1. NAME OF THE MEDICINAL PRODUCT

Doktacillin 1 g or 2 g, powder for solution for injection/infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1g
1 vial contains 1063 mg ampicillin sodium equivalent to 1 g ampicillin.

2g
1 vial contains 2126 mg ampicillin sodium equivalent to 2 g ampicillin.

3. PHARMACEUTICAL FORM

Powder for solution for injection/infusion

White to off-white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Acute exacerbation of chronic bronchitis. Upper urinary tract infection caused by enterococci. Septicaemia and endocarditis caused by enterococci. Acute meningitis caused by *Listeria monocytogenes*. Neonatal septicaemia.

In community-acquired pneumonia, Doktacillin should be reserved for patients for whom penicillin G has not produced the desired effect or is unsuitable for other reasons.

4.2 Posology and method of administration

Posology
Adults:
Intramuscularly: 500 mg 4 times daily.
Intravenous injection: 500 mg–2 g 4–6 times daily. Given slowly, 2 g over at least 3–4 minutes.
Continuous intravenous infusion: 6–12 g daily. An infusion pump should be used where possible.
Intermittent intravenous infusion: 2 g 4–6 times daily.

Higher doses than those recommended can be given intravenously if necessary.

Children:
Intramuscularly: 50 mg/kg body weight daily. The daily dose should be administered in four divided doses at 6-hourly intervals. For neonates and premature infants, 25–50 mg/kg divided into two doses is recommended.
Intravenously: 100–200 mg/kg body weight daily in severe infections. In bacterial meningitis, intravenous dosing in children can be increased if necessary to 400 mg/kg body weight daily.

Therapeutic monitoring
In long-term treatment, (> 2–3 weeks), hepatic and renal function and blood cell counts should be monitored.

In *acute meningitis caused by Listeria monocytogenes* and in *neonatal septicaemia*, Doktacillin should be given in combination with another antibiotic.

4.3 Contraindications

Hypersensitivity to the active substance or other penicillins.

4.4 Special warnings and precautions for use

There is cross-reactivity between penicillins and cephalosporins. High urine concentrations of Doktacillin may cause false positive reactions in some tests for the presence of glucose.
Diarrhoea/pseudomembranous colitis caused by *Clostridium difficile* may occur. Patients with diarrhoea must therefore be monitored closely.

Doktacillin 1 g
This medicinal product contains 65.8 mg sodium per injection vial, equivalent to 3.3 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Doktacillin 2 g
This medicinal product contains 131.6 mg sodium per injection vial, equivalent to 6.6 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

If the product is dissolved or diluted in isotonic sodium chloride solution, the additional amount of sodium from the solvent should also be taken into consideration (see section 6.6).

4.5 Interaction with other medicinal products and other forms of interaction

Dose adjustment may be required when Doktacillin is used in combination with the following medications: allopurinol and methotrexate.

Coadministration of *allopurinol* with ampicillin increases the risk of allergic skin reactions.

A serious case of a severe toxic reaction to *methotrexate* has been described, where the patient was treated concomitantly with furosemide and penicillin V, organic acids that may inhibit the tubular secretion of methotrexate. A possible interaction has also been described after combination of methotrexate and mezlocillin, and another case after combination of methotrexate and amoxicillin.

4.6 Fertility, pregnancy and lactation

Pregnancy: There are no known risks associated with the use of Doktacillin in pregnancy.

Breast-feeding: Ampicillin is excreted in human milk, but at therapeutic doses, effects on the breastfed infant are considered unlikely.

4.7 Effects on ability to drive and use machines

Doktacillin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequency of adverse reactions is defined using the following convention: 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 (cannot be estimated from the available data).

The most common undesirable effect is a skin rash which occurs in 5% of treated patients.

System organ class	Frequency	Undesirable effects
Infections and infestations	Uncommon	Pseudomembranous colitis
Blood and lymph disorders	Uncommon	Anaemia, thrombocytopaenia, eosinophilia, leukopaenia and agranulocytosis
Immune system disorders	Rare	Anaphylactic reaction
Gastrointestinal disorders	Common	Soft faeces
	Uncommon	Glossitis, stomatitis, nausea, vomiting, enterocolitis, diarrhoea
Skin and subcutaneous tissue disorders	Common	Exanthem
	Uncommon	Urticaria
	Rare	Exfoliative dermatitis and erythema multiforme

Fungal overgrowth in the oral cavity and vagina may occur. Local pain may occur after intramuscular injection.

The incidence of exanthem is higher in patients with infectious mononucleosis. A higher incidence of exanthem has also been observed in patients with leukaemia.
Raised AST values have been demonstrated to occur due to local release at the injection site and need not suggest hepatic involvement.
For treatment of anaphylactic reaction, see Section 4.9. Overdose.

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 to (see details below).

The Swedish Medical Products Agency
Box 26
751 03 Uppsala
www.lakemedelsverket.se

4.9 Overdose

Toxicity: Large doses are generally well tolerated. However in cases of, e.g., renal impairment and defective blood-cerebrospinal fluid barrier, parenteral administration of high doses have given rise to toxic symptoms. Acute reactions are mainly due to hypersensitisation.

Symptoms: Toxic reactions: nausea, vomiting, diarrhoea, electrolyte disturbance, reduced level of consciousness, muscle fasciculations, myoclonias, seizures, coma. Haemolytic reactions, renal failure, acidosis.
In exceptional cases, an anaphylactic reaction may occur within 20–40 minutes.

Treatment: Symptomatic treatment. In severe cases, haemoperfusion or haemodialysis. *Treatment of anaphylactic reaction:* Epinephrine (adrenaline) 0.1–0.5 mg slow intravenous route. Hydrocortisone 200 mg intravenously, possibly promethazine 25 mg intravenously. Fluids. Acidosis correction.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Penicillins with extended spectrum, ATC code: J01CA01.

Doktacillin (ampicillin) is a penicillin with a broad antibacterial spectrum. Ampicillin inhibits bacterial cell wall synthesis. The effect is bactericidal.

Antibacterial spectrum

Susceptible	Pneumococci Streptococci Enterococci *Listeria monocytogenes* Meningococci *Haemophilus influenzae* *Proteus mirabilis* Anaerobic streptococci and peptostreptococci
Intermediate	*E. coli* and *Acinetobacter*
Resistant	Staphylococci *Moraxella catarrhalis* Beta-lactamase-producing *Haemophilus influenzae* *Citrobacter* *Klebsiella* *Enterobacter* *Morganella morganii* *Proteus vulgaris* *Providencia* *Serratia* *Pseudomonas* *Legionella* *Clostridium difficile* *Bacteroides fragilis* Mycoplasma *Chlamydia*

Resistance occurs (1–10%) in pneumococci and *Enterococcus faecalis*.
Resistance is common (> 10%) in *Enterococcus faecium, Haemophilus influenzae* and gram-negative intestinal bacteria.

Mechanism of resistance
Resistance may arise due to bacterial synthesis of a large number of beta-lactamase enzymes that hydrolyse the penicillin. Several of these can be inhibited by clavulanic acid. Furthermore, resistance may arise due to the production of altered penicillin-binding proteins (PBP). The resistance is often plasmid-mediated.
Cross-resistance arises within the beta-lactam group (penicillins and cephalosporins).

Resistance development
Penicillin-resistant pneumococci are resistant to ampicillin. These strains of pneumococci are rare in Sweden but common in certain parts of Europe.

Resistance rates vary geographically and information on the local situation should be obtained from the relevant microbiological laboratory.

Susceptibility testing breakpoints
MIC (minimum inhibitory concentration) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for ampicillin and are listed here: https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

5.2 Pharmacokinetic properties

Following administration of Doktacillin 2 g as an intermittent infusion, a peak serum concentration of approx. 100 microgram/ml is reached. After 4 hours, serum concentration falls to approx. 4 microgram/ml. The biological half-life in serum is approximately 55–60 minutes. Ampicillin penetrates the blood-CSF barrier more readily in meningitis than in the presence of intact meninges. On average, the CSF concentration reaches 10–35% of the concentration in serum.

5.3 Preclinical safety data

There are no preclinical data considered relevant to clinical safety beyond data included in other sections of the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Doktacillin powder for solution for injection/infusion contains no excipients.

6.2 Incompatibilities

In the absence of compatibility studies, penicillin solutions should not be mixed with other medicinal products.

6.3 Shelf life

3 years.
Injectable solutions should be used immediately after reconstitution. Freshly prepared solutions may have a yellowish colour. Solutions intended for infusion should be added to the infusion immediately.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

Vial 10 x 1 g or 10 x 2 g

6.6 Special precautions for disposal and other handling

1 g Doktacillin contains 3 mmol Na^+, which is equivalent to approx. 20 ml isotonic sodium chloride solution.

The osmolarity of the final solution is dependent on the amount of Doktacillin used and which solvent is used for dilution. Depending on the amount of Doktacillin to be administered, water for injections *or* sodium chloride solution is recommended for dilution (see table below).

Type of solution	*Instructions for reconstitution*
Solution for intramuscular injection	1 g should be dissolved in 4 ml water for injections.
Solution for intravenous injection	1 g should be dissolved in 10 ml water for injections, 2 g should be dissolved in 20 ml water for injections.
Solution for intermittent infusion	1 g should be dissolved in 100 ml isotonic sodium chloride solution, 2 g should be dissolved in 100 ml water for injections or isotonic sodium chloride solution. Preferably, the solution obtained should be administered through a multi-way stopcock. The solution should be infused over 20–30 minutes. Mini-Set: The solution should be prepared in a Mini-bag plastic container with the help of a transfer adapter.
Solution for continuous infusion	2 g should be dissolved in 15 ml water for injections The obtained solution should be mixed with an appropriate infusion solution: Isotonic sodium chloride solution, Ringer's acetate, glucose solution 50 mg/ml with sodium and potassium, Rehydrex with glucose.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31 March 1964
Date of the last renewal: 01 January 2007

10. DATE OF REVISION OF THE TEXT

2024-09-30