Isoproterenol Hydrochloride

**Categories:**

**Ingredients:** Isoproterenol Hydrochloride.

**Indications:** Bronchitis, chronic; Emphysema; Asthma; Heart failure, congestive; Heart block; Cardiac arrest; Shock, hypovolemic; Adams-Stokes; Bronchospasm, secondary to anesthesia; Shock, cardiogenic; Shock, septic.

**Off-label Indications:** Not clinically relevant: Coronary Artery Disease (diagnosis); Pulmonary Embolism (to reverse cardiac output).

**Pregnancy Category C.**

**FDA Approved 1947-11-01.**

**Drug Class:** Adrenergic agonists; Bronchodilators.

**Brand Names:** Isolin (India); Isoprenalin (Sweden); Isuprel HCl (US, Belgium, France, Hong-kong, Thailand); Isuprel Mistometer (Bahrain, Cyprus, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Libya, Oman, Qatar, Republic-of-Yemen, Saudi-Arabia, Syria, United-Arab-Emirates, US); Isuprel Nebulimetro (Peru); Proternol L (Taiwan); Saventrine (Finland, Greece, Singapore). (International brand names outside U.S. in italics)

**Description:**

Chemically, isoproterenol hydrochloride is 3,4-dihydroxy-α-[(isopropylamino) methyl]-benzyl alcohol hydrochloride, a synthetic sympathomimetic amine that is structurally related to epinephrine but acts almost exclusively on beta receptors.

Isoproterenol hydrochloride is a racemic compound with a molecular weight of 247.72 and the molecular formula C_{11}H_{17}NO_3·HCl.

**Injection**

Each milliliter of the sterile 1:5000 Isuprel solution contains:

- Isoproterenol hydrochloride injection 0.2 mg
- Lactic acid 0.12 mg
- Sodium chloride 7.0 mg
- Sodium lactate 1.8 mg
- Sodium metabisulfite (as preservative) 1.0 mg
- Water for injection qs ad 1.0 ml

The pH is adjusted between 3.5 and 4.5 with hydrochloric acid. The air in the ampuls has been displaced by nitrogen gas.

The sterile 1:5000 solution can be administered by intravenous, intramuscular, subcutaneous, or intracardiac routes.

**Storage**

Store in a cool place between 8-15°C (46-50°F).

Do not use if the injection is pinkish to brownish in color or contains a precipitate.

**Inhalation Aerosol**

Isuprel Mistometer is a beta agonist sympathomimetic bronchodilator. It is a complete nebulizing unit consisting of a plastic-coated vial of aerosol solution, detachable plastic mouthpiece with built-in nebulizer, and protective cap. The vial contains isoproterenol hydrochloride 0.25% (w/w) with inert ingredients of alcohol 33% (w/w) and ascorbic acid 0.1% (w/w) and, as propellants, dichlorodifluoromethane and dichlorotetrafluoroethane.
The contents permit the delivery of not less than 200 actuations from the 11.2 g (10 ml) vial and not less than 300 actuations from the 16.8 (15 ml) vial. The Mistometer delivers a measured dose of 131 μg of the bronchodilator in a fine, even mist for inhalation.

**Storage**

Store at controlled room temperature 15°C to -30°C (59-86°F).

**Inhalation Solution**

Isuprel hydrochloride, brand of isoproterenol inhalation solution, is a beta agonist sympathomimetic bronchodilator.

**Solution 1:200:** Contains isoproterenol hydrochloride 5 mg/ml. *Inactive Ingredients:* Chlorobutanol 0.5% and sodium metabisulfite 0.3% as preservatives, citric acid, glycerin, purified water, and sodium chloride.

**Solution 1:100:** Contains isoproterenol hydrochloride 10 mg/ml. *Inactive Ingredients:* Chlorobutanol 0.5% and sodium metabisulfite 0.3% as preservatives, citric acid, purified water, saccharin sodium, sodium chloride, and sodium citrate.

Isoproterenol hydrochloride is soluble in water (1 g isoproterenol hydrochloride dissolves in 3 ml H₂O). The solutions have a pH range of 3-4.5.

The air in the bottles has been displaced by nitrogen gas.

**Storage**

Protect from light. Do not use the inhalation solution of their color are pinkish to brownish or if they contain a precipitate. Although solutions of isoproterenol HCl left in nebulizers will remain clear and potent for many days, for sanitary reasons it is recommended that they be changed daily.

Store at controlled room temperature 15-30°C (59-86°F).

**CLINICAL PHARMACOLOGY:**

**Injection**

Isoproterenol HCl injection acts primarily on the heart and on smooth muscle of bronchi, skeletal muscle vasculature, and alimentary tract. The positive inotropic and chronotropic actions of the drug result in an increase in minute blood flow. There is an increase in heart rate, an approximately unchanged stroke volume, and an increase in ejection velocity. The rate of discharge of cardiac pacemakers is increased with isoproterenol HCl injection. Venous return to the heart is increased through a decreased compliance of the venous bed. Systemic resistance and pulmonary vascular resistance are decreased, and there is an increase in coronary and renal blood flow. Systolic blood pressure may increase and diastolic blood pressure may decrease. Mean arterial blood pressure is usually unchanged or reduced. The peripheral and coronary vasodilating effects of the drug may aid tissue perfusion.

Isoproterenol HCl injection relaxes most smooth muscle, the most pronounced effect being on bronchial and gastrointestinal smooth muscle. It produces marked relaxation in the smaller bronchi and may even dilate the trachea and main bronchi past the resting diameter.

Isoproterenol HCl injection is metabolized primarily in the liver by COMT. The duration of action of isoproterenol HCl injection may be longer than epinephrine, but it is still brief.

**Inhalation Aerosol and Inhalation Solution**

Isoproterenol HCl relaxes bronchial spasm and facilitates expectoration of pulmonary secretions by acting almost exclusively on beta receptors. It is frequently effective when epinephrine and other drugs fail, and it has a wide margin of safety.
Isoproterenol HCl is readily absorbed when given as an aerosol. It is metabolized primarily in the liver and other tissues by catechol-0-methyltransferase (COMT).

Recent studies in laboratory animals (minipigs, rodents, and dogs) recorded the occurrence of cardiac arrhythmias and sudden death (with histologic evidence of myocardial necrosis) when beta agonists and methylxanthines were concomitantly administered. The significance of these findings when applied to human usage is currently unknown.

**INDICATIONS AND USAGE:**

**Injection:**

*Isoproterenol* HCl injection is indicated:

- For mild or transient episodes of heart block that do not require electric shock or pacemaker therapy.
- For serious episodes of heart block and Adams-Stokes attacks (except when caused by ventricular tachycardia or fibrillation). (See CONTRAINDICATIONS)
- For use in cardiac arrest until electric shock or pacemaker therapy, the treatments of choice, is available. (See CONTRAINDICATIONS)
- For bronchospasm occurring during anesthesia.
- As an adjunct to fluid and electrolyte replacement therapy and the use of other drugs and procedures in the treatment of hypovolemic and septic shock, low cardiac output (hypoperfusion) states, congestive heart failure, and cardiogenic shock. (See WARNINGS)

**Inhalation Aerosol and Inhalation Solution**

*Isoproterenol* HCl is indicated for the relief of bronchospasm associated with acute and chronic asthma and reversible bronchospasm which may be associated with chronic bronchitis or emphysema.

**CONTRAINDICATIONS:**

**Injection**

Use of *isoproterenol* HCl injection is contraindicated in patients with tachyarrhythmias; tachycardia or heart block caused by digitalis intoxication; ventricular arrhythmias which require inotropic therapy; and angina pectoris.

**Inhalation Aerosol and Inhalation Solution**

Use of *isoproterenol* in patients with preexisting cardiac arrhythmias associated with tachycardia is generally considered contraindicated because the cardiac stimulant effect of the drug may aggravate such disorders. The use of this medication is contraindicated in those patients who have a known hypersensitivity to *isoproterenol* or to any of the other components of this drug.

**WARNINGS:**

**Injection**

*Isoproterenol* HCl injection, by increasing myocardial oxygen requirements while decreasing effective coronary perfusion, may have a deleterious effect on the injured or failing heart. Most experts discourage its use as the initial agent in treating cardiogenic shock following myocardial infarction. However, when a low arterial pressure has been elevated by other means, *isoproterenol* HCl injection may produce beneficial hemodynamic and metabolic effects.

In a few patients, presumably with organic disease of the AV node and its branches, *isoproterenol* HCl injection has paradoxically been reported to worsen heart block or to precipitate Adams-Stokes attacks during normal sinus rhythm or transient heart block.

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 nonasthmatic people.

**Inhalation Solution**

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 nonasthmatic people.

Excessive use of an adrenergic aerosol should be discouraged as it may lose its effectiveness.

**Isoproterenol** administration as a solution for nebulization has been associated with a decrease in arterial $pO_2$ in asthmatic patients as a result of ventilation-perfusion abnormalities despite improvement in airway obstruction. The clinical significance of this relative hypoxemia is unclear.

As with other inhaled beta adrenergic agonists, **isoproterenol** HCl can produce paradoxical bronchospasm, that can be life threatening. If this occurs, the product should be discontinued immediately and alternative therapy instituted.

Deaths have been reported following excessive use of **isoproterenol** inhalation preparations and the exact cause is unknown. Cardiac arrest was noted in several instances. It is therefore essential that the physician instruct the patient in the need for further evaluation if his/her asthma worsens.

**Inhalation Aerosol**

Excessive use of an adrenergic aerosol should be discouraged as it may lose its effectiveness.

In patients with status asthmaticus and abnormal blood gas tensions, improvement in vital capacity and in blood gas tensions may not accompany apparent relief of bronchospasm. Facilities for administering oxygen mixtures and ventilatory assistance are necessary for such patients.

Occasional patients have been reported to develop severe paradoxical airway resistance with repeated, excessive use of **isoproterenol** inhalation preparations. The cause of this refractory state is unknown. It is advisable that in such instances the use of this preparation be discontinued immediately and alternative therapy instituted, since in the reported cases the patients did not respond to other forms of therapy until the drug was withdrawn.

Deaths have been reported following excessive use of **isoproterenol** inhalation preparations and the exact cause is unknown. Cardiac arrest was noted in several instances. It is therefore essential that the physician instruct the patient in the need for further evaluation if his/her asthma worsens.

**PRECAUTIONS:**

**General Injection**

**Isoproterenol** HCl injection should generally be started at the lowest recommended dose. This may be gradually increased if necessary while carefully monitoring the patient. Doses sufficient to increase the heart rate to more than 130 beats per minute may increase the likelihood of inducing ventricular arrhythmias. Such increases in heart rate will also tend to increase cardiac work and oxygen requirements which may adversely affect the failing heart or the heart with a significant degree of arteriosclerosis.

Particular caution is necessary in administering **isoproterenol** HCl injection to patients with coronary artery disease, coronary insufficiency, diabetes, hyperthyroidism, and sensitivity to sympathomimetic amines.

Adequate filling of the intravascular compartment by suitable volume expanders is of primary importance in most cases of shock and should precede the administration of vasoactive drugs. In patients with normal cardiac function, determination of central venous pressure is a reliable guide during volume replacement. If evidence of hypoperfusion persists after adequate volume replacement, **isoproterenol** HCl injection may be given.
In addition to the routine monitoring of systemic blood pressure, heart rate, urine flow, and the electrocardiograph, the response to therapy should also be monitored by frequent determination of the central venous pressure and blood gases. Patients in shock should be closely observed during isoproterenol HCl injection administration. If the heart rate exceeds 110 beats per minute, it may be advisable to decrease the infusion rate or temporarily discontinue the infusion. Determinations of cardiac output and circulation time may also be helpful. Appropriate measures should be taken to ensure adequate ventilation. Careful attention should be paid to acid-base balance and to the correction of electrolyte disturbances. In cases of shock associated with bacteremia, suitable antimicrobial therapy is, of course, imperative.

**Inhalation Aerosol**

**Isoproterenol** should be used with caution in patients with cardiovascular disorders including coronary insufficiency, diabetes, or hyperthyroidism, and in persons sensitive to sympathomimetic amines.

A single treatment with the isoproterenol HCl aerosol is usually sufficient for controlling isolated attacks of asthma.

Any patient who requires more than 3 aerosol treatments within a 24 hour period should be under the close supervision of a physician. Further therapy with the bronchodilator aerosol alone is inadvisable when 3-5 treatments within 6-12 hours produce minimal or no relief.

**Inhalation Solution**

**Isoproterenol** HCl, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension; in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines. Clinically significant changes in systolic and diastolic blood pressure have been seen in some patients after use of any beta adrenergic bronchodilator.

When compressed oxygen is employed as the aerosol propellant, the percentage of oxygen used should be determined by the patient's individual requirements to avoid depression of respiratory drive.

Any patient who requires more than 3 aerosol treatments within a 24 hour period should be under the close supervision of a physician. Further therapy with the bronchodilator aerosol alone is inadvisable when 3-5 treatments within 6-12 hours produce minimal or no relief.

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

Long-term studies in animals to evaluate the carcinogenic potential of isoproterenol HCl have not been done. Mutagenic potential and effect on fertility have not been determined. There is no evidence from human experience that isoproterenol HCl injection may be carcinogenic or mutagenic or that it impairs fertility.

**Pregnancy Category C**

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

**Nursing Mothers**

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when isoproterenol HCl is administered to a nursing woman.

**Information for the Patient Inhalation Aerosol**

Do not inhale more often than directed by your physician. Read instructions enclosed with the prescription before using. Do not exceed the dose prescribed by your physician. If difficulty in breathing persists, contact your physician immediately. Avoid spraying in eyes. Contents under pressure. Do not break or incinerate. Do not store at temperatures above 120°F. Keep out of reach of children.
**Pediatric Use Inhalation Aerosol and Inhalation Solution**

In general, the technique of isoproterenol HCl aerosol and isoproterenol HCl solution in administration to children is similar to that of adults, since children's smaller ventilatory exchange capacity automatically provides proportionally smaller aerosol intake. However, it is generally recommended that the 1:200 solution (rather than the 1:100) be used for an acute attack of bronchospasm, and no more than 0.25 ml of the 1:200 solution should be used for each 10-15 minute programmed treatment in chronic bronchospastic disease.

**INTERACTIONS:**

**Injection**

Isoproterenol HCl injection and epinephrine should not be administered simultaneously because both drugs are direct cardiac stimulants and their combined effects may induce serious arrhythmias. The drugs may, however, be administered alternately provided a proper interval has elapsed between doses.

Isoproterenol HCl should be used with caution, if at all, when potent inhalational anesthetics such as halothane are employed because of potential to sensitize the myocardium to effects of sympathomimetic amines.

**Inhalation Aerosol**

Epinephrine should not be administered concomitantly with isoproterenol HCl, as both drugs are direct cardiac stimulants and their combined effects may induce serious arrhythmia. If desired they may, however, be alternated, provided an interval of at least 4 hours has elapse.

**Inhalation Solution**

Other sympathomimetic aerosol bronchodilators or epinephrine should not be used concomitantly with isoproterenol HCl. If additional adrenergic drugs are to be administered by any route to the patient using isoproterenol HCl, they should be used with caution to avoid deleterious cardiovascular effects.

Beta adrenergic agonists should be administered with caution to patients being treated with MAO inhibitors or tricyclic antidepressants since the action of the beta adrenergic agonists on the vascular system may be potentiated.

Beta receptor blocking agents and isoproterenol HCl inhibit the effects of each other.

**ADVERSE REACTIONS:**

**Injection**

The following reactions to isoproterenol HCl have been reported:

**CNS:** Nervousness, headache, dizziness.

**Cardiovascular:** Tachycardia, palpitations, angina, Adams-Stokes attacks, pulmonary edema, hypertension, hypotension, ventricular arrhythmias, tachyarrhythmias.

In a few patients, presumably with organic disease of the AV node and its branches, isoproterenol HCl injection has been reported to precipitate Adams-Stokes seizures during normal sinus rhythm or transient heart block.

**Other:** Flushing of the skin, sweating, mild tremors, weakness.

**Inhalation Aerosol and Inhalation Solution**

The mist from the isoproterenol HCl aerosol contains alcohol but is generally very well tolerated. An occasional patient may experience some transient throat irritation which has been attributed to the alcohol content.

Serious reactions to isoproterenol HCl are infrequent. The following reactions, however, have been reported:

**CNS:** Nervousness, headache, dizziness, weakness.

**Gastrointestinal:** Nausea, vomiting.
Cardiovascular: Tachycardia, palpitations, precordial distress, angina-type pain.
Other: Flushing of the skin, tremor, and sweating.

The inhalation route is usually accompanied by a minimum of side effects. These untoward reactions disappear quickly and do not as a rule, inconvenience the patient to the extent that the drug must be discontinued. No cumulative effects have been reported.

OVERDOSAGE:

Injection

The acute toxicity of isoproterenol HCl in animals is much less than that of epinephrine. Excessive doses in animals or man can cause a striking drop in blood pressure, and repeated large doses in animals may result in cardiac enlargement and focal myocarditis.

In case of accidental overdosage as evidenced mainly by tachycardia or other arrhythmias, palpitations, angina, hypotension, or hypertension, reduce rate of administration or discontinue isoproterenol HCl injection until patient's condition stabilizes. Blood pressure, pulse, respiration, and EKG should be monitored.

It is not known whether isoproterenol HCl is dialyzable.

The oral LD_{50} of isoproterenol HCl in mice is 3850 mg/kg ± 1190 mg/kg of pure drug in solution.

Inhalation Aerosol and Inhalation Solution

Overdosage of isoproterenol HCl may produce signs and symptoms typical of excessive sympathomimetic effects, including tachycardia, palpitations, nervousness, nausea, and vomiting. Excessive use of adrenergic aerosols may result in loss of effectiveness or severe paradoxical airway resistance. Cardiac arrest has been noted in several instances. In all cases of overdose or excessive use of isoproterenol HCl, the drug should be discontinued immediately and vital functions supported until the patient is stabilized. It is not known whether isoproterenol HCl is dialyzable.

The acute oral LD_{50} in mice is 3850 mg/kg ± 1190 mg/kg of pure drug in solution (isoproterenol HCl). In dogs, the toxic dose is 1,000 times the therapeutic dose. Converted to the amount used clinically in man, this would be about 2,500 times the therapeutic dose.

DOSAGE AND ADMINISTRATION:

Injection

Isoproterenol HCl injection 1:5000 should generally be started at the lowest recommended dose and the rate of administration gradually increased if necessary while carefully monitoring the patient. The usual route of administration is by intravenous infusion or bolus intravenous injection. In dire emergencies, the drug may be administered by intracardiac injection. If time is not of the utmost importance, initial therapy by intramuscular or subcutaneous injection is preferred (see TABLE 1).

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Preparation of Dilution</th>
<th>Initial Dose</th>
<th>Subsequent Dose Range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus intravenous injection</td>
<td>Dilute 1 ml (0.2 mg) to 10 ml with sodium chloride injection, or 5% dextrose injection</td>
<td>0.02-0.06 mg (1-3 ml of diluted solution)</td>
<td>0.01-0.2 mg (0.5-10 ml of diluted solution)</td>
</tr>
<tr>
<td>Intravenous infusion</td>
<td>Dilute 10 ml (2 mg) in 500 ml of 5% dextrose injection</td>
<td>5 μg/min. (1.25 ml of diluted solution per minute)</td>
<td></td>
</tr>
<tr>
<td>Intramuscular</td>
<td>Use Solution 1:5000 undiluted</td>
<td>0.2 mg (1 ml)</td>
<td>0.02-1 mg (0.1-5 ml)</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>Use Solution 1:5000 undiluted</td>
<td>0.2 mg (1 ml)</td>
<td>0.15-0.2 mg (0.75-1 ml)</td>
</tr>
</tbody>
</table>
TABLE 1 Recommended Dosage for Adults With Heart Block, Adams-Stokes Attacks, and Cardiac Arrest

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Preparation of Dilution</th>
<th>Initial Dose</th>
<th>Subsequent Dose Range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracardiac</td>
<td>Use Solution 1:5000 undiluted</td>
<td>0.02 mg (0.1 ml)</td>
<td></td>
</tr>
</tbody>
</table>

* Subsequent dosage and method of administration depend on the ventricular rate and the rapidity with which the cardiac pacemaker can take over when the drug is gradually withdrawn.

There are no well-controlled studies in children to establish appropriate dosing; however, the American Heart Association recommends an initial infusion rate of 0.1 μg/kg/min, with the usual range being 0.1-1.0 μg/kg/min (see TABLE 2).

TABLE 2 Recommended Dosage for Adults With Shock and Hypoperfusion States

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Preparation of Dilution*</th>
<th>Infusion Rate†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous infusion</td>
<td>Dilute 5 ml (1 mg) in 500 ml of 5% dextrose injection</td>
<td>0.5-5 μg/min (0.25-2.5 ml of diluted solution)</td>
</tr>
</tbody>
</table>

* Concentrations up to 10 times greater have been used when limitation of volume is essential.
† Rates over 30 μg/min have been used in advanced stages of shock. The rate of infusion should be adjusted on the basis of heart rate, central venous pressure, systemic blood pressure, and urine flow. If the heart rate exceeds 110 beats per minute, it may be advisable to decrease or temporarily discontinue the infusion (see TABLE 3).

TABLE 3 Recommended Dosage for Adults With Bronchospasm Occurring During Anesthesia

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Preparation of Dilution</th>
<th>Initial Dose</th>
<th>Subsequent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus intravenous injection</td>
<td>Dilute 1 ml (0.2 mg) to 10 ml with sodium chloride injection, or 5% dextrose injection</td>
<td>0.01-0.02 mg (0.5-1 ml of diluted solution)</td>
<td>The initial dose may be repeated when necessary</td>
</tr>
</tbody>
</table>

Inhalation Aerosol Acute Bronchial Asthma

Hold the aerosol in an inverted position. Close lips and teeth around open end of mouthpiece. Breathe out, expelling as much air from the lungs as possible; then inhale deeply while pressing down on the bottle to activate spray mechanism. Try to hold breath for a few seconds before exhaling. Wait one full minute in order to determine the effect before considering a second inhalation. A treatment may be repeated up to 5 times daily if necessary. (See PRECAUTIONS)

If carefully instructed, children quickly learn to keep the stream of mist clear of the teeth and tongue, thereby assuring inhalation into the lungs. Occlusion of the nares of very young children may be advisable to make inhalation certain.

Warm water should be run through the mouthpiece once daily to wash it and prevent clogging.

The mouthpiece may also be sanitized by immersion in alcohol.

Bronchospasm in Chronic Obstructive Lung Disease

The aerosol provides a convenient aerosol method for delivering isoproterenol HCl. The treatment described above for Acute Bronchial Asthma may be repeated at not less than 3-4 hour intervals as part of a programmed regimen of treatment of obstructive lung disease complicated by a reversible bronchospastic component. One application from the aerosol may be regarded as equivalent in effectiveness to 5-7 operations of a hand-bulb nebulizer using a 1:100 solution.

Children's Dosage

In general, the technique of isoproterenol HCl aerosol in administration to children is similar to that of adults, since children's smaller ventilatory exchange capacity automatically provides proportionally smaller aerosol intake.

Inhalation Solution
Isoproterenol HCl HCl solutions can be administered as an aerosol mist by hand-bulb nebulizer, compressed air or oxygen operated nebulizer, or by intermittent positive pressure breathing (IPPB) devices. The method of delivery, and the treatment regimen employed in the management of the reversible bronchospastic element accompanying bronchial asthma, chronic bronchitis, and chronic obstructive lung diseases, will depend on such factors as the severity of the bronchospasm, patient age, tolerance to the medication, complicating cardiopulmonary conditions, and whether therapy is for an intermittent acute attack of bronchospasm or is part of a programmed treatment regimen for constant bronchospasm.

**Acute Bronchial Asthma Hand-Bulb Nebulizer**

Depending on the frequency of treatment and the type of nebulizer used, a volume of solution of isoproterenol HCl, sufficient for not more than one day's treatment, should be placed in the nebulizer using the dropper provided. In time, the patient can learn to adjust the volume required. For adults and children, the 1:200 solution is administered by hand-bulb nebulization in a dosage of 5-15 deep inhalations (using an all glass or plastic nebulizer). In adults, the 1:100 solution may be used if a stronger solution seems to be indicated. The dose is 3-7 deep inhalations. If after about 5-10 minutes inadequate relief is observed, these doses may be repeated one more time. If the acute attack recurs, treatments may be repeated up to 5 times daily if necessary. (See PRECAUTIONS)

**Bronchospasm in Chronic Obstructive Lung Disease Hand-Bulb Nebulizer**

A solution of 1:200 or 1:100 of isoproterenol HCl may be administered daily at not less than 3-4 hour intervals for subacute bronchospastic attacks or as part of a programmed treatment regimen in patients with chronic obstructive lung disease with a reversible bronchospastic component. An adequate dose is usually 5-15 deep inhalations, using the 1:200 solution. Some patients with severe attacks of bronchospasm may require 3-7 deep inhalations using the 1:100 solution of isoproterenol HCl.

**Nebulization by Compressed Air or Oxygen**

A method often used in patients with severe chronic obstructive lung disease is to deliver the isoproterenol mist in more dilute form over a longer period of time. The purpose is, not so much to increase the dose supplied, as to achieve progressively deeper bronchodilation and thus insure that the mist achieves maximum penetration of the finer bronchioles. In this method, 0.5 ml of a 1:200 solution of isoproterenol HCl is diluted to 2 ml to 2.5 ml with water or isotonic saline to achieve a use concentration of 1:800 to 1:1000. If desired, 0.25 ml of the 1:100 solution may be similarly diluted to achieve the same use concentration. The diluted solution is placed in a nebulizer (e.g., DeVilbiss #640 unit) connected to either a source of compressed air or oxygen. The flow rate is regulated to suit the particular nebulizer so that the diluted solution of isoproterenol HCl will be delivered over approximately 10-20 minutes. A treatment may be repeated up to 5 times daily if necessary. Although the total delivered dose of isoproterenol HCl is somewhat higher than with the treatment regimen employing the hand-bulb nebulizer, patients usually tolerate it well because of the greater dilution and longer application-time factors.

**Intermittent Positive Pressure Breathing (IPPB)**

Diluted solutions of 1:200 or 1:100 of isoproterenol HCl are used in a programmed regimen for the treatment of reversible bronchospasm in patients with chronic obstructive lung disease who require intermittent positive pressure breathing therapy. These devices generally have a small nebulizer, usually of 3 ml to 5 ml capacity, on a patient-operated side arm. The effectiveness of IPPB therapy is greatly enhanced by the simultaneous use of aerosolized bronchodilators. As with compressed air or oxygen operated nebulizers, the usual regimen is to place 0.5 ml of 1:200 solution of isoproterenol HCl diluted to 2 ml to 2.5 ml with water or isotonic saline in the nebulizer cup and follow the IPPB manufacturer's operating instructions. IPPB-bronchodilator treatments are usually administered over 15-20 minutes, up to 5 times if necessary.

**Children's Dosage**

In general, the technique of isoproterenol HCl solution in administration to children is similar to that of adults, since children's smaller ventilatory exchange capacity automatically provides proportionally smaller aerosol intake. However, it is generally recommended that the 1:200 solution (rather than the 1:100) be used for an acute attack of bronchospasm, and no more than 0.25 ml of the 1:200 solution should be used for each 10-15 minute programmed treatment in chronic bronchospastic disease.