

# הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך \_\_\_\_\_ September 2, 2012 \_\_\_\_\_

שם תכשיר באנגלית: **PENICILLIN G SODIUM 5 MU, 10 MU**

מספר רישום: **5 MU: 024 73 21066 00, 10 MU: 025 45 21065 00**

שם בעל הרישום: **Salomon, Levin, & Elstein Ltd., P.O.Box 3696, Petach-Tikva**

## פרטים על השינויים המבוקשים

טקסט חדש	טקסט נוכחי	פרק בעלון
<p>Therefore, before initiating therapy with this drug, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens, because of the risk of anaphylactoid reactions (asthma, purpura, gastrointestinal symptoms) (1). Patients should be observed for 30 minutes after medicine administration and adrenaline or epinephrine should be made immediately available for injection (1). If an allergic reaction occurs, the drug should be discontinued and appropriate therapy instituted.</p> <p>Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management including intubation, should also be administered as indicated.</p> <p>If high-dose penicillin treatment is continued for more than 5 days, electrolyte balance, blood counts and renal function should be monitored (1).</p> <p>In patients receiving very high intravenous doses (more than 10 million IU daily) injection sites should be alternated every 2 days to prevent superinfections and thrombophlebitis (1).</p> <p><i>Pseudomembranous colitis/Clostridium difficile-associated diarrhea (CDAD) (2)</i> has been reported with nearly all antibacterial agents, including Penicillin G, and may range in severity from mild to life-threatening. <i>C. difficile</i> produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of <i>C difficile</i> 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. (2). Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.</p> <p><i>Use in Breastfeeding</i></p> <p>Since penicillins are excreted in breast milk, administration of this drug to nursing mothers may lead to sensitization, diarrhea, candidiasis and skin rash in infants.</p> <p>Residual benzylpenicillin may be present in breast milk at levels corresponding to approximately 0.8% of the maternal dose (1)</p>	<p>Therefore, before initiating therapy with this drug, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens, because of the risk of anaphylactoid reactions If an allergic reaction occurs, the drug should be discontinued and appropriate therapy instituted.</p> <p>Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids, and airway management including intubation, should also be administered as indicated.</p> <p><i>Pseudomembranous colitis</i> has been reported with nearly all antibacterial agents, including Penicillin G, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.</p> <p><i>Use in Breastfeeding</i></p> <p>Since penicillins are excreted in breast milk, administration of this drug to nursing mothers may lead to sensitization, diarrhea, candidiasis and skin rash in infants.</p> <p>Therefore, taking into account the importance of the drug to the mother, either discontinue nursing, or discontinue the drug.</p>	<p style="text-align: center;"><b>Warnings</b></p>

<p>Therefore, taking into account the importance of the drug to the mother, either discontinue nursing, or discontinue the drug.</p> <p><i>Use in <b>Pediatrics Infants</b></i></p> <p>Penicillins are excreted largely unchanged by the kidney. Because renal function is incompletely developed in infants, the rate of elimination of the drug tends to be slow. Penicillin-type drugs should therefore be administered with caution, <b>appropriate reductions in the dosage and frequency of administration should be made in these patients (2)</b>, particularly in neonates, and organ system function should be evaluated frequently.</p> <p><b>As infants have been found to develop severe local reactions to intramuscular injections, treatment should preferably be intravenous (1)</b></p> <p><i>Use in <b>Geriatrics (2)</b></i></p> <p>Clinical studies of Penicillin G Injection did not include sufficient numbers 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.</p> <p>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.</p>	<p><i>Use in <b>Infants</b></i></p> <p>Penicillins are excreted largely unchanged by the kidney. Because renal function is incompletely developed in infants, the rate of elimination of the drug tends to be slow. Penicillin-type drugs should therefore be administered with caution, particularly in neonates, and organ system function should be evaluated frequently.</p>	
<p><i><b>Other Precautions (1)</b></i></p> <p>Particular caution should be exercised when treating patients with an allergic diathesis such as urticaria or hay fever or with bronchial asthma.</p> <p>Caution is also necessary when treating newborns, patients with severe cardiopathies and other serious heart disease, hypovolaemia, epilepsy and renal or hepatic damage.</p> <p>Caution is required when treating concurrent infections in patients presenting mononucleosis and acute lymphatic leukaemia due to the increased risk of skin reactions.</p>		<p><b>Precautions</b></p>
<p>Cross allergenicity to cephalosporins, with a reported incidence, of 5 to 10%, is possible, and should be considered when treating patients known to be hypersensitive to these medicines. (1)</p>		<p><b>Contraindications</b></p>
<p>The reported incidence of allergic reactions to all penicillins ranges from 0.7 to 10% percent in different studies. Sensitization is usually the result of previous treatment with a penicillin, but some individuals have had immediate reactions when first treated. In such cases, it is postulated that prior exposure to penicillin may have occurred via trace amounts present in milk or vaccines (2).</p> <p>Immediate reactions usually occur within 20 minutes of administration and range in severity from urticaria and pruritus to angioneurotic edema, laryngospasm, bronchospasm, hypotension, vascular</p>	<p>Immediate reactions usually occur within 20 minutes of administration and range in severity from urticaria and pruritus to angioneurotic edema, laryngospasm, bronchospasm, hypotension, vascular collapse and death (see Warnings). Such immediate anaphylactic reactions are very rare and usually occur after parenteral therapy, but a few cases of anaphylaxis have been reported following oral therapy. Another type of immediate reaction, an accelerated reaction, may occur between 20 minutes and 45 hours after administration and may include urticaria, pruritus, fever and, occasionally, laryngeal edema.</p>	<p><b>Adverse events</b></p>

collapse and death (see Warnings). Such immediate anaphylactic reactions are very rare and usually occur after parenteral therapy, but a few cases of anaphylaxis have been reported following oral therapy. Another type of immediate reaction, an accelerated reaction, may occur between 20 minutes and 45 hours after administration and may include urticaria, pruritus, fever and, **angioneurotic edema, erythema multiforme, joint pain (1)** occasionally, laryngeal edema.

*Gastrointestinal system*

Pseudomembranous colitis has been reported with the onset occurring during or after Penicillin G treatment. Nausea, vomiting, stomatitis, **glossitis (1)**, black or hairy tongue, and other symptoms of gastrointestinal irritation may occur, especially during oral therapy.

**If diarrhoea develops during treatment, the possibility of pseudomembranous colitis should be excluded (1)**

*Hematological*

Hematological reactions including hemolytic anemia, granulocytopenia (neutropenia), thrombocytopenia, **pancytopenia (1)**, thrombocytopenic purpura, eosinophilia, leukopenia, and agranulocytosis have been observed in patients receiving prolonged high doses of Penicillin G (e.g. bacterial endocarditis). These are believed to be hypersensitivity phenomena and are usually reversible upon discontinuation of therapy.

***Hepatobiliary disorders (1)***

**Isolated cases**

**Hepatitis, cholestasis**

*Urogenital system*

Renal tubular damage and interstitial nephritis have been associated with large intravenous doses of Penicillin G. Manifestations of this reaction may include fever, rash, eosinophilia, proteinuria, eosinophiluria, hematuria and a rise in serum urea nitrogen. Discontinuation of Penicillin G results in resolution in the majority of patients.

**Oliguria and anuria occur rarely during high-dose penicillin therapy and usually disappear within 48 hours after discontinuing treatment. Diuresis can also be stimulated with 10% mannitol solution (1).**

*Local reactions*

**Rare**

**Severe local reactions on intramuscular administration to infants (1).**

Phlebitis and thrombophlebitis may occur with intravenous administration.

**As penicillins are only active against proliferating micro-organisms, Penicillin G sodium should not be combined with bacteriostatic antibiotics. Combinations with other antibiotics should only be considered if their effects can be expected to be synergistic or at least additive. In general, each component in the combination should be given at the individually effective dose for monotherapy. However for combinations with proven synergistic action, the dose of the more toxic component in the combination may be reduced.)**

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***Penicillins/Other Drugs that compete with Renal Tubular Secretion:*** Other drugs may compete with Penicillin G for renal tubular secretion and thus prolong the serum half-life of penicillin. These drugs include: aspirin/, phenylbutazone, sulfonamides, indomethacin thiazide diuretics, furosemide and ethacrynic acid.

**Drug Interactions**

If indicated, bactericidal antibiotic candidates for combination with Penicillin G sodium include isoxazolyl penicillins such as flucloxacillin and other narrow-spectrum beta-lactam antibiotics, aminopenicillins, aminoglycosides. These should be administered by slow IV injection prior to Penicillin G sodium infusions. Wherever possible, aminoglycosides should be administered separately by IM injection (1).

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**Laboratory Tests (see also Precautions) (2)**  
 Periodic assessment of organ system function, including frequent evaluation of electrolyte balance, hepatic, renal and hematopoietic systems, and cardiac and vascular status should be performed during prolonged therapy with high doses of intravenous penicillin G. If any impairment of function is suspected or known to exist, a reduction in the total dosage should be considered. In suspected staphylococcal infections, proper laboratory studies, including susceptibility tests should be performed. All infections due to Group A beta-hemolytic streptococci should be treated for at least 10 days.  
 Patients being treated for gonococcal infection should have a serologic test for syphilis before receiving penicillin. All cases of penicillin treated syphilis should receive adequate follow

**Laboratory  
Tests**

**Others**

