

 **17 January 2025**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**for**

**Rotacin, powder for solution for injection-/infusion**

**0. D.SP.NO.**

33451

**1. NAME OF THE MEDICINAL PRODUCT**

Rotacin

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Rotacin 500 mg powder for solution for injection/infusion

Each vial contains ampicillin sodium equivalent to 500 mg ampicillin.

Rotacin 1 g powder for solution for injection/infusion

Each vial contains ampicillin sodium equivalent to 1 g ampicillin.

Rotacin 2 g powder for solution for injection/infusion

Each vial contains ampicillin sodium equivalent to 2 g ampicillin.

Excipient with known effect: Sodium.

Rotacin 500 mg contains approximately 35 mg of sodium.

Rotacin 1 g contains approximately 70 mg of sodium.

Rotacin 2 g contains approximately 140 mg of sodium.

For the full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**

Powder for solution for injection/infusion.

White or almost white powder.

**4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications**

Rotacin is indicated for the treatment of the following infections in adults and children (see section 5.1):

* Acute exacerbation of chronic bronchitis
* Pyelonephritis
* Bacterial meningitis
* Community-acquired pneumonia when penicillin G has not given the desired effect or is unsuitable for other reasons
* Intra-abdominal infections
* Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above
* Treatment and prophylaxis of endocarditis.

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

**4.2 Posology and method of administration**

**Posology**

Adults

*Intramuscular*: 500 mg 4 times daily.

*Intravenous injection*: 500 mg to 2 g 4-6 times daily. Inject slowly 2 g for at least 3-4 minutes.

*Continuous intravenous infusion*: 6 to 12 g per day. Infusion pump should be used if possible.

*Intravenous intermittent infusion*: 2 g 4-6 times daily.

For prophylaxis of endocarditis, 2 g may be administered intravenously as a single dose 30 to 60 minutes before procedure.

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

Children

Intramuscular: 50 mg/kg body weight daily. The daily dose should be divided into four doses at 6 hour intervals.

For newborn and premature 25-50 mg/kg divided into two doses is recommended.

Intravenously: 100-200 mg/kg body weight daily in severe infection. In bacterial meningitis the intravenous dose for children may be increased to 400 mg / kg body weight daily (divided into four doses) if needed.

For prophylaxis of endocarditis in children, 50 mg/kg may be administered intravenously as a single dose 30 to 60 minutes before procedure.

Treatment control

For prolonged treatment (over 2-3 weeks) liver and kidney function and blood counts should be monitored.

In case of acute meningitis caused by *Listeria monocytogenes* and in neonatal septicemia, ampicillin is given in combination with another antibiotic.

In intraabdominal infections, ampicillin should be used in combination with other appropriate antibacterial agents when anaerobic pathogens and/or Gram-negative pathogens are known or suspected to be contributing to the infectious process.

Special populations

*Renal impairment*

No dose adjustment is required in patients with creatinine clearance (CrCI) >30 ml/min.

In case of severe renal impairment with 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 2/3,
* at a creatinine clearance below 20 ml/min, the normal dose should be reduced to 1/3.

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

**Method of administration**

Rotacin 500 mg, 1 g: For intramuscular or intravenous use after reconstitution.

Rotacin 2 g: For intravenous use after reconstitution.

Only freshly prepared, clear solutions prepared immediately before use should be used. Care must be taken to ensure complete dissolution. Reconstituted solutions are clear and slightly yellow.

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

**4.3 Contraindications**

Hypersensitivity to the active substance or to other beta-lactam antibiotics (e.g. penicillins, cephalosporins).

**4.4 Special warnings and precautions for use**

Cross allergy between penicillins and cephalosporins occurs.

High urine concentrations can give false positive reaction in some glucose tests.

Diarrhoea may be symptoms of pseudomembranous colitis caused by *Clostridioides difficile*. Therefore, patients with diarrhea should be followed closely.

Rotacin contains sodium.

Rotacin 500 mg contains 35 mg sodium per vial, equivalent to 1.75 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Rotacin 1 g contains 70 mg sodium per vial, equivalent to 3.5 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Rotacin 2 g contains 140 mg sodium per vial, equivalent to 7 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This should be particularly taken into account for those on a low salt diet.

If the product is dissolved or diluted with isotonic sodium chloride solution, the additional amount of sodium from the solvent should also be considered.

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

The following combinations with ampicillin may require dose adjustment: Allopurinol and methotrexate.

Allopurinol

Coadministration of allopurinol with ampicillin increases the risk of allergic skin reaction.

Methotrexate

Severe toxic reaction to methotrexate has been described in one patient who was treated concomitantly with furosemide and penicillin V. These organic acids may inhibit the tubular secretion of methotrexate.

This possible interaction has also been described following the combination of methotrexate and mezlocillin and methotrexate and amoxicillin.

**4.6 Fertility, pregnancy and lactation**

Pregnancy

Long clinical experience indicates a low risk of adverse reactions on pregnancy, the foetus or new-born 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

Ampicillin is excreted in human milk in small amounts at therapeutic doses (1μg/ml after injection of 2-4 g of ampicillin). Breast fed infants may therefore suffer hypersensitivity reactions, diarrhoea or mucosal yeast colonisation, which in some cases may necessitate the discontinuation of breastfeeding.

Fertility

In animal studies, ampicillin had no effect on fertility.

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

No traffic warning.

Rotacin has no or negligible effect on the ability to drive and use machines.

**4.8 Undesirable effects**

Adverse reactions are classified as follows: 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).

The most common is rash that occurs in about 5 % of treated patients.

| *System organ class* | *Frequency* | *Adverse reactions* |
| --- | --- | --- |
| Infections and infestations | Uncommon | pseudomembranous colitis |
| Blood and lymphatic system disorders | Uncommon | anemia, thrombocytopenia, eosinophilia, leukopenia and agranulocytosis |
| Immune system disorders | Rare | anaphylactic reaction |
| Gastrointestinal disorders | Common | loose stools |
| Uncommon | glossitis, stomatitis, nausea, vomiting, enterocolitis, diarrhea |
| Skin and subcutaneous tissue disorders | Common | exanthema |
| Uncommon | urticaria |
| Rare | exfoliative dermatitis and erythema multiformae |

Local pain may occur during intramuscular injection.

In the case of mononucleosis infection, the occurrence of exanthema is high. There is also an increased incidence of exanthema observed in leukemia.

An increased frequency of rash has also been observed in leukemia.

Elevated AST values have been shown to occur due to local release at the injection site and does not necessarily indicate liver involvement.

For treatment of anaphylactic reaction, see section 4.9.

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:

Lægemiddelstyrelsen

Axel Heides Gade 1

DK-2300 København S

Website: www.meldenbivirkning.dk

**4.9 Overdose**

*Toxicity*: Large doses are usually well tolerated. However, for example, impaired renal function and impaired cerebrospinal fluid barrier, high-dose parenteral administration has produced toxic symptoms. Acute reactions are mainly due to allergic reactions.

*Symptoms*: Toxic reactions; nausea, vomiting, diarrhea, electrolyte disturbances, lowering of consciousness, muscle fasciculations, myoclones, cramps, coma. Hemolytic reactions, kidney disturbances, acidosis.

In exceptional cases, anaphylactic reaction may occur within 20-40 minutes.

*Treatment*: Symptomatic treatment. In severe cases, hemoperfusion or hemodialysis.

In anaphylactic reaction: Epinephrine (adrenaline) 0.1-0.5 mg slowly intravenously. Hydrocortisone 200 mg intravenously, optionally prometazine 25 mg intravenously. Liquid. Acid correction.

**4.10 Legal status**

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**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Antibacterials for systemic use; beta-lactam antibacterials, penicillins; Penicillins with extended spectrum, ATC code: J01CA01.

Mechanism of action

Ampicillin is a penicillin with an extended antibacterial spectrum. Ampicillin inhibits the cell wall synthesis of bacteria. The effect is bactericidal.

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

| *Microorganism* | *MIC breakpoint (mg/L)* |
| --- | --- |
| *Susceptible* | *Resistant* |
| Enterobacterales | ≤8 | >8 |
| *Enterococcus* spp. | ≤4 | >8 |
| *Haemophilus influenzae*1,4 | ≤1 | >1 |
| *Staphylococcus* spp.2 | - | - |
| *Streptococcus* A, B, C, G3*Streptococcus pneumoniae*1*Streptococcus pneumoniae*5 | -≤0.5≤0.5 | ->1>0.5 |
| Viridans group streptococci | ≤0.5 | >2 |
| *Neisseria meningitidis*1 | ≤0.125 | >1 |
| Listeria monocytogenes | ≤1 | >1 |
| *Aerococcus sanguinicola* and *urinae* | ≤0.25 | >0.25 |
| Non-species related breakpoints6 | ≤2 | >8 |
| 1 For indications other than meningitis.2 Most staphylococci are penicillinase producers and some are methicillin resistant. Either mechanism renders staphylococci resistant to ampicillin. Isolates resistant to benzylpenicillin or cefoxitin are resistant to ampicillin. Benzylpenicillin susceptible Staphylococcus spp. are also susceptible to ampicillin.3 Susceptibility is inferred from benzylpenicillin.4 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.5 For the meningitis indication only.6 The non-species related breakpoints are based on doses of at least 2 g×3 or 4 times daily (6 to 8 g/day). |

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.

Antibacterial spectrum

|  |  |
| --- | --- |
| *Sensitive* | PneumococciStreptococciEnterococci*Listeria monocytogenes*Meningococci*Haemophilus influenzae**Proteus mirabilis*Anaerobic streptococcal and peptostreptococcal strains |
| *Intermediate* | *Escherichia coli* and *Acinetobacter* |
| *Resistant* | *Staphylococci**Moraxella catarrhalis*Beta lactamase-producing *Haemophilus influenzae**Citrobacter**Klebsiella**Enterobacter**Morganella morganii**Proteus vulgaris**Providencia**Serratia**Pseudomonas**Legionella**Clostridioides difficile**Bacteroides fragilis**Mycoplasma* spp.*Chlamydia* |

Resistance occurs (1-10 %) in pneumococci and *Enterococcus faecalis*.

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

Mechanisms of resistance

Resistance may be due to bacterial synthesis of a large number of beta-lactamase hydrolyzes the penicillin. Several of these can be inhibited with clavulanic acid. In addition, resistance may occur due to production of altered pencillin binding proteins (PBPs). Resistance is often plasmid mediated.

Cross resistance occurs within the beta-lactam group (penicillins and cephalosporins).

Development of resistance

Penicillin-resistant pneumococci are resistant to ampicillin. These are unusual rare in Sweden but common in some parts of Europe.

The bacterial resistance varies geographically and information on the local resistance conditions should be obtained from the local microbiological laboratory.

**5.2 Pharmacokinetic properties**

When 2 g of ampicillin is given as an intermittent infusion, a maximum serum concentration of about 100 micrograms/ml is achieved, after about 4 hours about 4 micrograms/ml. The biological half-life in serum is 55-60 minutes. Ampicillin penetrates the blood cerebrospinal fluid barrier better in meningitis. On average concentration is 10-35 % of the serum concentration.

**5.3 Preclinical safety data**

There are no preclinical data of relevance to the safety assessment beyond what has already been taken into account in the SPC.

**6. PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

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**6.2 Incompatibilities**

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

**6.3 Shelf life**

36 months.

After reconstitution the solution should be used immediately after preparation.

**6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

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

**6.5 Nature and contents of container**

Clear glass (type III) vials of nominal capacity 8 ml or 20 ml (only for 2g) sealed with a chlorobutyl rubber stopper and aluminium cap (with or without a plastic grey flip-off seal).

Pack sizes

Boxes of 1, 10, 25, 50 and 100 vials.

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

Only freshly prepared, clear solutions prepared immediately before use should be used. Care must be taken to ensure complete dissolution. Reconstituted solutions are clear and slightly yellow.

For single withdrawal only.

Rotacin 500 mg

*- Solution for i.m. injection:*

The contents of the 500 mg vial are dissolved in 1.8 ml solvent (water for injections).

The solution should be used immediately after reconstitution.

*- solution for i.v. injection:*

Dissolve the contents of the 500 mg vial in 5 ml solvent (water for injections).

Chemical and physical in-use stability has been demonstrated for 0.5 hour at 25 °C.

*- solution for i.v. Infusion:*

Dissolve the contents of the 500 mg vial in 5 ml solvent (water for injections). The finished solution can be diluted with the infusion fluids mentioned below with the desired volume to achieve the final concentration also mentioned in the below table.

Rotacin 1 g

*- Solution for i.m. injection:*

The contents of the 1 g vial are dissolved in 3.4 ml solvent (water for injections).

The solution should be used immediately after reconstitution.

*- solution for i.v. injection:*

Dissolve the contents of the 1 g vial in 7.4 ml solvent (water for injections).

Chemical and physical in-use stability has been demonstrated for 0.5 hour at 25 °C.

*- solution for i.v. Infusion:*

Dissolve the contents of the 1 g vial in 7.4 ml solvent (water for injections). The finished solution can be diluted with the infusion fluids mentioned below with the desired volume to achieve the final concentration also mentioned in the below table.

Rotacin 2 g

*- solution for i.v. injection:*

Dissolve the contents of the 2 g vial in 10 ml solvent (water for injections).

The solution should be used immediately after reconstitution.

*- solution for i.v. Infusion:*

Dissolve the contents of the 2 g vial in 10 ml solvent (water for injections). The finished solution can be diluted with the infusion fluids mentioned below with the desired volume to achieve the final concentration also mentioned in the below table.

|  |
| --- |
| **For IV infusion** |
| **Strength** | **Diluent** | **Final concentration** |
| 500 mg, 1 g, 2 g | Sodium chloride 0.9 % | 30 mg/ml |
| 500 mg, 1 g, 2 g | M/6 Sodium lactate | 30 mg/ml |
| 500 mg, 1 g, 2 g | Ringer’s Lactate | 30 mg/ml |

Chemical and physical in-use stability has been demonstrated for 1 hour at 15-30°C.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

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

**7. MARKETING AUTHORISATION HOLDER**

Adelco Chromatourgia Athinon E. Colocotronis Bros S.A.

Moschato

Pireos Avenue 37

183 46 Athens, Attiki

Grækenland

**8. MARKETING AUTHORISATION NUMBER(S)**

500 mg: 69533

1 g: 69536

2 g: 69537

**9. DATE OF FIRST AUTHORISATION**

17 January 2025

**10. DATE OF REVISION OF THE TEXT**

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