

## **PRESCRIBING INFORMATION**

**Pr ISOPROTERENOL**

**Isoproterenol HCl Injection USP**

**1: 5 000 (0.2 mg/mL)**

Sandoz Canada Inc.  
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**Isoproterenol**  
**(Isoproterenol HCl Injection USP)**  
**1: 5 000 (0.2 mg/mL)**

**THERAPEUTIC CLASSIFICATION**

Sympathomimetic

**INDICATIONS**

Symptomatic relief of bronchial asthma and in cases of emphysema, bronchitis and other chronic bronchopulmonary disorders in which bronchospasm is a complicating factor.

Injectable form is particularly suitable for the treatment and prevention of (1) Adams-Stokes syndrome and other episodes of heart-block, except when caused by ventricular tachycardia of fibrillation (2) cardiac arrest (3) carotid sinus hypersensitivity (4) ventricular tachycardia and fibrillation (5) laryngobronchospasm during anesthesia (6) as adjunctive therapy in shock.

**CONTRAINDICATIONS**

Patients with tachyarrhythmias; tachycardia of heart-block caused by digitalis intoxication; ventricular arrhythmias which require inotropic therapy and angina pectoris. Do not administer concomitantly with epinephrine. May be used alternately with epinephrine if indicated, provided a 4-hour interval elapses.

**PRECAUTIONS**

Use with caution in patients sensitive to sympathomimetic amines and in the presence of hypertension, cardiovascular disorders (including coronary artery disease and coronary insufficiency), diabetes, hyperthyroidism, in patients with a potential for cardiac arrhythmias and in those patients receiving MAO inhibitors. Potent inhalational anesthetics such as halothane may sensitize the myocardium to effects of sympathomimetic amines.

Rarely, patients have been reported to develop severe paradoxical airway resistance with repeated, excessive use of aerosol preparations containing sympathomimetic amines. The cause of this refractory state is unknown. It is advisable that in such instances the use of the aerosol be discontinued immediately and alternative therapy instituted, since in the reported cases the patients did not respond to other forms of therapy until the aerosol was withdrawn. Deaths have been reported following excessive use of aerosol preparations containing sympathomimetic amines, the exact cause of which is unknown. Cardiac arrest was noted in several instances.

Close supervision and careful adjustment of dosages are required when isoproterenol is given with tricyclic antidepressants, since the effect of the two drugs may be cumulative.

In neutral or alkaline solution, isoproterenol may become red on exposure to air. Accordingly, the saliva or sputum may appear pink or red in colour after oral inhalation of the drug. This is not harmful but should be explained to patients to allay possible apprehension or confusion with bleeding.

Isoproterenol 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 injection may produce beneficial hemodynamic and metabolic effects.

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

May contain sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in 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.

Isoproterenol 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/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.

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 injection may be given.

In addition to the routine monitoring of systemic blood pressure, heart rate, urine flow, and the ECG, 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 hydrochloride injection administration. 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.

## ADVERSE EFFECTS

The following reactions to isoproterenol injection 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 hydrochloride 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, swelling of the parotids with prolonged use, nausea and vomiting.

## OVERDOSAGE: SYMPTOMS AND TREATMENT

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 hydrochloride injection until patient's condition stabilizes. Blood pressure, pulse, respiration, and ECG should be monitored.

It is not known whether isoproterenol is dialysable.

## DOSAGE

### Parenteral

**Cardiac Disorders:** SC or IM injection of 200 mcg (1 mL of 1:5 000 solution), IV injection of 20 mcg (0.1 mL of 1:5 000 solution). IV infusion of solution containing 1 mg in 200 mL of 5% glucose at a rate of 1 mL (5 mcg) per minute. Intracardiac injection of 20 mcg (0.1 mL of 1:5 000 solution).

**Laryngobronchospasm:** IV injection from 10 to 20 mcg (0.5 to 1 mL of 1:50 000 solution). To prepare 1:50 000 solution dilute 1 mL of 1:5 000 solution to 10 mL with 5% dextrose in water.

**Adjunctive Rherapy in Shock:** IV infusion of 1 mg in 500 mL of 5% dextrose in water administered (after initial 5 mL dose of solution) at a rate of 0.5 mcg to 5 mcg/minute.

Infusion rate (up to 30 mcg/minute in advanced shock) 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/minute, it may be advisable to decrease the infusion rate or temporarily discontinue the infusion.

## **SUPPLIED**

Isoproterenol Hydrochloride 1:5 000 (0.2 mg/mL) in sterile aqueous solution.

Each mL of Isoproterenol Hydrochloride 1:5 000 (0.2 mg/mL) contains isoproterenol hydrochloride 0.2 mg, lactic acid 0.1 mg, sodium lactate 1.8 mg, sodium metabisulfite, sodium chloride for isotonicity, hydrochloric acid to adjust pH and water for injection.

Isoproterenol 1: 5 000 (0.2 mg/mL) is available in 1 mL and 5 mL ampoules, boxes of 10.

Store between 15 and 30°C. Protect from light. Discard unused portion.

The injection is not to be used if the colour is pinkish or darker than slightly yellow or if it contains a precipitate.