**Procainamide Hydrochloride**

**Ingredients:** Procainamide Hydrochloride

**Indications:** Arrhythmia, ventricular; Tachycardia, ventricular

**Off-label Indications:** Not clinically relevant: Arrhythmias, Atrial; Arrhythmias, Supraventricular; Arrhythmias, Ventricular, Asymptomatic; Atrial Fibrillation, Conversion of; Atrial Flutter, Conversion of; Hyperthermia, Malignant; Tachycardias, Wide-complex, Uncertain Mechanism; Ventricular Premature Complexes.

FDA Approved 1950-06-01.

**DRUG CLASS:** Antiarrhythmics, class IA

**Brand Names:** Amisalin (Taiwan); Biocoryl (Spain); Cardiorytmin (Finland); Gima (Indonesia); Procanbid (US); Procan-SR (Canada); Pronestyl (US, Australia, Belgium, England, Ethiopia, India, Ireland, Japan, Kenya, Malaysia, Netherlands, South-africa, Switzerland, Taiwan, Tanzania, Uganda, Uruguay); Pronestyl-SR (US, Canada) (International brand names outside U.S. in italics).

**WARNING:**

The prolonged administration of procainamide often leads to the development of a positive anti-nuclear antibody (ANA) test, with or without symptoms of a lupus erythematosus-like syndrome. If a positive ANA titer develops, the benefits versus risks of continued procainamide therapy should be assessed.

**DESCRIPTION:**

**Note:** This monograph contains information on procainamide hydrochloride (procainamide HCl) tablets, extended release tablets, capsules, and injection. Procainamide hydrochloride, a Group 1A cardiac antiarrhythmic drug, is p-amino-N-(2-(diethylamino)ethyl)-benzamide monohydrochloride, molecular weight 271.79. It differs from procaine which is the p-aminobenzoyl ester of 2-(diethylamino)-ethanol. Procainamide as the free base has a pKa of 9.23; the monohydrochloride is very soluble in water. Procainamide hydrochloride is supplied for oral administration as capsules and tablets in potencies of 250, 375, and 500 mg.

**Inactive Ingredients Pronestyl Tablets**

Calcium silicate, microcrystalline cellulose, colorants (FD&C yellow no. 5 (tartrazine) and yellow no. 6), flavor, povidone, starch, stearic acid, and other ingredients.

**Pronestyl Capsules**

Colorants (D&C yellow no. 10, except 375 mg; FD&C yellow no. 6), gelatin, lactose (except 500 mg), magnesium stearate, talc, and titanium dioxide.

**Pronestyl Extended-Release Tablets**

Procainamide extended-release tablets are available for oral administration as green, film-coated tablets containing 250 mg procainamide hydrochloride, as yellow scored, film-coated tablets containing 500 mg procainamide hydrochloride; as orange, scored, film coated tablets containing 750 mg procainamide hydrochloride; and as red, scored, film-coated tablets containing 1000 mg procainamide hydrochloride.

All strengths of Pronestyl extended release tablets contain candeilla wax; colloidal silicon dioxide; magnesium stearate; titanium dioxide, vanillin; and other ingredients. The individual strengths contain additional ingredients as follows: 250 mg: D&C yellow no. 10 Al lake; FD&C blue no. 1 Al lake; FD&C yellow no. 6 Al lake; lactose; may also contain methylparaben; or simethicone emulsion and polysorbate 80. 500 mg: D&C yellow no.10 Al lake; FD &C blue no.2 Al lake; FD&C yellow no. 6 Al lake; sucrose; may also contain methylparaben; and propylparaben; or simethicone and emulsion and polysorbate 80. 750 mg: FD&C yellow no. 6 Al lake; may also contain propylene glycol; or simethicone emulsion and polysorbate 80. 1000 mg: D&C red no. 7 calcium lake; FD&C yellow no. 6 Al lake; propylene glycol.
**Pronestyl Injection**

Procainamide hydrochloride is available for parenteral use as a sterile, aqueous solution providing 100 mg or 500 mg/ml. The 100 mg/ml concentration in each ml procainamide hydrochloride 100 mg, benzyl alcohol 0.009 ml and sodium metabisulfite 0.9 mg in water for injection. The 500 mg/ml concentration contains in each ml procainamide hydrochloride 500 mg, benzyl alcohol 0.009 ml and sodium metabisulfite 2 mg in water for injection. For both concentrations, pH is 4.0-6.0; sodium hydroxide and/or hydrochloric acid added, if needed, for pH adjustment. Vials are sealed under nitrogen.

**Storage**

Store at controlled room temperature 15-30°C (59-86°F). Discard solution if darker than slightly yellow or otherwise discolored.

**Oral Forms**

Store at room temperature; avoid excessive heat (104° F); protect from moisture.

**CLINICAL PHARMACOLOGY:**

Procainamide (PA) 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 (A-V) node, a direct slowing action and a weaker vagolytic effect which may speed A-V 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 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 PA may exert vagolytic effects and produce slight acceleration of heart rate, while high or toxic concentrations may prolong A-V conduction time or induce A-V 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. These direct effects of PA on electrical activity, conduction, responsiveness, excitability and automaticity are characteristic of a Group 1A antiarrhythmic agent, the prototype for which is quinidine; PA effects are very similar. However, PA has weaker vagal blocking action than does quinidine, does not induce alpha-adrenergic blockade, and is less depressing to cardiac contractility.

Ingested PA is resistant to digestive hydrolysis, and the drug is well absorbed from the entire small intestinal surface, but individual patients vary in their completeness of absorption of PA. Following oral administration of PA, plasma PA levels reach about 50% of peak in 30 minutes, 90% at an hour, and peak at about 90-120 minutes. About 15-20% of PA is reversibly bound to plasma proteins, and considerable amounts are more slowly and reversibly bound to tissues of the heart, liver, lung, and kidney. The apparent volume of distribution eventually reaches about 2 L/kg body weight with a half-time of approximately 5 minutes. While PA has been shown in the dog to cross the blood-brain barrier, it did not concentrate in the brain at levels higher than in plasma. It is not known if PA crosses the placenta. Plasma esterases are far less active in hydrolysis of PA than of procaine. The half-time for elimination of PA is 3-4 hours in patients with normal renal function, but reduced creatinine clearance and advancing age each prolong the half-time of elimination of PA.

A significant fraction of the circulating PA may be metabolized in hepatocytes to N-acetylprocainamide (NAPA), ranging from 16-21% of an administered dose in "slow acetylators" to 24-33% in "fast-acetylators". Since NAPA also has significant antiarrhythmic activity and somewhat slower renal clearance than PA, both hepatic acetylation rate capability and renal function, as well as age, have significant effects on the effective biologic half-time of therapeutic action of administered PA and the NAPA derivative. Trace amounts may be excreted in the urine as free and conjugated p-aminobenzoic acid, 30-60% as unchanged PA, and 6-52% as the NAPA derivative. Both PA and NAPA are eliminated by active tubular secretion as well as by glomerular filtration. Action of PA on the central nervous system is not prominent, but high plasma concentrations may cause tremors. While therapeutic plasma levels for PA have been reported to be 3-10 μg/ml, certain patients such as those with sustained ventricular tachycardia, may need higher
levels for adequate control. This may justify the increased risk of toxicity (see OVERDOSAGE). Where programmed ventricular stimulation has been used to evaluate efficacy of PA in preventing recurrent ventricular tachyarrhythmias, higher plasma levels (mean, 13.6 μg/ml) of PA were found necessary for adequate control.

Additional Information for Procainamide HCl Injection

Following IM injection, this drug is rapidly absorbed into the blood stream, and plasma levels peak in about 15-60 minutes, considerably faster than orally administered forms. IV administration of procainamide HCl can produce therapeutic procainamide levels within minutes after the infusion is started.

INDICATIONS AND USAGE:

Procainamide HCl is indicated for the treatment of documented ventricular arrhythmias, such as sustained ventricular tachycardia, that, in the judgement of the physician, are life-threatening. Because of the proarrhythmic effects of procainamide HCl, its use with lesser arrhythmias is generally not recommended. Treatment of patients with asymptomatic ventricular premature contractions should be avoided. Initiation of procainamide HCl treatment, as with other antiarrhythmic agents used to treat life-threatening arrhythmias, should be carried out in the hospital. Antiarrhythmic drugs have not been shown to enhance survival in patients with ventricular arrhythmias. Because procainamide has the potential to produce serious hematological disorders (0.5%) particularly leukopenia or agranulocytosis (sometimes fatal), its use should be reserved for patients in whom, in the opinion of the physician, the benefits of treatment clearly outweigh the risks. (See WARNINGS and BOXED WARNING)

CONTRAINDICATIONS:

Complete Heart Block

Procainamide should not be administered to patients with complete heart block because of its effects in suppressing nodal or ventricular pacemakers and the hazard of asystole. It may be difficult to recognize complete heart block in patients with ventricular tachycardia, but if significant slowing of ventricular rate occurs during PA treatment without evidence of A-V conduction appearing, PA should be stopped. In cases of second degree A-V block or various types of hemiblock, PA should be avoided or discontinued because of the possibility of increased severity of block, unless the ventricular rate is controlled by an electrical pacemaker.

Idiosyncratic Hypersensitivity

In patients sensitive to procaine or other ester-type local anesthetics, cross sensitivity to PA is unlikely; however, it should be borne in mind, and PA should not be used if it produces acute allergic dermatitis, asthma, or anaphylactic symptoms.

Lupus Erythematosus

An established diagnosis of systemic lupus erythematosus is a contraindication to PA therapy, since aggravation of symptoms is highly likely.

Torsades de Pointes

In the unusual ventricular arrhythmia called "les torsades de pointes" (Twistings of the points), characterized by alternation of one or more ventricular premature beats in the directions of the QRS complexes on ECG in persons with prolonged Q-T and often enhanced U waves, Group 1A antiarrhythmic drugs are contraindicated. Administration of PA in such cases may aggravate this special type of ventricular extrasystole or tachycardia instead of suppressing it.

WARNINGS:

Mortality

In the National Heart, Lung and Blood Institute's Cardiac Arrhythmia Suppression Trial (CAST), a long-term, multicentered, randomized, double-blind study in patients with asymptomatic non-life-threatening ventricular arrhythmias who had had myocardial infarctions more than 6 days but less than 2 years previously, an excessive
mortality or non-fatal cardiac arrest rate was seen in patients treated with encainide or flecainide (56/730) compared with that seen in patients assigned to matched placebo-treated groups (22/725). The average duration of treatment with encainide or flecainide in this study was 10 months. The applicability of these results to other populations (e.g., those without recent myocardial infarctions) or to other antiarrhythmic drugs is uncertain, but at present it is prudent to consider any antiarrhythmic agent to have a significant risk in patients with structural heart disease.

**BLOOD DYSCRASIAS:** Agranulocytosis, bone marrow depression, neutropenia, hypoplastic anemia and thrombocytopenia in patients receiving procainamide hydrochloride have been reported 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 1 month of discontinuation. Caution should be used in patients with pre-existing marrow failure or cytopenia of any type (see ADVERSE REACTIONS).

**Digitalis Intoxication**

Caution should be exercised in the use of procainamide in arrhythmias associated with digitalis intoxication. Procainamide can suppress digitalis-induced arrhythmias; however, if there is concomitant marked disturbance of atrioventricular conduction, additional depression of conduction and ventricular asystole or fibrillation may result. Therefore, use of procainamide should be considered only if discontinuation of digitalis, and therapy with potassium, lidocaine, or phenytoin are ineffective.

**First Degree Heart Block**

Caution should be exercised also if the patient exhibits or develops first degree heart block while taking PA, and dosage reduction is advised in such cases. If the block persists despite dosage reduction, continuation of PA administration must be evaluated on the basis of current benefit versus risk of increased heart block.

**Predigialization for Atrial Flutter or Fibrillation**

Patients with atrial flutter or fibrillation should be cardioverted or digitalized prior to PA administration to avoid enhancement of A-V conduction which may result in ventricular rate acceleration beyond tolerable limits. Adequate digitalization reduces but does not eliminate the possibility of sudden increase in ventricular rate as the atrial rate is slowed by PA in these arrhythmias.

**Congestive Heart Failure**

For patients in congestive heart failure, and those with acute ischemic heart disease or cardiomyopathy, caution should be used in PA therapy, since even slight depression of myocardial contractility may further reduce cardiac output of the damaged heart.

**Concurrent Other Antiarrhythmic Agents**

Concurrent use of PA with other Group 1A antiarrhythmic agents such as quinidine or disopyramide may produce enhanced prolongation of conduction or depression of contractility and hypotension, especially in patients with cardiac decompensation. Such use should be reserved for patients with serious arrhythmias unresponsive to a single drug and employed only if close observation is possible.

**Renal Insufficiency**

Renal insufficiency may lead to accumulation of high plasma levels from conventional oral doses of PA, with effects similar to those of overdosage (see OVERDOSAGE), unless dosage is adjusted for the individual patient.

**Myasthenia Gravis**
Patients with myasthenia gravis may show worsening of symptoms from PA due to its procaine-like effect on diminishing acetylcholine release at skeletal muscle motor nerve endings, so that PA administration may be hazardous without optimal adjustment of anticholinesterase medications and other precautions.

Additional Information for the Injection

This contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

PRECAUTIONS:

General

Immediately after initiation of PA therapy, patients should be closely observed for possible hypersensitivity reactions, especially if procaine or local anesthetic sensitivity is suspected, and for muscular weakness if myasthenia gravis is a possibility. In conversion of atrial fibrillation to normal sinus rhythm by any means, dislodgement of mural thrombi may lead to embolization, which should be kept in mind.

After a day or so, steady state plasma PA levels are produced following regular oral administration of a given dose of procainamide HCl tablets; procainamide HCl capsules at set intervals, with peak plasma concentrations at about 90-120 minutes after each dose. After achieving and maintaining therapeutic plasma concentrations and satisfactory electrocardiographic and clinical responses, continued frequent periodic monitoring of vital signs and electrocardiograms is advised. If evidence of QRS widening of more than 25% or marked prolongation of the Q-T interval occurs, concern for overdosage is appropriate, and reduction in dosage is advisable if a 50% increase occurs. Elevated serum creatinine or urea nitrogen, reduced creatinine clearance, or history of renal insufficiency, as well as use in older patients (over age 50), provide grounds to anticipate that less than the usual dosage and longer time intervals between doses may suffice, since the urinary elimination of PA and NAPA may be reduced, leading to gradual accumulation beyond normally-predicted amounts. If facilities are available for measurement of plasma PA and NAPA, or acetylation capability, individual dose adjustment for optimal therapeutic levels may be easier, but close observation of clinical effectiveness is the most important criterion.

In the longer term, periodic complete blood counts are useful to detect possible idiosyncratic hematologic effects of PA on neutrophil, platelet or red cell homeostasis; agranulocytosis has been reported to occur occasionally in patients on long-term PA therapy. A rising titer of serum ANA may precede clinical symptoms of the lupoid syndrome (see BOXED WARNING and ADVERSE REACTIONS). If the lupus erythematosus-like syndrome develops in a patient with recurrent life-threatening arrhythmias not controlled by other agents, corticosteroid suppressive therapy may be used concomitantly with PA. Since the PA-induced lupoid syndrome rarely includes the dangerous pathologic renal changes, PA therapy may not necessarily have to be stopped unless the symptoms of serositis and the possibility of further lupoid effects are of greater risk than the benefit of PA in controlling arrhythmias. Patients with rapid acetylation capability are less likely to develop the lupoid syndrome after prolonged PA therapy.

Procainamide HCl tablets contain FD&C yellow no. 5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals. Although the overall incidence of FD&C yellow no. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

Additional Information for the Injection

Blood pressure should be monitored with the patient supine during parenteral, especially intravenous, administration of Procainamide (see DOSAGE AND ADMINISTRATION). There is a possibility that relatively high, although transient, plasma levels of procainamide may be attained and cause hypotension before the procainamide can be disturbed from the plasma volume to its full apparently volume to its full apparent volume of distribution, which is approximately 50 times greater. Therefore, caution should be exercised to avoid overly rapid administration of procainamide. If the blood pressure falls 15 mm Hg or more, procainamide administration should be temporarily discontinued. ECG monitoring is advisable as well, both for observation of the progress and response of the arrhythmia under treatment, and for early detection of any tendency to excessive widening of the QRS complex, prolongation of the P-R interval or any signs of the heat block (see OVERDOSAGE). Parenteral therapy with procainamide should be limited to use in hospitals in
which monitoring and intensive supportive care are available or to emergency situations in which equivalent
observation and treatment can be provided.

**Information for the Patient**

The physician is advised to explain to the patient that close cooperation in adhering to the prescribed dosage schedule
is of great importance in controlling the cardiac arrhythmia safely. The patient should understand clearly that more
medication is not necessarily better and may be dangerous, that skipping doses or increasing intervals between doses
to suit personal convenience may lead to loss of control of the heart problem, and that "making up" missed doses by
doubling up later may be hazardous.

The patient should be encouraged to disclose any past history of drug sensitivity, especially to procaine or other local
anesthetic agents, or aspirin, and to report any history of kidney disease, congestive heart failure, myasthenia gravis,
liver disease, or lupus erythematosus. The patient should be counseled to report promptly any symptoms of arthralgia,
myalgia, fever, chills, skin rash, easy bruising, sore throat or sore mouth, infections, dark urine or icterus, wheezing,
muscular weakness, chest or abdominal pain, palpitations, nausea, vomiting, anorexia, diarrhea, hallucinations,
dizziness, or depression.

**Laboratory Tests**

Laboratory tests such as complete blood count (CBC), electrocardiogram, and serum creatinine or urea nitrogen may
be indicated, depending on the clinical situation, and periodic rechecking of the CBC and ANA may be helpful in early
detection of untoward reactions.

**Drug/Laboratory Test Interactions**

Suprapharmacologic concentrations of lidocaine and meprobamate may inhibit fluorescence of PA and NAPA, and
propranolol shows a native fluorescence close to the PA/NAPA peak wavelengths, so that tests which depend on
fluorescence measurement may be affected.

**Carcinogenesis, Mutagenesis, and Impairment of Fertility**

Long term studies in animals have not been performed.

**Pregnancy, Teratogenic Effects, Pregnancy Category C**

Animal reproduction studies have not been conducted with PA. It also is not known whether PA can cause fetal harm
when administered to a pregnant woman or can affect reproduction capacity. PA should be given to a pregnant woman
only if clearly needed.

**Nursing Mothers**

Both PA and NAPA are excreted in human milk, and absorbed by the nursing infant. Because of the potential for
serious adverse reactions in nursing infants, a decision to discontinue nursing or the drug should be made, taking into
account the importance of the drug to the mother.

**Pediatric Use**

Safety and effectiveness in children have not been established.

**INTERACTIONS:**

If other antiarrhythmic drugs are being used, additive effects on the heart may occur with PA administration, and
dosage reduction may be necessary (see WARNINGS).

Anticholinergic drugs administered concurrently with PA may produce additive antivagal effects on A-V nodal
conduction, although this is not as well documented for PA as for quinidine.
Patients taking PA who require neuromuscular blocking agents such as succinylcholine may require less than usual doses of the latter, due to PA effects on reducing acetylcholine release.

**ADVERSE REACTIONS:**

**Cardiovascular**

Hypotension following oral PA administration is rare. Hypotension and serious disturbances of cardiorhythm such as ventricular asystole or fibrillation are more common after intravenous administration (see OVERDOSAGE and WARNINGS). Second degree heart block has been reported in 2 of almost 500 patients taking PA orally.

**Multisystem**

A lupus erythematosus-like syndrome of arthralgia, pleural or abdominal pain, and sometimes arthritis, pleural effusion, pericarditis, fever, chills, myalgia, and possibly related hematologic or skin lesions is fairly common after prolonged PA administration, perhaps more often in patients who are slow acetylators (see BOXED WARNING and PRECAUTIONS). While some series have reported less than 1 in 500, others have reported the syndrome in up to 30% of patients on long term oral PA therapy. If discontinuation of PA does not reverse the lupoid symptoms, corticosteroid treatment may be effective.

**Hematologic**

Neutropenia, thrombocytopenia, or hemolytic anemia may rarely be encountered. Agranulocytosis has occurred after repeated use of PA, and deaths have been reported. (See BOXED WARNING and WARNINGS)

**Skin**

Angioneurotic edema, urticaria, pruritus, flushing, and maculopapular rash have also occurred occasionally.

**Gastrointestinal**

Anorexia, nausea, vomiting, abdominal pain, bitter taste, or diarrhea may occur in 3-4% of patients taking oral procainamide. Hepatomegaly with increased serum aminotransferase activity have been reported after a single oral dose.

**Nervous System**

Dizziness or giddiness, weakness, mental depression, and psychosis with hallucinations have been reported occasionally.

**OVERDOSAGE:**

Progressive widening of the QRS complex, prolonged Q-T and P-R intervals, lowering of the R and T waves, as well as increasing A-V block, may be seen with doses which are excessive for a given patient. Increased ventricular extrasystoles, or even ventricular tachycardia or fibrillation may occur. After intravenous administration but seldom after oral therapy, transient high plasma levels of PA may induce hypotension, affecting systolic more than diastolic pressures, especially in hypertensive patients. Such high levels may also produce central nervous depression, tremor, and even respiratory depression.

Plasma levels above 10 μg/ml are increasingly associated with toxic findings, which are seen occasionally in the 10-12 μg/ml range, more often in the 12-15 μg/ml range, and commonly in patients with plasma levels greater than 15 μg/ml. Overdosage symptoms may result following a single 2 g dose; while 3 g may be dangerous, especially if the patient is a slow acetylator, has decreased renal function, or underlying organic heart disease.

Treatment of overdosage or toxic manifestations includes general supportive measures, close observation, monitoring of vital signs and possibly intravenous pressor agents and mechanical cardiorespiratory support. If available, PA and NAPA plasma levels may be helpful in assessing the potential degree of toxicity and response to therapy. Both PA and
NAPA are removed from the circulation by hemodialysis but not peritoneal dialysis. No specific antidote for PA is known.

**DOSAGE AND ADMINISTRATION:**

**Oral Forms**

The oral dose and interval of administration should be adjusted for the individual patient, based on clinical assessment of the degree of underlying myocardial disease, the patient's age, and renal function. As a general guide, for younger adult patients with normal renal function, an initial total daily oral dose of up to 50 mg/kg of body weight of capsules or tablets may be used, given in divided doses, every 3 hours, to maintain therapeutic blood levels. For older patients, especially those over 50 years of age, or for patients with renal, hepatic, or cardiac insufficiency, lesser amounts or longer intervals may produce adequate blood levels, and decrease the probability of occurrence of dose related adverse reactions. For the tablets and capsules, the total daily dose should be administered in divided doses at 3, 4, or 6 hour intervals and adjusted according to the patient's response (TABLE 1 and TABLE 2).

**TABLE 1 Capsules and Tablets**

To provide up to 50 mg/kg of body weight/day:*

<table>
<thead>
<tr>
<th>Patients Weighing</th>
<th>Capsules and Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>lb</td>
<td>kg</td>
</tr>
<tr>
<td>88-110</td>
<td>40-50</td>
</tr>
<tr>
<td>132-154</td>
<td>60-70</td>
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<tr>
<td>176-198</td>
<td>80-90</td>
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<tr>
<td>&gt;220</td>
<td>&gt;100</td>
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</tbody>
</table>

**TABLE 2 Extended Release Tablets**

To provide up to 50 mg/kg of body weight/day:*

<table>
<thead>
<tr>
<th>Patients Weighing</th>
<th>Extended Release Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>lb</td>
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<td>88-110</td>
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</table>

* Initial dosage schedule guide only, to be adjusted for each patient individually, based on age, cardiorenal function, blood level (if available), and clinical response.

**Injection**

Procainamide HCl injection is useful for arrhythmias which require immediate suppression and for maintenance of arrhythmia control. IV therapy allows most rapid control of serious arrhythmias, including those following myocardial infarction; it should be carried out in circumstances where close observation and monitoring of the patient are possible, such as hospital or emergency facilities. IM administration is less opt to produce temporary high plasma levels but therapeutic plasma levels are not obtained as rapidly as with IV administration. Oral procainamide dosage forms are preferable for less urgent arrhythmias as well as long-term maintenance after initial parenteral procainamide therapy.

IM administration may be used as an alternative to the oral route for patients with less threatening arrhythmias but who are nauseated or vomiting, who are ordered to receive nothing by mouth preoperatively or who may have malabsorptive problems. An initial dose of 50 mg/kg body weight may be estimated. This amount should be divided into fractional doses of one-eighth to one-quarter to be injected by the IM route every 3-6 hours until oral therapy is possible. If more than three injections are given, the physician may wish to assess the patient factors such as age and renal function, clinical response, and if available, blood levels of procainamide and NAPA in adjusting further doses for that individual. For treatment of arrhythmias associated with anesthesia or surgical operation, the suggested dose is 100-500 mg by IM injection.

IV administration for procainamide HCl injection should be done cautiously to avoid a possible hypotensive response (see PRECAUTIONS and OVERDOSAGE). Initial arrhythmia control, under ECG monitoring, may usually be accomplished safely within a half-hour by either of the two methods which follow:
1 A) Direct injection into a vein or tubing an established infusion line should be done slowly at a rate not to exceed 50 mg per minute. It is advisable to dilute either the 100 mg/ml or the 500 mg/ml concentrations of procainamide HCl injection prior to IV injection to facilitate control of dosage rate. Doses of 100 mg may be administered every 5 minutes at this rate until the arrhythmia is suppressed or until 500 mg has been administered, after which it is advisable to wait 10 minutes or longer to allow for more distribution into tissues before resuming.

2 B) Alternatively, a loading infusion containing 20 mg of procainamide HCl per ml (1 g diluted to 50 ml with 5% dextrose injection) may be administered at a constant rate of 1 ml/min for 25-30 minutes to deliver 500-600 mg of procainamide. Some effects may be seen after the infusion of the first 100 or 200 mg; it is unusual to require more than 600 mg to achieve satisfactory antiarrhythmic effects.

The maximum advisable dosage to be given either by repeated bolus injections or such loading infusion is 1 g.

To maintain therapeutic levels, a more dilute IV infusion at a concentration of 2 mg/ml is convenient (1 g procainamide HCl in 500 ml of 5% dextrose injection), and may be administered at 1-3 ml/minute. If daily total fluid intake must be limited, a 4 mg/ml concentration (1 g procainamide HCl injection in 250 ml of 5% dextrose injection) administered at 0.5-1.5 ml/minute will deliver an equivalent 2-6 mg per minute. The amount needed in a given patient to maintain therapeutic level should be assessed principally from the clinical response and will depend upon the patient's weight and age, renal elimination, hepatic acetylation rate and cardiac status, but should be adjusted for each patient based upon close observation. A maintenance infusion rate of 50 μg/min/kg body weight to a person with a normal renal procainamide elimination half-time of 3 hours may be expected to produce a plasma level of approximately 6.5 μg/ml (see TABLE 3).

Since the principle route for elimination of procainamide and NAPA is renal excretion, reduced excretion will prolong the half-life of elimination and lower the dose rate needed to maintain therapeutic levels. Advancing age reduces the renal excretion of procainamide and NAPA independently of reductions in creatine clearance; compared to normal young adults, there is approximately 25% reduction at age 50 and 50% at age 75. IV therapy should be terminated if persistent conduction disturbances or hypotension develop. As soon as the patient's basic cardiac rhythm appears to be stabilized, oral antiarrhythmic maintenance therapy is preferable, if indicated and possible. A period of about 3 to 4 hours (one half-time for renal elimination, ordinarily) should elapse after the last IV dose before administering the first dose of procainamide tablets or capsules.

### TABLE 3 Dilutions and Rates for IV Infusions* Procainamide HCl Injection

<table>
<thead>
<tr>
<th>Final Concentration</th>
<th>Infusion Volume†</th>
<th>Procainamide To Be Added</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Loading Infusion</td>
<td>20 mg/ml</td>
<td>50 ml</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Maintenance</td>
<td>2 mg/ml or</td>
<td>500 ml</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Infusion</td>
<td>4 mg/ml</td>
<td>250 ml</td>
<td>1000 mg</td>
</tr>
</tbody>
</table>

The maintenance infusion rates are calculated to deliver 2-6 mg/min depending on body weight, renal elimination rate and steady-state plasma level needed to maintain control of the arrhythmia*.

The 4 mg/ml maintenance concentration may be preferred if total infusion volume is to be limited.

* Please see text under DOSAGE AND ADMINISTRATION for further details. The flow rate of any IV Procainamide infusion must be monitored closely to avoid transientsly high plasma levels and possible hypotension (see PRECAUTIONS).
† All infusions should be made up to final volume with 5% dextrose injection.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.