OXACILLIN- oxacillin sodium injection, powder, for solution
Renaissance SSA, LLC

Oxacillin for Injection 1 and 2 gram

OXACILLIN for Injection, USP

For Intramuscular or Intravenous Injection

To reduce the development of drug-resistant bacteria and maintain the effectiveness of oxacillin for injection and other antibacterial drugs, oxacillin for injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION

Oxacillin for Injection, USP is a semisynthetic penicillin antibiotic derived from the penicillin nucleus, 6-amino-penicillanic acid. It is resistant to inactivation by the enzyme penicillinase (beta-lactamase). It is the sodium salt in a parenteral dosage form for intramuscular or intravenous use.

Each vial of oxacillin for injection, USP contains oxacillin sodium equivalent to 1 gram or 2 grams of oxacillin. The sodium content is 64.4 mg (2.8 mEq) per gram of oxacillin. The product is buffered with 22 mg dibasic sodium phosphate per gram of oxacillin. Oxacillin for injection, USP is white to off white powder and gives a clear solution upon reconstitution.

OXACILLIN SODIUM

The chemical name of oxacillin sodium is 4-Thia-1-azabicyclo [3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-6-[(5-methyl-3-phenyl-4isoxazolyl) carbonyl] amino]-7-oxo-monosodium salt, monohydrate, [2S(2α,5α,6β)]. It is resistant to inactivation by the enzyme penicillinase (beta-lactamase). The molecular formula of oxacillin sodium is C_{19}H_{18}N_{4}NaO_{4}S•H_{2}O. The molecular weight is 441.44.

CLINICAL PHARMACOLOGY

Intravenous administration provides peak serum levels approximately 5 minutes after the injection is completed. Slow IV administration of 500 mg gives a peak serum level of 43 mcg/mL after 5 minutes with a half-life of 20-30 minutes.

Oxacillin sodium, with normal doses, has insignificant concentrations in the cerebrospinal and ascitic fluids. It is found in therapeutic concentrations in the pleural, bile, and amniotic fluids.

Oxacillin sodium is rapidly excreted as unchanged drug in the urine by glomerular filtration and active tubular secretion. The elimination half-life for oxacillin is about 0.5 hours. Nonrenal elimination includes hepatic inactivation and excretion in bile.

Oxacillin sodium binds to serum protein, mainly albumin. The degree of protein binding reported varies with the method of study and the investigator, but generally has been found to be 94.2% ± 2.1%.

Probenecid blocks the renal tubular secretion of penicillins. Therefore, the concurrent administration of probenecid prolongs the elimination of oxacillin and, consequently, increases the serum concentration.

Intramuscular injections give peak serum levels 30 minutes after injection. A 250 mg dose gives a level of 5.3 mcg/mL, while a 500 mg dose peaks at 10.9 mcg/mL. Intravenous injection gives a peak about 5 minutes after the injection is completed. Slow IV dosing with 500 mg gives a 5 minute peak of 43 mcg/mL with a half-life of 20 to 30 minutes.

Microbiology

Mode of Action

Penicillinase-resistant penicillins exert a bactericidal action against penicillin susceptible microorganisms during the state of active multiplication. All penicillins inhibit the biosynthesis of the bacterial cell wall.

Mechanism of Resistance

Resistance to penicillins may be mediated by destruction of the beta-lactam ring by a beta-lactamase, altered affinity of penicillin for target, or decreased penetration of the antibiotic to reach the target site.

Cross-Resistance

Resistance to oxacillin (or cefoxitin) implies resistance to all other beta-lactam agents, except newer agents with activity against methicillin-resistant Staphylococcus aureus.

Susceptibility Testing

For specific information regarding susceptibility test interpretive criteria and associated test methods and quality control standards recognized by FDA for this drug, please see: https://www.fda.gov/STIC.

INDICATIONS AND USAGE

Oxacillin is indicated in the treatment of infections caused by penicillinase producing staphylococci which have demonstrated susceptibility to the drug. Cultures and susceptibility tests should be performed initially to determine the causative organism and its susceptibility to the drug. (See CLINICAL PHARMACOLOGY: Susceptibility Testing)
Oxacillin may be used to initiate therapy in suspected cases of resistant staphylococcal infections prior to the availability of susceptibility test results. Oxacillin should not be used in infections caused by an organism susceptible to penicillin G. If the susceptibility tests indicate that the infection is due to an organism other than a resistant Staphylococcus, therapy should not be continued with oxacillin.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Oxacillin for Injection, USP and other antibacterial drugs, Oxacillin for Injection, USP should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

CONTRAINDICATIONS
A history of a hypersensitivity (anaphylactic) reaction to any penicillin is a contraindication.

WARNINGS
Serious and occasionally fatal hypersensitivity (anaphylactic shock with collapse) reactions have occurred in patients receiving penicillin. The incidence of anaphylactic shock in all penicillin-treated patients is between 0.015 and 0.04 percent. Anaphylactic shock resulting in death has occurred in approximately 0.002 percent of the patients treated.

When oxacillin therapy is initiated, it should be initiated only after a comprehensive patient drug and allergy history has been obtained. If an allergic reaction occurs, oxacillin should be discontinued and appropriate therapy instituted.

\textit{Clostridium difficile} associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including oxacillin for injection, USP, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of \textit{C. difficile}.

\textit{C. difficile} produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of \textit{C. difficile} cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against \textit{C. difficile} may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of \textit{C. difficile}, and surgical evaluation should be instituted as clinically indicated.

PRECAUTIONS

General
Oxacillin should generally not be administered to patients with a history of sensitivity to any penicillin. Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma. Whenever allergic reactions occur, penicillin should be withdrawn unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. The use of antibiotics may result in overgrowth of non-susceptible organisms. If new infections due to bacteria or fungi occur, the drug should be discontinued and appropriate measures taken.

Prescribing Oxacillin for Injection, USP in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Laboratory Tests
Bacteriologic studies to determine the causative organism and their susceptibility to oxacillin should be performed (see CLINICAL PHARMACOLOGY-Microbiology). In the treatment of suspected staphylococcal infections, therapy should be changed to another active agent if culture tests fail to demonstrate the presence of staphylococci.

Periodic assessment of organ system function including renal, hepatic, and hematopoietic should be made during prolonged therapy with oxacillin.

Blood cultures, white blood cell, and differential cell counts should be obtained prior to initiation of therapy and at least weekly during therapy with oxacillin.

Periodic urinalysis, blood urea nitrogen, and creatinine determinations should be performed during therapy with oxacillin and dosage alterations should be considered if these values become elevated. If any impairment of renal function is suspected or known to exist, a reduction in the total dosage should be considered and blood levels monitored to avoid possible neurotoxic reactions. AST (SGOT) and ALT (SGPT) values should be obtained periodically during therapy to monitor for possible liver function abnormalities.

Drug Interactions
Tetracycline, a bacteriostatic antibiotic, may antagonize the bactericidal effect of penicillin and concurrent use of these drugs should be avoided.

Oxacillin blood levels may be increased and prolonged by concurrent administration of probenecid which blocks the renal tubular secretion of penicillin. Probenecid decreases the apparent volume of distribution and slows the rate of excretion by competitively inhibiting renal tubular secretion of penicillin.

Oxacillin-probenecid therapy should be limited to those infections where very high serum levels of oxacillin are necessary.

Carcinogenesis, Mutagenesis, Impairment of Fertility
No long-term animal studies have been conducted with these drugs. Studies on reproduction (nafcillin)
in rats and rabbits reveal no fetal or maternal abnormalities before conception and continuously through
weaning (one generation).

Pregnancy
Teratogenic Effects

Pregnancy Category B
Reproduction studies performed in the mouse, rat, and rabbit have revealed no evidence of impaired
fertility or harm to the fetus due to the penicillinase-resistant penicillin. Human experience with the
penicillins during pregnancy has not shown any positive evidence of adverse effects on the fetus. There
are, however, no adequate or well-controlled studies in pregnant women showing conclusively that
harmful effects of these drugs on the fetus can be excluded. Because animal reproduction studies are
not always predictive of human response, this drug should be used during pregnancy only if clearly
needed.

Nursing Mothers
Penicillins are excreted in human milk. Caution should be exercised when penicillins are administered to
a nursing woman.

Pediatric Use
Because of incompletely developed renal function in pediatric patients, oxacillin may not be completely
excreted, with abnormally high blood levels resulting. Frequent blood levels are advisable in this group
with dosage adjustments when necessary. All pediatric patients treated with penicillins should be
monitored closely for clinical and laboratory evidence of toxic or adverse effects. Safety and
effectiveness in pediatric patients have not been established.

Geriatric Use
Clinical studies of oxacillin for injection did not include sufficient number of subjects aged 65 and over
to determine whether they respond differently from younger subjects. Other reported clinical
experience has not identified differences in responses between the elderly and younger patients. In
general, dose selection for an elderly patient should be cautious, usually starting at the low end of the
dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of
concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug
may be greater in patients with impaired renal function. Because elderly patients are more likely to have
decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal
function.

Oxacillin for Injection contains 64.4 mg (2.8 mEq) of sodium per gram of oxacillin. At the usual
recommended doses, patients would receive between 64.4 and 386.4 mg/day (2.8 and 16.8 mEq) of
sodium. The geriatric population may respond with a blunted natriuresis to salt loading. This may be
clinically important with regard to such diseases as congestive heart failure.

Information for Patients
Patients should be counseled that antibacterial drugs including Oxacillin for Injection, USP should only
be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When
Oxacillin for Injection, USP is prescribed to treat a bacterial infection, patients should be told that
although it is common to feel better early in the course of therapy, the medication should be taken
exactly as directed. Skipping doses or not completing the full course of therapy may: (1) decrease the
effectiveness of the immediate treatment, and (2) increase the likelihood bacteria will develop
resistance and will not be treatable by Oxacillin for Injection or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is
discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody
stools (with or without stomach cramps and fever) even as late as two or more months after having taken
the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

ADVERSE REACTIONS

Body as a Whole
The reported incidence of allergic reactions to penicillin ranges from 0.7 to 10 percent (see
WARNINGS). Sensitization is usually the result of treatment but some individuals have had immediate
reactions to penicillin when first treated. In such cases, it is thought that the patients may have had prior
exposure to the drug via trace amounts present in milk and vaccines.

Two types of allergic reactions to penicillins are noted clinically, immediate and delayed.
Immediate reactions usually occur within 20 minutes of administration and range in severity from
urticaria and pruritus to angioedematous edema, laryngospasm, bronchospasm, hypotension, vascular
collapse, and death. Such immediate anaphylactic reactions are very rare (see WARNINGS) and usually
occur after parenteral therapy but have occurred in patients receiving oral therapy. Another type of
immediate reaction, an accelerated reaction, may occur between 20 minutes and 48 hours after
administration and may include urticaria, pruritus, and fever. Although laryngeal edema, laryngospasm,
and hypotension occasionally occur, fatalities is uncommon.

Delayed allergic reactions to penicillin therapy usually occur after 48 hours and sometimes as late as 2
to 4 weeks after initiation of therapy.
Manifestations of this type of reaction include serum sickness-like symptoms (i.e., fever, malaise,
urticaria, myalgia, arthralgia, abdominal pain) and various skin rashes. Nausea, vomiting, diarrhea,
 stomatitis, black or hairy tongue, and other symptoms of gastrointestinal irritation may occur, especially
during oral penicillin therapy.

Nervous System Reactions
Neurotoxic reactions similar to those observed with penicillin G may occur with large intravenous
doses of oxacillin, especially in patients with renal insufficiency.
Urogenital Reactions
Renal tubular damage and interstitial nephritis have been associated infrequently with the administration of oxacillin. Manifestations of this reaction may include rash, fever, eosinophilia, hematuria, proteinuria, and renal insufficiency. Nephropathy induced by penicillins does not appear to be dose-related and is generally reversible upon prompt discontinuation of therapy.

Gastrointestinal Reactions
Pseudomembranous colitis has been reported with the use of oxacillin. The onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).

Metabolic Reactions
Agranulocytosis, neutropenia, and bone marrow depression have been associated with the use of oxacillin. Hepatotoxicity, characterized by fever, nausea, and vomiting associated with abnormal liver function tests, mainly elevated SGOT levels, has been associated with the use of oxacillin.

To report SUSPECTED ADVERSE REACTIONS, contact Renaissance SSA, LLC at 1-855-273-0153 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE
The signs and symptoms of oxacillin overdosage are those described in the ADVERSE REACTIONS section. If signs or symptoms occur, discontinue use of the medication, treat symptomatically, and institute appropriate supportive measures.

DOSAGE AND ADMINISTRATION
Bacteriologic studies to determine the causative organisms and their susceptibility to oxacillin should always be performed. Duration of therapy varies with the type and severity of infection as well as the overall condition of the patient, therefore it should be determined by the clinical and bacteriological response of the patient. In severe staphylococcal infections, therapy with oxacillin should be continued for at least 14 days. Therapy should be continued for at least 48 hours after the patient has become afebrile, asymptomatic, and cultures are negative. The treatment of endocarditis and osteomyelitis may require a longer term of therapy.

With intravenous administration, particularly in elderly patients, care should be taken because of the possibility of thrombophlebitis.

RECOMMENDED DOSAGES FOR OXACILLIN FOR INJECTION, USP

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adults</th>
<th>Infants and Children ≤40 kg (88 lbs)</th>
<th>Other Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxacillin</td>
<td>250 to 500 mg IM or IV every 4 to 6 hours (mild to moderate infections)</td>
<td>50 mg/kg/day IM or IV in equally divided doses every 6 hours (mild to moderate infections)</td>
<td>1 gram IM or IV every 4 to 6 hours (severe infections) 100 mg/kg/day IM or IV in equally divided doses every 4 to 6 hours (severe infections) Premature and Neonates 25 mg/kg/day IM or IV</td>
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</tbody>
</table>

Directions for use
For Intramuscular Use: Use Sterile Water for Injection, USP. Add 5.4 mL to the 1 gram vial, 10.6 mL to the 2 gram vial. Shake well until a clear solution is obtained. After reconstitution, vials will contain 250 mg of active drug per 1.5 mL of solution. The reconstituted solution is stable for 3 days at 70° F or for one week under refrigeration (40° F).

For Direct Intravenous Use: Use Sterile Water for Injection, USP or Sodium Chloride Injection, USP. Add 10 mL to the 1 gram vial, 20 mL to the 2 gram vial. Withdraw the entire contents and administer slowly over a period of approximately 10 minutes.

For Administration by Intravenous Drip: Reconstitute as directed above (For Direct Intravenous Use) prior to diluting with Intravenous Solution.

STABILITY PERIODS FOR OXACILLIN FOR INJECTION, USP
Stability studies on oxacillin sodium at concentrations of 0.5 mg/mL and 2 mg/mL in various intravenous solutions listed below indicate the drug will lose less than 10% activity at room temperature (70° F) during a 6-hour period.

<table>
<thead>
<tr>
<th>IV Solution</th>
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<tbody>
<tr>
<td>5% Dextrose in Normal Saline</td>
</tr>
<tr>
<td>10% D-Fructose in Water</td>
</tr>
<tr>
<td>10% D-Fructose in Normal Saline</td>
</tr>
<tr>
<td>Lactated Potassic Saline Injection</td>
</tr>
<tr>
<td>10% Invert Sugar in Normal Saline</td>
</tr>
<tr>
<td>10% Invert Sugar Plus 0.3% Potassium Chloride in Water</td>
</tr>
<tr>
<td>Travert 10% Electrolyte #1</td>
</tr>
<tr>
<td>Travert 10% Electrolyte #2</td>
</tr>
<tr>
<td>Travert 10% Electrolyte #3</td>
</tr>
</tbody>
</table>

Only those solutions listed above should be used for the intravenous infusion of oxacillin sodium. The concentration of the antibiotic should fall within the range specified. The drug concentration and the rate and volume of the infusion should be adjusted so that the total dose of oxacillin is administered before the drug loses its stability in the solution in use.

If another agent is used in conjunction with oxacillin therapy, it should not be physically mixed with oxacillin but should be administered separately.

**HOW SUPPLIED**

Oxacillin for Injection, USP contains oxacillin sodium equivalent to 1 gram or 2 grams oxacillin per vial.

NDC 70655-099-95 1 gram vial packaged in 10s
NDC 70655-109-95 2 grams vial packaged in 10s

Store the dry powder at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature].

Manufactured for:
Renaissance SSA, LLC
Newtown, PA 18940

Manufactured by:
Haupt Pharma Latina S.r.l.
Latina, Italy

Rev.11/18

**PRINCIPAL DISPLAY PANEL**

NDC 70655-099-95
Oxacillin for injection, USP
Rx Only
1 Gram
10 x 1 gram vials
**Product Information**

**Product Type**: HUMAN PRESCRIPTION DRUG  
**Item Code (Source)**: NDC:70655-099

**Route of Administration**: INTRAMUSCULAR, INTRAVENOUS

**Active Ingredient/Active Moiety**

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<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
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<tr>
<td>OXACILLIN SODIUM (UNII: G0V6C994Q5) (OXACILLIN - UNII:UH95VD7V76)</td>
<td>OXACILLIN</td>
<td>1 g in 1 g</td>
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**Inactive Ingredients**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
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<tbody>
<tr>
<td>SODIUM PHOSPHATE, DIBASIC (UNII: GB6BHAB7A7)</td>
<td>22 mg in 1 g</td>
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**Packaging**

<table>
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<th>Marketing End Date</th>
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<tr>
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**Marketing Information**

**Marketing Category**: ANDA  
**Application Number or Monograph Citation**: ANDA206681  
**Marketing Start Date**: 06/01/2018  
**Marketing End Date**: 06/01/2018

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**OXACILLIN**

oxacillin sodium injection, powder, for solution

**Product Information**

**Product Type**: HUMAN PRESCRIPTION DRUG  
**Item Code (Source)**: NDC:70655-109

**Route of Administration**: INTRAMUSCULAR, INTRAVENOUS

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**OXACILLIN**

oxacillin sodium injection, powder, for solution

**Product Information**

**Product Type**: HUMAN PRESCRIPTION DRUG  
**Item Code (Source)**: NDC:70655-109

**Route of Administration**: INTRAMUSCULAR, INTRAVENOUS
### Active Ingredient/Active Moiety

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<tr>
<td>OXACILLIN SODIUM (UNII: G0V6C994Q5) (OXACILLIN - UNII:UH95VD7V76)</td>
<td>OXACILLIN</td>
<td>2 g in 2 g</td>
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### Inactive Ingredients

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<th>Strength</th>
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<tbody>
<tr>
<td>SODIUM PHOSPHATE, DIBASIC (UNII: G86861BA74)</td>
<td>44 mg in 2 g</td>
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**Labeler** - Renaissance SSA, LLC (079777043)

Revised: 4/2019