximum serum concentration in the area of 80–100 µg/mL is attained after an intravenous infusion of 2 g.

Distribution
Approx. 20% of ampicillin is bound to serum proteins. Penetration into cerebrospinal fluid and the brain only occurs in cases of inflammation of the meninges. Concentration in bile is higher than in serum.

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 new borns (2 to 4 hours). The renal clearance of ampicillin is about 194 ml/min after intravenous administration.

5.3 Preclinical safety data

Carcinogenic potential studies in animals have not been carried out.

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 medicinal products except those mentioned in section 6.6.
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

2 years.

Shelf-life after preparation of the ready-to-use solution
Reconstituted/diluted solution should be used immediately.

6.4 Special precautions for storage

Do not store above 25°C.
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

<Product Name> 250 mg
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and light yellow flip off aluminium seal containing 266 mg powder for solution for injection/infusion.

<Product Name> 500 mg
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and electric blue flip off aluminium seal containing 531 mg powder for solution for injection/infusion.

<Product Name> 1 g
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and green flip off aluminium seal containing 1063 mg powder for solution for injection/infusion.

<Product Name> 2 g
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and brown flip off aluminium seal containing 2126 mg powder for solution for injection/infusion.

6.6 Special precautions for disposal and other handling

Ampicillin solutions are compatible with 0.9 % (9 mg/ml) sodium chloride solution, 5 % (50 mg/ml) glucose solution and Ringer solution.

<Product Name> 250 mg
The 10 % injection/infusion solution is prepared by dissolving 0.26 g powder in 2.5 ml water for injections.

<Product Name> 500 mg
The 10 % injection/infusion solution is prepared by dissolving 0.53 g powder in 5 ml water for injections.

<Product Name> 1 g
The 10 % injection/infusion solution is prepared by dissolving 1.06 g powder in 10 ml water for injections.

<Product Name> 2 g
The 10 % injection/infusion solution is prepared by dissolving 2.12 g powder in 20 ml water for injections.

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. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]

<Detailed information on this medicinal product is available on the website of {name of MS Agency}>

LABELLING AND PACKAGE LEAFLET

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

<Product Name> 250 mg powder for solution for injection/infusion
<Product Name> 500 mg powder for solution for injection/infusion
<Product Name> 1 g powder for solution for injection/infusion
<Product Name> 2 g powder for solution for injection/infusion
Ampicillin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains: ampicillin sodium equivalent to 250 mg of ampicillin.
Each vial contains: ampicillin sodium equivalent to 500 mg of ampicillin.
Each vial contains: ampicillin sodium equivalent to 1 g of ampicillin.
Each vial contains: ampicillin sodium equivalent to 2 g of ampicillin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection/infusion
1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intramuscular or intravenous use only.
For single use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use as directed by the Physician.

8. EXPIRY DATE

EXP

Reconstituted/diluted solution should be used immediately.

9. SPECIAL STORAGE CONDITIONS

Unopened vial: Do not store above 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Any unused portion must be discarded appropriately.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

<2D barcode carrying the unique identifier included.>

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC: {number}
SN: {number}
NN: {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial (10 ml and 20 ml)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

<Product Name> 250 mg powder for solution for injection/infusion
<Product Name> 500 mg powder for solution for injection/infusion
<Product Name> 1 g powder for solution for injection/infusion
<Product Name> 2 g powder for solution for injection/infusion
Ampicillin
For intramuscular or intravenous use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Vial of 10 ml.
Vial of 10 ml.
Vial of 10 ml.
Vial of 20 ml.

6. OTHER

PACKAGE LEAFLET

Package leaflet: information for the patient

<Product Name> 250 mg powder for solution for injection/infusion
<Product Name> 500 mg powder for solution for injection/infusion
<Product Name> 1 g powder for solution for injection/infusion
<Product Name> 2 g powder for solution for injection/infusion

Ampicillin

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 <Product Name> is and what it is used for

Please be aware that your doctor may have prescribed the medicine for a different use and/or at a dose different from those mentioned in this leaflet. Always follow the doctor's prescription given on the packaging label.

<Product Name> is a medicine for the treatment of bacterial infections (antibiotic) and works by killing bacteria that cause infections. It contains the active substance ampicillin. Ampicillin belongs to a group of medicines called 'penicillins'.

<Product Name> is used to treat the following:
• complicated acute bacterial sinusitis
• meningitis caused by the listeria bacteria
• infections of the heart
• kidney infections
• female genital organ infections
• infections inside the abdomen
• urinary bladder infections

2. What you need to know before you are given <Product Name>

Do not use <Product Name>
- if you are allergic to ampicillin, other penicillins or to cephalosporins

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using <Product Name> if you:
- have a condition known as 'infectious mononucleosis' (your doctor will have told you) – as there is a greater risk that you will develop a skin rash
- have diarrhoea

If you are having blood or urine tests for glucose, let your doctor or nurse know that you are taking <Product Name>. This is because <Product Name> can affect the results of these types of tests.

Other medicines and <Product Name>
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without prescription and natural remedies.

This is especially important if you are taking the following medicines:
- allopurinol (a medicine used for gout); it may be more likely that you will have an allergic skin reaction.
- probenecid (a medicine used for gout); your doctor may decide to adjust your dose of <Product Name>.
- methotrexate (a medicine used to treat cancer or rheumatism); as <Product Name> can affect how methotrexate works.
- contraceptive pills, as <Product Name> may reduce their effectiveness.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
Ampicillin may be used during pregnancy if your doctor thinks it is necessary.
It is possible that breastfeeding infants can be affected. Consult your doctor before using Ampicillin when breast-feeding.

Driving and using machines
The medicine is not thought to affect the ability to drive or use machines.
Medicines may affect your ability to drive or carry out potentially hazardous work. Read the information in the package leaflet carefully. If you are unsure about anything, talk to your doctor or pharmacist.

<Product Name> contains sodium
Ampicillin 250 mg
This medicine contains less than 1 mmol sodium (23 mg) per vial of 2.5 ml, that is to say essentially 'sodium-free'.

Ampicillin 500 mg
This medicine contains 32.9 mg sodium (main component of cooking/table salt) in each vial of 5 ml. This is equivalent to 1.64% of the recommended maximum daily dietary intake of sodium for an adult.

Ampicillin 1 g
This medicine contains 65.8 mg sodium (main component of cooking/table salt) in each vial of 10 ml. This is equivalent to 3.29% of the recommended maximum daily dietary intake of sodium for an adult.

Ampicillin 2 g
This medicine contains 131.6 mg sodium (main component of cooking/table salt) in each vial of 20 ml. This is equivalent to 6.58% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use <Product Name>

<Product Name> is only available from hospital personnel, who will be able to provide further information. <Product name> is injected into muscle or vein. The dosage is determined by a doctor, who will adjust it for you.

Use in adults and adolescents
The recommended dose is 500 mg every 4 to 6 hours (the daily dose can be increased to 6 g in case of severe infection)

Use in children
Intravenous injection or infusion

Child 1 month – 12 years
The recommended dose is 25 mg/kg (max 1g) every 6 hours (the dose can be increased to 50 mg/kg (max 2 g) every 6 hours in case of severe infection).

Neonate 21 – 28 days
The recommended dose is 30 mg/kg every 6 hours (the dose can be doubled in case of severe infection).

Neonate 7 – 21 days
The recommended dose is 30 mg/kg every 8 hours (the dose can be doubled in case of severe infection).

Neonate under 7 days
The recommended dose is 30 mg/kg every 12 hours (the dose can be doubled in case of severe infection).

Dosage for patients with impaired kidney function
No dose adjustment is required in patients with mild to moderate kidney problems.

For severely impaired renal function with a glomerular filtration rate of 30 ml/min and less, a reduction in the dose (administered amount) is recommended, since an accumulation of ampicillin is to be expected:
- at a creatinine clearance of 20 to 30 ml/min, the normal dose should be reduced to ⅔,
- at a creatinine clearance below 20 ml/min, the normal dose should be reduced to ⅓.

As a general rule, a dose of 1 g ampicillin in 8 hours should not be exceeded in patients with severe renal insufficiency.

How <Product Name> will be given to you
It will be given as an injection into a vein, or by intravenous infusion, or into a muscle in your body.

Duration of treatment
The duration of treatment depends on the course of the disease. As a general rule, ampicillin is used for 7 to 10 days, but for at least another 2 to 3 days after the signs of disease have subsided.

If you use more <Product Name> than you should
It is unlikely you will be given too much, but if you think you have been given too much <Product Name> tell your doctor, pharmacist or nurse immediately.
Signs may be an upset stomach (feeling sick (nausea), being sick (vomiting) or diarrhoea), muscle twitching, nervousness, tingling around the mouth, tinnitus, tremor, dizziness, blurred vision, altered

consciousness including coma, a change in levels of sodium or potassium in your blood, other problems with your blood, kidney failure or an increase of acid in the blood or convulsions (fits).

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop taking <Product Name> and immediately contact your doctor or go to your nearest hospital emergency department if you get the following:

- An increase in the number of infections causing fever, severe chills, sore throat, mouth ulcers, chest infections or you may feel tired, short of breath, have pale skin, yellowing of the skin or whites of the eyes, unexplained bruising or bleeding more easily than normal. These may be signs of changes to the type or number of blood cells in the blood.
- An allergic reaction: such as a rash, hives, redness, itching or swelling of the face, mouth, lips, tongue or throat that may cause difficulty breathing.
- Widespread red skin rash which may have small pus-containing blisters (exfoliative dermatitis)
- Skin rash, which may blister, and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge (erythema multiforme)
- A widespread rash with blisters and peeling skin, particularly around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome), and a more severe form, causing extensive peeling of the skin (more than 30% of the body surface (toxic epidermal necrolysis))
- Severe diarrhoea containing blood (pseudomonas colitis).
- Severe diarrhoea due to inflammation of the bowel (enterocolitis)

Common side effects (may affect more than 1 in 100 patients):

- diarrhoea (loose bowel movements),
- skin rash.

Uncommon side effects (may affect more than 1 in 1,000 patients):

- swollen/sore tongue,
- sore mouth,
- brownish discoloured tongue with a rough or hairy feel (‘hairy tongue’),
- nausea,
- vomiting,
- itchy rash with red bumps (hives).

Side effects with unknown frequency (cannot be estimated from the available data):

- Increase in liver enzymes.

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 listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store <Product Name>

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the label after EXP. The expiry date refers to the last day of that month.

Do not store above 25 °C.
Reconstituted/diluted solution should be used immediately.
Do not use this medicine if you notice cloudiness or precipitations.

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 <Product Name> contains
- The active substance is ampicillin (as ampicillin sodium).
- There are no other ingredients.

<Product Name> 250 mg:
One vial contains 266 mg of ampicillin sodium (equivalent to 250 mg of ampicillin).

<Product Name> 500 mg:
One vial contains 531 mg of ampicillin sodium (equivalent to 500 mg of ampicillin).

<Product Name> 1 g:
One vial contains 1063 mg of ampicillin sodium (equivalent to 1000 mg of ampicillin).

<Product Name> 2 g:
One vial contains 2126 mg of ampicillin sodium (equivalent to 2000 mg of ampicillin).

What <Product Name> looks like and contents of the pack
White to off white crystalline powder

<Product Name> 250 mg:
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and light yellow flip off aluminium seal containing 266 mg powder for solution for injection/infusion.

<Product Name> 500 mg:
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and blue flip off aluminium seal containing 531 mg powder for solution for injection/infusion.

<Product Name> 1 g:
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and green flip off aluminium seal containing 1063 mg powder for solution for injection/infusion.

<Product Name> 2 g:
Pack with 1 glass vial with dark grey bromobutyl rubber stopper and brown flip off aluminium seal containing 2126 mg powder for solution for injection/infusion.

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

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

<Denmark> <Ampicillin Mylan 250 mg pulver til injektions-og infusionsvæske, opløsning>
<Ampicillin Mylan 500 mg pulver til injektions-og infusionsvæske, opløsning>
<Ampicillin Mylan 1 g pulver til injektions-og infusionsvæske, opløsning>
<Ampicillin Mylan 2 g pulver til injektions-og infusionsvæske, opløsning>

<Finland> <Ampicillin Mylan 250 mg injektio-/infuusiokuiva-aine liuosta varten>
<Ampicillin Mylan 500 mg injektio-/infuusiokuiva-aine liuosta varten>
<Ampicillin Mylan 1 g injektio-/infuusiokuiva-aine liuosta varten>
<Ampicillin Mylan 2 g injektio-/infuusiokuiva-aine liuosta varten>

<Norway> <Ampicillin Mylan 250 mg pulver til injeksjons-/infusjonsvæske, oppløsning>
<Ampicillin Mylan 500 mg pulver til injeksjons-/infusjonsvæske, oppløsning>
<Ampicillin Mylan 1 g pulver til injeksjons-/infusjonsvæske, oppløsning>
<Ampicillin Mylan 2 g pulver til injeksjons-/infusjonsvæske, oppløsning>

<United-Kingdom> <Ampicillin 250 mg powder for solution for injection/infusion>
<Ampicillin 500 mg powder for solution for injection/infusion>
<Ampicillin 1 g powder for solution for injection/infusion>
<Ampicillin 2 g powder for solution for injection/infusion>

This leaflet was last revised in {**MM/YYYY**}.
[To be completed nationally]

<Other sources of information>

<Detailed information on this medicine is available on the website of {name of MS Agency}>

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The following information is intended for healthcare professionals only:

Preparation of the injection solution:
<Product Name> 250 mg
The 10 % injection/infusion solution is prepared by dissolving 0.26 g powder in 2.5 ml water for injections.

<Product Name> 500 mg
The 10 % injection/infusion solution is prepared by dissolving 0.53 g powder in 5 ml water for injections.

<Product Name> 1 g
The 10 % injection/infusion solution is prepared by dissolving 1.06 g powder in 10 ml water for injections.

<Product Name> 2 g
The 10 % injection/infusion solution is prepared by dissolving 2.12 g powder in 20 ml water for injections.

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.
Compatibility
Ampicillin solutions should always be administered separately, unless the compatibility with other infusion solutions or medicines has been established.
Ampicillin solutions are compatible with 0.9 % (9 mg/ml) sodium chloride solution, 5 % (50 mg/ml) glucose solution and Ringer solution.
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 discolouration.