PRODUCT MONOGRAPH

PProcainamide Hydrochloride Injection USP

100 mg/mL

Antiarrhythmic Agent

Sandoz Canada Inc.
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Boucherville, QC, Canada
J4B 7K8

Date of Revision: 24 July 2014

Control No. 23913
ACTION AND CLINICAL PHARMACOLOGY

Procainamide increases the effective refractory period of the atria, and to a lesser extent the bundle of His-Purkinje system and ventricles of the heart. It reduces impulse conduction velocity in the atria, His-Purkinje fibers, and ventricular muscle, but has variable effects on the atrioventricular node, a direct slowing action and a weaker vagolytic effect which may speed atrioventricular conduction slightly. Myocardial excitability is reduced in the atria, Purkinje fibers, papillary muscles, and ventricles by an increase in the threshold for excitation, combined with inhibition of ectopic pacemaker activity by retardation of the slow phase of diastolic depolarization, thus decreasing automaticity especially in ectopic sites. Contractility of the undamaged heart is usually not affected by therapeutic concentrations, although slight reduction of cardiac output may occur, and may be significant in the presence of myocardial damage. Therapeutic levels of procainamide may exert vagolytic effects and produce slight acceleration of heart rate, while high or toxic concentrations may prolong atrioventricular conduction time or induce atrioventricular block, or even cause abnormal automaticity and spontaneous firing, by unknown mechanisms.

The electrocardiogram may reflect these effects by showing slight sinus tachycardia (due to the anticholinergic action) and widened QRS complexes and, less regularly, prolonged Q-T and P-R intervals (due to longer systole and slower conduction), as well as some decrease in QRS and T wave amplitude. As a Group 1A antiarrhythmic agent with similar actions as quinidine, procainamide demonstrates direct effects on electrical activity, conduction, responsiveness, excitability and automaticity. However, procainamide has weaker vagal blocking action than does quinidine, does not induce alpha-adrenergic blockade, and is less depressing to cardiac contractility.

Pharmacokinetics
The action of procainamide begins almost immediately after intravenous administration. Following intramuscular injection, the therapeutic effect appears in 15 to 60 minutes. For ventricular arrhythmias, therapeutic plasma levels have been reported to be 3 to 10 mcg/mL, with those for the majority of patients in the range of 4 to 8 mcg/mL.

Procainamide's apparent volume of distribution (Vd) is usually between 1.75 and 2.5 L/kg body weight. About 75% of the procainamide is concentrated in highly perfused tissues. Approximately 20% is bound to plasma albumin.

On the average, about 60% (range 30-80%) of the drug is excreted unchanged. The half-time for elimination from the body may vary from 2.5 to 6 hours or longer. The plasma clearance of procainamide is 400-600 mL/minute; renal clearance is 200-400 mL/minute.
In humans, procainamide is acetylated, and N-acetylprocainamide (NAPA), an active metabolite, can be detected in both plasma and urine. The dose fraction of procainamide excreted as N-acetylprocainamide is extremely variable, ranging from 6% to 52%.

**INDICATIONS AND CLINICAL USE**

| No antiarrhythmic drug has been shown to reduce the incidence of sudden death in patients with asymptomatic ventricular arrhythmias. Most antiarrhythmic drugs have the potential to cause dangerous arrhythmias; some have been shown to be associated with an increased incidence of sudden death. In light of the above, physicians should carefully consider the risks and benefits of antiarrhythmic therapy for all patients with ventricular arrhythmias. |

**Ventricular Arrhythmias**

Procainamide Hydrochloride Injection USP is indicated for the treatment of documented life-threatening ventricular arrhythmias, such as sustained ventricular tachycardia. Procainamide Hydrochloride Injection USP may also be used for the treatment of patients with documented symptomatic ventricular arrhythmias when the symptoms are of sufficient severity to require treatment. Because of the proarrhythmic effects of procainamide, its use should be reserved for patients in whom, in the opinion of the physician, the benefit of treatment clearly outweighs the risks.

For patients with sustained ventricular tachycardia, procainamide therapy should be initiated in the hospital. Hospitalization may also be required for certain other patients depending on their cardiac status and underlying cardiac disease.

The effects of procainamide therapy in patients with recent myocardial infarction have not been adequately studied and, therefore, its use in this condition cannot be recommended.

**Supraventricular Arrhythmias**

Procainamide Hydrochloride Injection USP is also indicated in the treatment of atrial fibrillation, particularly if the condition is of recent development and the treatments of choice cannot be used or are ineffective. The drug may also be used in paroxysmal atrial tachycardia which cannot be controlled by reflex stimulation or by other measures.

**CONTRAINDICATIONS**

Hypersensitivity to the drug is an absolute contraindication; in this connection, cross-sensitivity to procaine and related drugs must be borne in mind. Procainamide should not be administered to patients with complete atrioventricular heart block. Procainamide is also contraindicated in cases of high degree AV block unless an electrical pacemaker is operative. Procainamide should not be used in patients with myasthenia gravis.
Because of the possibility of precipitous lowering of blood pressure with intravenous administration of procainamide, it should not be used in patients with severe congestive heart failure, renal failure or shock.

Procainamide therapy is contraindicated where there is an established diagnosis of systemic lupus erythematosus since aggravation of symptoms is highly likely.

In the particular ventricular arrhythmia called "Torsades de Pointes", Group 1A antiarrhythmic drugs are contraindicated. Administration of procainamide in such cases may aggravate this type of ventricular tachycardia instead of suppressing it.

**WARNINGS**

**Mortality**
The results of the Cardiac Arrhythmia Suppression Trial (CAST) in post-myocardial infarction patients with asymptomatic ventricular arrhythmias showed a significant increase in mortality and in nonfatal cardiac arrest rate in patients treated with encainide or flecainide compared with a matched placebo-treated group. CAST was continued using a revised protocol with the moricizine and placebo arms only. The trial was prematurely terminated because of a trend towards an increase in mortality in the moricizine-treated group.

The applicability of these results to other populations or other antiarrhythmic agents is uncertain, but at present it is prudent to consider these results when using any antiarrhythmic agent.

**Blood Dyscrasias**
Prolonged therapy with procainamide has produced cases of agranulocytosis, bone marrow depression, neutropenia, hypoplastic anemia and thrombocytopenia at a rate of approximately 0.5%. Most of these patients received procainamide within the recommended dosage range. Fatalities have occurred (with approximately 20-25% mortality in reported cases of agranulocytosis). Since most of these events have been noted during the first 12 weeks of therapy, it is recommended that complete blood counts including white cell, differential and platelet counts be performed at weekly intervals for the first 3 months of therapy, and periodically thereafter. Complete blood counts should be performed promptly if the patient develops any signs of infection (such as fever, chills, sore throat or stomatitis), bruising or bleeding. If any of these hematologic disorders are identified, procainamide therapy should be discontinued. Blood counts usually return to normal within one month of discontinuation. Caution should be used in patients with preexisting marrow failure or cytopenia of any type (see ADVERSE REACTIONS).

Patients should be instructed to report promptly any flu-type symptoms such as malaise and aches, as well as any soreness of the mouth, throat or gums, unexplained fever, skin rash, unusual bleeding or bruising, symptoms that resemble arthritis or symptoms of an upper respiratory tract infection.
**Positive ANA**
The prolonged administration of procainamide often leads to the development of a positive antinuclear antibody (ANA) test with or without symptoms of lupus erythematosus-like syndrome. If a positive ANA titer develops, the benefit/risk ratio related to continued procainamide therapy should be assessed. This may necessitate discontinuation of procainamide and substitution of alternative antiarrhythmic therapy.

**PRECAUTIONS**

Procainamide Hydrochloride Injection USP should be diluted prior to intravenous administration (see DOSAGE AND ADMINISTRATION).

During administration of the drug, evidence of untoward myocardial responses should be carefully watched for in all patients, especially in those patients with abnormal myocardium. In atrial fibrillation or flutter, the ventricular rate may increase suddenly as the atrial rate is slowed. Adequate digitalization reduces, but does not abolish this danger. If myocardial damage exists, ventricular tachycardia is particularly hazardous. Correction of atrial fibrillation, with resultant forceful contractions of the atrium, may cause a dislodgement of mural thrombi and produce an embolic episode. However, it has been suggested that in a patient who is already discharging emboli, procainamide is more likely to stop than to aggravate the process.

Adjustment of the heart rate in a patient who has developed ventricular tachycardia during an occlusive coronary episode should be carried out with extreme caution. Caution is also required in marked disturbances of atrioventricular conduction such as AV block, bundle-branch block, or severe digitalis intoxication, where the use of procainamide may result in additional depression of conduction and ventricular asystole or fibrillation. Widening of the QRS complex on the electrocardiograph calls for extreme caution. The effects of procainamide in digitalis intoxication, particularly where the arrhythmia is accompanied by marked conduction disturbances, are unpredictable and fatalities have occurred.

Electrocardiographic monitoring should be carried out during intravenous therapy and, whenever practical, during intramuscular therapy. If electrocardiograms give evidence of impending heart block, parenteral administration should be discontinued at once. Since patients with severe organic heart disease and ventricular tachycardia may also have complete heart block which is difficult to diagnose under these circumstances, this complication should always be kept in mind when treating ventricular arrhythmias with procainamide. If the ventricular rate is significantly slowed by procainamide without attainment of regular atrioventricular conduction, the drug should be discontinued and the patient re-evaluated as asystole may result under these circumstances.

Serious hypotension can result from peripheral vasodilation and by depressing myocardial contractility and cardiac output. At high plasma levels, procainamide may produce sinus tachycardia due to reflex sympathetic response to its hypotensive effect. Large doses may
increase cardiac automaticity and can induce complete atrioventricular block, cardiac standstill or ventricular extrasystoles that may proceed to ventricular fibrillation. These effects on the myocardium are reflected in the electrocardiogram; a widening of the QRS complex occurs most consistently; less regularly, the P-R and Q-T intervals are prolonged; and the QRS and T waves show some decrease in voltage. These actions of procainamide may be intensified in patients with congestive heart failure.

During the first day following acute myocardial infarction, absorption of oral procainamide can be very poor. Therefore, when warranted, it is suggested that the drug be administered intramuscularly or intravenously.

Plasma procainamide and NAPA concentrations rise markedly with increases in blood urea nitrogen and correlate well with creatinine clearance. Should patients with impaired kidney function and/or liver disease receive unadjusted dosage, symptoms of overdosage (principally ventricular tachycardia and severe hypotension) may occur due to drug accumulation. Similarly, plasma concentrations have been found to be increased in elderly patients possibly due to declining renal function in this age group. The frequency of administration should be reduced in patients with renal or hepatic insufficiency or in elderly patients.

Plasma concentrations of procainamide and NAPA should be monitored in patients with renal disease, hepatic disease, cardiac failure or low cardiac output states.

In patients with cardiac failure or shock or in patients with low cardiac output and extrarenal azotemia, the apparent volume of distribution and/or the elimination rate of procainamide can decrease considerably for a given dose, thereby resulting in increased plasma concentrations. Such patients should therefore be carefully monitored and the dose or frequency of administration reduced if warranted.

Instances of a syndrome resembling systemic lupus erythematosus have been reported in connection with oral maintenance procainamide therapy. The mechanism of this lupus erythematosus-like syndrome is uncertain. Polyarthritis, arthritis, fever, pleuritic pain and skin lesions are common symptoms; to a lesser extent myalgia, pleural effusion and pericarditis may occur. Rare cases of thrombocytopenia or Coombs' positive hemolytic anemia have been reported, and may be related to this syndrome. Patients receiving procainamide for extended periods of time or in whom symptoms suggestive of lupus erythematosus-like syndrome appear, should have antinuclear antibody titers measured at regular intervals. The drug should be discontinued if there is a rising titer (antinuclear antibody) or clinical symptoms of lupus erythematosus-like syndrome appear. Lupus erythematosus-like syndrome is usually reversible upon discontinuation of the drug. If discontinuation of the drug does not cause remission of the symptoms, steroid therapy may be effective. If lupus erythematosus-like syndrome develops in a patient with recurrent life-threatening arrhythmias not controllable by other antiarrhythmic agents, steroid suppressive therapy may be used concomitantly with procainamide.

**Special Populations**

**Pregnant Women:** Animal reproduction studies have not been conducted with procainamide. It is also not known whether procainamide can cause fetal harm when administered to a pregnant
woman or can affect reproduction capacity.

There has been some evidence of the diffusion of procainamide across the placental membrane. Therefore, due to the potential accumulation and slow rate of elimination of procainamide and N-acetylprocainamide in the fetus, the potential benefit of the use of procainamide during pregnancy should be weighed against the possible hazard to the fetus.

**Nursing Women:** It is known that this drug is excreted in human milk. Caution should be exercised when procainamide is administered to a nursing woman.

**Pediatrics:** Safety and effectiveness in children have not been established.

**DRUG INTERACTIONS**

**Antiarrhythmics:** Concurrent use with procainamide may result in additive cardiac effects and/or additive toxic effects.

**Beta Blockers:** Procainamide may potentiate the cardiac depressant action of beta-blocking agents such as propranolol.

**Anticholinergics:** Procainamide enhances the anticholinergic effects. Extreme caution must be exercised with such a combination.

**Anticholinesterases:** Procainamide antagonizes the effect of anticholinesterases in myasthenia gravis and paralysis returns.

**Antihypertensives:** Procainamide may potentiate the hypotensive effects of thiazide diuretics and other antihypertensive agents. Adjustment of dosage may be required.

**Cimetidine:** It has been reported that the histamine H₂-antagonist cimetidine reduces renal clearance of procainamide and NAPA resulting in higher plasma concentrations for longer durations. Caution should be exercised when administering these drugs concurrently, especially in the elderly who have a reduced ability to clear all three. Dosage modification may be required.

**Neuromuscular Blocking Agents:** Procainamide potentiates the effects of skeletal muscle relaxants such as succinylcholine. It also may enhance or prolong the neuromuscular blocking activity of bacitracin, colistimethate, dihydrostreptomycin, gentamicin, gramicidin, kanamycin, neomycin, polymyxin B, streptomycin, and viomycin, producing respiratory depression.

**Antibiotics:** Procainamide has also been reported to interact with kanamycin, neomycin and streptomycin to cause apnea and muscle weakness, due to an additive neuromuscular blocking effect.
ADVERSE REACTIONS

The overall incidence of adverse effects with procainamide is about 9%. The most commonly occurring are gastrointestinal upset 3.9%, cardiovascular effects (ventricular dysrhythmias, bradycardia, hypotension and shock) 3.3% and drug fever 1.6%.

The most serious adverse reactions reported are granulocytopenia and the development of antinuclear antibodies (ANA). Granulocytopenia is most likely to occur within the first three months of therapy. Prolonged administration of procainamide often leads to the development of a positive ANA test with or without symptoms of lupus erythematosus-like syndrome (see WARNINGS).

Because procainamide is a peripheral vasodilator, rapid intravenous administration may produce transient but at times severe lowering of blood pressure, particularly in conscious patients. Intramuscular injection is less likely to be accompanied by serious falls in blood pressure, and hypotension following oral administration is rare. Serious disturbances of cardiac rhythm such as ventricular asystole or fibrillation are also more common with intravenous administration. Precautionary measures to be followed during intravenous injection are given in the section on DOSAGE AND ADMINISTRATION.

Incidence Greater than 1%
* Elevated ANA (antinuclear antibodies), sometimes associated with drug-induced lupus syndrome.

* Gastrointestinal symptoms, especially with large oral doses: Anorexia, nausea, vomiting, diarrhea.

Cardiovascular effects: Bradycardia, arrhythmias, cardiac failure, shock.

Hypersensitivity reactions, which may be manifested by one or more of the following: Pruritus, urticaria, angioneurotic edema, maculopapular rash, fever, eosinophilia, hypergammaglobulinemia

* In patients on long-term procainamide therapy with sustained-release preparations, the above reactions have been reported with an incidence greater than 5%.

Incidence Less than 1%
* Granulocytopenia (incidence about 0.5%, sometimes resulting in death)
* Thrombocytopenia
* Immune hemolytic anemia
* Convulsions
* Psychosis with hallucinations
* Confusion
* Mental depression
* Giddiness
• Lightheadedness
• Weakness
• Bitter taste

**Rare**

• Hypotension.
• A case was reported with fever and chills plus nausea, vomiting, abdominal pain, acute hepatomegaly, and a rise in serum glutamic oxaloacetic transaminase following a single dose of the drug.
• Vasculitis (hypersensitivity-type).

**REPORTING SUSPECTED SIDE EFFECTS**

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    - Health Canada
    - Postal Locator 0701E
    - Ottawa, Ontario
    - K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

*NOTE*: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

**OVERDOSAGE**

Signs and symptoms of overdosage of procainamide include severe hypotension, ventricular fibrillation, widening of the QRS complex, junctional tachycardia, intraventricular conduction delay, oliguria, lethargy, confusion, nausea and vomiting.

If ingestion is recent, gastric lavage or emesis may reduce absorption. Dopamine, phenylephrine or levaterenol may be helpful in reversing severe hypotensive responses.

Management of overdosage includes symptomatic treatment with ECG and blood pressure monitoring. Procainamide toxicity can usually be treated, if necessary, by administering
vasopressors after adequate fluid volume replacement. Intravenous infusion of 1/6 molar sodium lactate injection reportedly reduces the cardiotoxic effects of procainamide.

The urinary elimination of procainamide is proportional to the glomerular filtration rate but is also affected by changes in urinary pH. Procainamide is relatively lipid-soluble as a free base but the ionized form is not. Acid urine, therefore, leads to ion trapping of procainamide which enters the urine by passive diffusion from the plasma. Accordingly, renal clearance of procainamide can be considerably increased by maintaining a low urinary pH and high flow rates.

If procainamide toxicity causes severe hypotension and renal insufficiency, urinary elimination of procainamide and NAPA is decreased and hemodialysis may be required. Hemodialysis significantly reduces the serum half-life of procainamide and effectively removes procainamide and NAPA. Peritoneal dialysis is not effective.

It has been reported that one patient who ingested approximately 7 g of procainamide hydrochloride recovered after treatment consisting of IV norepinephrine, IV furosemide, attempted volume expansion with albumin, and hemodialysis. Also reported is the case of an elderly patient who recovered after ingestion of approximately 19 g of procainamide hydrochloride. The patient was treated with IV isoproterenol and IV epinephrine. The latter report suggested that insertion of a ventricular pacing electrode is a reasonable precautionary measure in case high-grade AV block develops.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

**DOSAGE AND ADMINISTRATION**

Selection of the dose and route of administration should be made with the following facts in mind:

- The optimum plasma level is 4 to 8 mcg/mL.
- **Therapeutic Urgency:** Oral administration is preferred. When parenteral therapy is necessary, intramuscular administration is the method of choice. Intravenous use should be limited to emergencies and continuous ECG monitoring is mandatory when this route is used.
- Excretion is delayed in elderly patients and in patients with impaired renal function (decreased creatinine clearance), and reduced frequency of administration is required (see PRECAUTIONS).
- Excretion rate is reduced by an alkaline urine, necessitating a reduced frequency of administration.
- Patients with cardiac failure, shock, low cardiac output and extrarenal azotemia should be carefully monitored and the dose or frequency of administration reduced if necessary.
- Excretion rates appear to be unchanged by furosemide and other diuretics but are decreased by the use of acetazolamide, due to the production of alkaline urine.
- Following stabilization on intravenous therapy, conversion to oral procainamide should be carried out as soon as practical.
- Should toxic or subtherapeutic levels be suspected, the patient's plasma procainamide should be
determined and adjusted accordingly.

Patients vary in response to a dose of procainamide. Nevertheless, the following guidelines should be considered when deciding upon the patient's actual requirements:

**Intramuscular Dose:** If the oral route is not feasible because of vomiting or unreliable absorption, 0.5 to 1 g may be given intramuscularly, repeated every 3 hours until oral therapy is possible.

**Intravenous Dose:** Procainamide Hydrochloride Injection USP should be further diluted to facilitate accurate control of dosage. The dose should be administered at a rate not greater than 25-50 mg per minute by either direct intravenous administration or infusion. Slow administration allows some initial tissue distribution. Solutions prepared with 5% dextrose should be used immediately after preparation.

**Caution:** Intravenous use of procainamide may be accompanied by a hypotensive response, sometimes precipitous. For this reason, the dose schedules described below should be monitored electrocardiographically, so that the drug may be stopped when the arrhythmia is interrupted or when excessive widening of the QRS complex or prolongation of the P-R interval suggest the occurrence of myocardial toxicity. Patients should be kept in a supine position and blood pressure should be measured almost continuously during IV administration. If the fall in blood pressure exceeds 15 mmHg, the intravenous administration should be temporarily discontinued. Solutions of phenylephrine hydrochloride injection, or levarterenol bitartrate injection, should be available to counteract severe hypotensive responses.

**Direct Intravenous Administration:** Each mL of the 10% (100 mg/mL) solution should be further diluted to 10 to 20 mL with 5% dextrose prior to direct intravenous administration to facilitate control of dosage rate. The diluted solution should be used immediately after preparation.

To reduce the possibility of a hypotensive response, 100 mg doses may be administered every 5 minutes by direct intravenous injection, at a rate not exceeding 50 mg per minute, until the arrhythmia is suppressed or a dose of 1 g has been administered. Blood pressure must be monitored and the electrocardiogram read before each dose. An effect is usually seen after the first or second injection. It is unusual to require more than 5 or 6 injections to achieve satisfactory antiarrhythmic effects.

To maintain therapeutic levels, procainamide infusion may then be started at a rate of 2 to 6 mg of Procainamide Hydrochloride Injection USP per minute (see Table) depending on the patient's body weight, circulatory condition and renal function.

**Intravenous Infusion:** An alternative method of achieving and then maintaining a therapeutic plasma concentration is to infuse 500 to 600 mg of Procainamide Hydrochloride Injection USP at a constant rate over a period of 25 to 30 minutes and then to change to another infusion for maintenance at a rate of 2 to 6 mg/minute (see Table).
### Dilutions and Rates for Intravenous Infusions *

<table>
<thead>
<tr>
<th>Approximate Final Concentration</th>
<th>Infusion Bottle Size (mL)</th>
<th>mL of Procainamide HCl Injection USP (100 mg/mL) to be added</th>
<th>Infusion Rate</th>
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</thead>
<tbody>
<tr>
<td>0.2% (2 mg/mL)</td>
<td>500</td>
<td>10</td>
<td>1-3 mL/min</td>
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<tr>
<td></td>
<td>250</td>
<td>5</td>
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<tr>
<td>0.4% (4 mg/mL)</td>
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<td>20</td>
<td>0.5-1.5 mL/min</td>
</tr>
<tr>
<td></td>
<td>250</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

* Caution: The flow rate of all intravenous infusion solutions must be closely monitored. These dilutions are calculated to deliver 2-6 mg per minute at the infusion rates listed.

Diluted solutions should be inspected visually for discoloration, precipitation or particulate matter prior to administration whenever solution and container permit. Discard any unused portion.

Intravenous therapy should be terminated as soon as the patient's basic cardiac rhythm appears to be stabilized and, if indicated, the patient should be placed on oral procainamide maintenance therapy. A period of about 3 to 4 hours (one half-life) should elapse after the last intravenous dose of Procainamide Hydrochloride Injection USP before administering the first oral dose of procainamide.

**Surgical Use:** For arrhythmias occurring during surgery, the suggested parenteral dose is 0.5 to 1.0 g preferably given intramuscularly.
PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Procainamide hydrochloride

Chemical Name: p-Amino-N-(2-diethylaminoethyl) benzamide hydrochloride

Molecular formula and molecular mass: \( \text{C}_{13}\text{H}_{21}\text{N}_{3}\text{O} \cdot \text{HCl} ; 271.79 \text{ g/mol} \)

Structural Formula:

![Structural Formula]

Physicochemical properties: Procainamide hydrochloride is an odourless, white to tan-coloured, crystalline powder. It is very soluble in water, soluble in alcohol, slightly soluble in chloroform and very slightly soluble in benzene and ether. Procainamide hydrochloride has a melting point of 165 to 169°C. The pH of a 10% aqueous solution is 5.5.

STORAGE AND STABILITY

Store Procainamide Hydrochloride Injection USP between 15 and 30°C. Do not freeze. The solution, which is colourless initially, may in time develop a slightly yellow colour. This change does not prevent its use, but a solution which becomes discoloured in any other way should not be used.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Each mL of Procainamide Hydrochloride Injection USP contains procainamide hydrochloride 100 mg, benzyl alcohol 0.9% v/v as preservative, hydrochloric acid and/or sodium hydroxide to adjust pH, and water for injection q.s.

Procainamide Hydrochloride Injection USP is available as a 10% parenteral solution (100 mg/mL) in 10 mL amber glass multidose vials, boxes of 10.

LATEX FREE STOPPER: Stopper contains no dry natural rubber.
PHARMACOLOGY

Procainamide exerts many actions on the heart and the circulation. It slows conduction in the atrium, ventricle and the bundle of His. The effect is greatest across the AV node, suggesting the greater sensitivity of this tissue to the drug. The refractory period is prolonged with the atrium being much more affected than the ventricle. With therapeutic plasma levels of the drug contractility of the heart is usually not affected by procainamide unless myocardial damage exists. Excitability of the ventricle and the atrium to electric stimulation is profoundly depressed. In addition, the rate of pacemaker is also depressed. Procainamide has been shown to be effective in preventing the development of epinephrine-induced ventricular arrhythmia in dogs under cyclopropane anesthesia. It also suppressed ventricular tachycardia produced by ligation of coronary arteries in the dog.

TOXICOLOGY

Acute

The LD$_{50}$ of procainamide hydrochloride is reported to be as follows:

<table>
<thead>
<tr>
<th>Species</th>
<th>Route of Administration</th>
<th>LD$_{50}$ (mg/kg)</th>
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<tbody>
<tr>
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REFERENCES


Procainamide Hydrochloride Injection USP