PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr] ORCIPRENALINE

Orciprenaline Sulfate Syrup

Syrup 2 mg/mL and Oral

House Standard

Beta-Adrenergic Agonist
Bronchodilator

AA PHARMA INC.
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RECENT MAJOR LABEL CHANGES

7 Warnings and Precautions	10/2022

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ORCIPRENALINE (Orciprenaline Sulfate Syrup) has been found useful in the following conditions:

- Bronchial asthma
- Chronic bronchitis
- Pulmonary emphysema

Orciprenaline sulfate may also be useful when bronchospasm is present in sarcoidosis, silicosis, carcinoma of the lung and tuberculosis.

Limitation of use: Orciprenaline should not be used for the treatment of acute episodes of bronchospasm.

1.1 Pediatrics

Pediatrics (<4 years of age): No data in patients less than 4 years of age are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use in patients less than 4 years of age (See 4 DOSAGE AND ADMINISTRATION).

1.2 Geriatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

2 CONTRAINDICATIONS

- ORCIPRENALINE is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- ORCIPRENALINE is contraindicated in patients with a known sensitivity to this drug or other sympathomimetic amines.
- ORCIPRENALINE is contraindicated in patients with hypertrophic obstructive cardiomyopathy and cardiac arrhythmias associated with tachycardia.
- ORCIPRENALINE is contraindicated in concomitant use with beta–adrenergic blocking agents, such as propranolol.

As a tocolytic in patients at risk of premature labour or threatened abortion.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- The dosage should be individualized, and the patient's response should be monitored by the prescribing physician on an ongoing basis.

Asthma

- Like other beta-agonists, ORCIPRENALINE should not be used without appropriate concomitant anti-inflammatory therapy.
- If a previously effective dosage regimen fails to provide the usual relief, or the effects of a dose last for less than three hours, patients should seek prompt medical advice as this is a sign of seriously worsening asthma that requires reassessment of therapy.
- As there may be adverse effects associated with excessive dosing, the dosage or frequency of administration should not be increased.
- The effect of an inhalant bronchodilator may be potentiated by oral administration of 20 mg of orciprenaline sulfate 90 minutes prior to use of the inhalant. No additive effect occurs when the drugs are given in reverse order (see 10.2 Pharmacodynamics).

4.2 Recommended Dose and Dosage Adjustment

The recommended doses of ORCIPRENALINE syrup are:

Adults: Two teaspoons (10 mL) of syrup (20 mg) three or four times daily.

Adolescents 12 to <18 years of age: Two teaspoons (10 mL) of syrup (20 mg) three times daily.

Children 4 to < 12 years of age: One teaspoon (5 mL) of syrup (10 mg) three times daily.

- The maximum daily dose is 80 mg.

4.4 Administration

ORCIPRENALINE syrup should be administered orally. ORCIPRENALINE syrup should be measured by a spoon to ensure the appropriate dose is administered.

4.5 Missed Dose

If a dose of ORCIPRENALINE is missed, it should be taken as soon as the patient remembers. Patients should not take two doses at the same time to make up for a missed dose.

5 OVERDOSAGE

The symptoms of overdosage are those of excess beta stimulation including exaggeration of the known pharmacological effects, i.e. any of the symptoms listed under adverse reactions, the most prominent being tachycardia, palpitation, tremor, hypertension, hypotension, widening of the pulse pressure, anginal pain, arrhythmias, hypokalemia and flushing. Serum potassium levels should be monitored.

Treatment

Treatment should be discontinued and appropriate symptomatic therapy should be considered.

To antagonise the effect of orciprenaline, the judicious use of a cardioselective beta-adrenergic blocking agent (e.g. metoprolol, atenolol, propranolol) may be considered but only under the supervision of a healthcare professional since bronchospasm may be induced. The dose should be adjusted carefully in patients suffering from asthma.

Therapy may include administration of sedative, tranquilizers or in severe cases, intensive therapy.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths and Composition

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Syrup 2 mg/mL	Artificial grape flavour, edetate disodium, glycerin, hydroxyethyl cellulose, methylparaben, propylparaben, purified water and sorbitol.

ORCIPRENALINE (orciprenaline sulfate) syrup is clear and grape–flavoured. Each mL contains 2 mg of active ingredient orciprenaline sulfate.

Available in amber–coloured bottles containing 250 mL of clear syrup.

7 WARNINGS AND PRECAUTIONS

General

ORCIPRENALINE should not be initiated in patients with significantly worsening or acutely deteriorating asthma, which may be life threatening. Like other β_2 agonists, ORCIPRENALINE (orciprenaline sulfate) should not be used on a regular daily basis without appropriate concomitant anti-inflammatory therapy (see 4.1 Dosing Considerations).

Deterioration of asthma

Patients should be advised to seek medical aid in the event that they do not respond to their dose of a rescue medication inhaler (e.g. salbutamol).

In acute tests, orciprenaline sulfate has been shown to have minimal effect on blood pressure and pulse. The drug should be used with care, however, in asthmatic or emphysematous patients who also have systemic hypertension, coronary artery disease, acute and recurring congestive heart failure, diabetes mellitus, glaucoma or hyperthyroidism or in patients sensitive to sympathomimetic amines.

Cardiovascular

Beta-adrenergic agonists may have clinically significant cardiac effects. Orciprenaline is a non-selective beta-adrenergic agonist and may have more cardiac side effects than more selective beta$_2$-adrenergic agonists.

Care should be taken with patients suffering from cardiovascular disorders, especially coronary insufficiency, myocardial insufficiency, cardiac arrhythmias, recent myocardial infarction, severe organic heart and/or other vascular disorders, hypertension, hyperthyroidism phaeochromocytoma or diabetes mellitus.

Endocrine and Metabolism

Potentially serious hypokalemia may result from β_2–agonist therapy, mainly from parenteral and nebulized administration. Particular caution is advised in acute severe asthma as this may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics; the adverse effects of hypokalemia on cardiac rhythm may be exacerbated by hypoxia. It is recommended that serum potassium levels be monitored in such situations. Hypokalemia will increase the susceptibility of digitalis–treated patients to cardiac arrhythmias.

If therapy does not produce a significant improvement or if the patient's condition gets worse, medical advice must be sought in order to determine a new plan of treatment. In the case of acute or rapidly worsening dyspnea, a doctor should be consulted immediately.

Immune

Hypersensitivity

Immediate hypersensitivity reactions may occur after administration of orciprenaline sulfate. Care should be taken in patients who are unusually responsive to sympathomimetic amines.

Respiratory

Deterioration of asthma

Increasing use of $ß_2$–agonists to control symptoms of bronchial obstruction, especially administration on a regular basis or in high amounts, indicates deterioration of asthma control. Under these conditions, the patient's therapy plan has to be revised. It is inadequate simply to increase the use of bronchodilators under these circumstances, in particular over extended periods of time (see 4. DOSAGE AND ADMINISTRATION).

Paradoxical Bronchospasm

Paradoxical bronchospasm may occur with inhaled medications and is characterized by an immediate increase in wheezing after the dose. This should be treated immediately with an alternative presentation or a different fast-acting inhaled bronchodilator to relieve acute asthmatic symptoms. The use of the preparation should be discontinued immediately and alternate therapy instituted. The cause of this refractory state is unknown. It is advisable that in such instances the use of the preparation be discontinued immediately and alternate therapy instituted since, in the reported cases, the patients Fatalities have been reported following excessive use of isoproterenol inhalation preparations and the exact cause is unknown. Cardiac arrest was noted in several instances.

7.1 Special Populations

7.1.1 Pregnant Women

ORCIPRENALINE should not be administered to pregnant women or to women of childbearing potential unless in the opinion of the physician the expected benefits outweigh the possible risks to the fetus. Clinical evidence presently available from the use of ORCIPRENALINE in pregnancy is limited. In rabbits, high oral doses (100 mg/kg) and low subcutaneous doses (0.2 mg/kg) have resulted in malformed offspring in some experiments, but not in others. Studies in the rat, mouse and rhesus monkey have shown no adverse effects on the developing fetus. Other sympathomimetic drugs tested, viz., ephedrine and phenylephrine, produced teratogenic effects in the rabbit when given orally at high doses as did isoproterenol given subcutaneously at low doses. The significance of these findings is not known.

There is no well documented experience in pregnant women. Orciprenaline sulfate should only be used during pregnancy if the potential benefit outweighs the potential risk to the fetus.

Use in labour and delivery

Beta–agonists should be used with caution before and during childbirth in view of their inhibiting effect on uterine contractions. Orciprenaline is contraindicated as a tocolytic in patients at risk of premature labour or threatened abortion.

7.1.2 Breast-feeding

It is not known whether orciprenaline sulfate is excreted in human milk; therefore, orciprenaline sulfate should be used during nursing only if the potential benefit justifies the possible risk to the newborn.

7.1.3 Pediatrics

Pediatrics (< 4 years of age): The safety and efficacy in children below the age of 4 years have not been established.

7.1.4 Geriatrics

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use. As with other beta-agonists, special caution should be observed when using Orciprenaline in elderly patients who have concomitant cardiovascular disease that could be adversely affected by this class of drug.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most frequently observed adverse reactions to orciprenaline sulfate at the recommended dosage include, fine tremor of skeletal muscles, nervousness, headache, dizziness, tachycardia, and palpitations.

As with other beta-mimetics, nausea, vomiting, sweating, weakness and myalgia/muscle cramps may occur. In rare cases decrease in diastolic blood pressure, increase in systolic blood pressure, arrhythmia, particularly after higher doses, may occur.

In rare cases skin reactions or allergic reactions have been reported, especially in hypersensitive patients. There have been isolated cases of anaphylactic or anaphylactoid reactions.

In individual cases psychological alterations have been reported under inhalational therapy with beta-mimetics.

Potentially serious hypokalemia may result from beta$_2$-agonist therapy.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

Sympathomimetics: Concomitant use of orciprenaline sulfate with other sympathomimetic agents is not recommended since the combined use may lead to deleterious cardiovascular effects. If concomitant use is necessary, this should take place only under strict medical supervision.
Beta-adrenergic Blockers: beta-adrenergic blockers may weaken or antagonise the effect of orciprenaline. Therefore, orciprenaline should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use.

Monoamine Oxidase Inhibitors and Tricyclic Antidepressants: Extreme care should be exercised in the concomitant use of orciprenaline sulfate with epinephrine, monoamine oxidase inhibitors or tricyclic antidepressants since the action of beta adrenergic agonists may be enhanced.

Corticosteroids, Methylxanthines and Diuretics: Concomitant treatment with xanthine derivatives, steroids, or non-potassium sparing diuretics may potentiate a possible hypokalemic effect of beta2-agonists (See 7 WARNINGS AND PRECAUTIONS, Cardiovascular). Hypokalemia may increase susceptibility to cardiac arrhythmias in patients treated with digitalis.

Anaesthetics: Inhalation of halogenated hydrocarbon anaesthetics such as halothane, trichloroethylene and enflurane may increase the susceptibility to the cardiovascular effects of beta-agonists.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Orciprenaline sulfate is a bronchodilating agent that acts through stimulation of beta2-adrenergic receptors in bronchial smooth muscle, thereby causing relaxation of bronchial muscle fibres. The bronchospasm associated with various pulmonary diseases - chronic bronchitis, pulmonary emphysema, bronchial asthma, silicosis, tuberculosis, sarcoidosis and carcinoma of the lung, has been successfully reversed by therapy with orciprenaline sulfate.

Orciprenaline is considered a non-selective beta-adrenergic agonist. It is an agonist for beta2-adrenergic receptors in bronchial smooth muscle as well as cardiac beta1-adrenergic receptors. It is less selective for beta2-adrenergic receptors than salbutamol, a beta2-adrenergic agonist, used for the acute relief of bronchospasm.

Receptor sites in the bronchi and bronchioles are somewhat more sensitive to the drug than those in the heart and blood vessels, so that the ratio of bronchodilating to cardiovascular effects is favourable. Consequently, it is usually possible clinically to produce good bronchodilation at dosage levels which are unlikely to cause cardiovascular side effects.

The efficacy of the bronchodilator after both oral and inhalation administration has been demonstrated by pulmonary function studies (spirometry, and by measurement of airways resistance by body plethysmography).

Following oral administration, the effect is usually noted within 30 minutes. The peak effect of bronchodilator activity following orciprenaline sulfate generally occurs within 60 to 90 minutes, and this activity lasts for 3 to 6 hours.

Orciprenaline sulfate taken orally potentiates the action of a bronchodilator inhalant administered 90 minutes later, whereas no additive effect occurs when the drugs are given in reverse order.

Tolerance to the drug during prolonged therapy has not been observed.

10.2 Pharmacodynamics

Bronchodilator Action

In guinea–pigs and dogs, orciprenaline sulfate has a marked relaxing effect on bronchospasm induced by histamine, acetylcholine, or serotonin. When administered orally, orciprenaline sulfate protects guinea–pigs from histamine–induced asthma. In dogs, orciprenaline sulfate is better absorbed and acts longer than isoproterenol. In dogs in which bronchospasm has been induced with morphine or pilocarpine, 1 mg/kg isoproterenol and 30 mg/kg orciprenaline

sulfate administered intravenously, have the same degree of bronchodilator action; however, the effect of orciprenaline sulfate lasts considerably longer than that of isoproterenol.

The efficacy of orciprenaline sulfate has been demonstrated by improvement of flow rates (FEV1, MMFR, MEFR) and airways resistance measurements (body plethysmography). Repeated measurements of pulmonary function made over a 4–hour period showed that orciprenaline sulfate 20 mg orally gives a generally better result regarding duration of action and magnitude of response than placebo, 100 mg methoxyphenamine, 30 mg ephedrine by mouth, or 10 mg isoproterenol sublingually.

Studies have shown that patients with bronchitis and emphysema respond to continuous therapy with orciprenaline sulfate. The frequency and severity of acute attacks decrease, and patients experience relief of wheezing, chest congestion and shortness of breath. A close association is apparent between objective measurements of pulmonary function and the subjective response.

The effect of an inhalant bronchodilator may be potentiated by oral administration of 20 mg of orciprenaline sulfate 90 minutes prior to use of the inhalant. No additive effect occurs when the drugs are given in reverse order. The probable reason for this is that a bronchodilator delivered to the lungs via the vascular system (intravenous or oral medication) acts upon bronchioles whether or not they are occluded. Such an effect causes a wider distribution in the lungs of a subsequently given drug, and consequently the bronchodilation is more intense. Knowledge of this interaction is of value when instructing patients in the combined use of oral orciprenaline sulfate and an inhaled bronchodilator.

Cardiovascular Effects

Orciprenaline sulfate administered intravenously to anesthetized dogs in equivalent bronchodilator doses tends to have less effect on blood pressure and heart rate than isoproterenol. In dogs, with small intravenous doses there is occasionally a fall in diastolic pressure and, because of the increase in the cardiac output, there is an increase in systolic pressure with a consequent increase in pulse pressure. The ratio between intramuscular and oral effects is 1:67 for orciprenaline sulfate and 1:333 for isoproterenol. Thus the oral absorption of orciprenaline sulfate in dogs is approximately 5 times better than that of isoproterenol.

In various isolated heart preparations, orciprenaline sulfate has positive inotropic and chronotropic effects. In the spontaneously beating right atrium (cat) a dose of orciprenaline sulfate 41 times greater than that of isoproterenol is required to achieve the same inotropic effect but with electrically stimulated atrium and papillary muscle, concentrations only 1.2 and 2.7 times greater were required respectively. Thus in heart preparations which lack a pacemaker, the effects of orciprenaline sulfate and isoproterenol are similar whereas when a pacemaker is present, as in the right atrium, the effect of orciprenaline sulfate is much less than that of isoproterenol. It can be concluded that orciprenaline sulfate, like isoproterenol, acts

mainly on the sinus node in the right atrium and that the affinity of orciprenaline sulfate for the pacemaker is appreciably less than that of isoproterenol. In heart preparations which ordinarily do not beat spontaneously, orciprenaline sulfate induced spontaneous activity much less frequently than isoproterenol. In guinea–pigs, doses of orciprenaline sulfate from 1 to 100 mg/kg intravenously failed to induce any cardiac arrhythmia. On the other hand, orciprenaline sulfate provided protection against arrhythmias experimentally induced by adrenaline. For example, 30 minutes to 2 hours after 30-100 mg/kg of orciprenaline sulfate had been administered intravenously, arrhythmias were not induced by doses of adrenaline from 3 to 30 times greater than those which formerly produced arrhythmias.

Although orciprenaline has lower cardiovascular effects than isoproterenol, a non-selective beta-adrenergic agonist, orciprenaline has the potential for more cardiovascular effects than selective beta2-adrenergic agonists, e.g. salbutamol.

Effects on Other Systems

Orciprenaline sulfate produces an inhibitory effect on the smooth muscle of the gastrointestinal tract, as demonstrated by its action on histamine and acetylcholine–induced contractions of the isolated guinea–pig ileum and on serotonin–induced spasm of the rat duodenum. The inhibitory effect on the gastrointestinal tract was further demonstrated by studying charcoal meal progression in the guinea–pig.

A mild mydriatic effect has been shown in mice and on the enucleated eyes of cattle.

10.3 Pharmacokinetics

Absorption

Excretion studies in humans with the orally administered labelled compound have demonstrated that an average of approximately 40% of the drug is absorbed. Animal studies (rat, rabbit and monkey) have also demonstrated good absorption as evidenced by recovery of substantial amounts in the urine.

Distribution:

The concentration of radioactivity in blood plasma was determined in rabbits following intravenous administration of radiolabelled orciprenaline sulfate. Radioactivity decreased in two phases of different velocity. During the first phase, the decrease is linear on the semilogarithmic scale with a half–life of about 40 minutes. This may represent tissue penetration. The second phase is considerably slower and has a half–life of approximately 15 hours.

Metabolism:

The major metabolite in animals is also the conjugated form of the drug.

Elimination

The drug is excreted primarily as glucuronic acid conjugates.

11 STORAGE, STABILITY AND DISPOSAL

ORCIPRENALINE syrup should be stored at room temperature (15 °C to 30 °C).

Protect from light.

Keep out of reach and sight of children.

12 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions for ORCIPRENALINE syrup.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

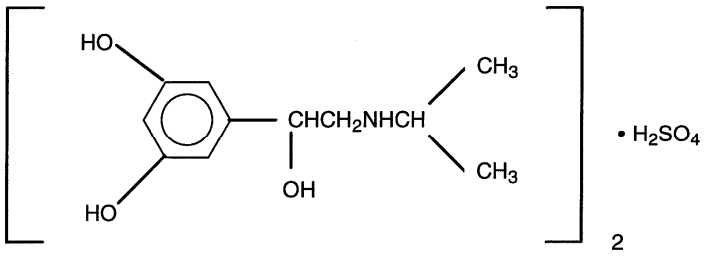
Proper Name: Orciprenaline sulfate

Chemical Names: 1)1,3-Benzenediol,5-[1-hydroxy-2-[1-methylethyl)-amino]ethyl]-,sulfate (2:1)(salt);

2)3,5-Dihydroxy-α–[(iso-propylamino)methyl]benzyl alcohol sulfate (2:1).

Molecular Formula and Molecular Mass: $(C_{11}H_{17}NO_3)_2 \bullet H_2SO_4$ and 520.60

Structural Formula:



Physicochemical properties: White to off–white crystalline powder, freely soluble in water

14 CLINICAL TRIALS

There are no clinical trial data available for this drug product.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology

The toxic effects of orciprenaline sulfate have been studied in 5 species: rat, mouse, rabbit, dog and monkey. In acute and subchronic studies, orciprenaline sulfate was given by various routes

including oral, inhalation, intravenous, intraperitoneal, and subcutaneous and in doses ranging from 0.2 mg to 500 mg/kg.

Acute Toxicity

The following table compares the LD_{50}'s in various species for oral orciprenaline sulfate.

Species	LD_{50} (mg/kg)
Rat	4420-5276
Mouse	4800-8130
Rabbit	3114-5000
Dog	50-900
Monkey	4000

The oral LD_{50} ranges represent values found by different investigators.

In mice, for an oral LD_{50} of 4800 mg/kg, the subcutaneous LD_{50} is 200 mg/kg and the intravenous LD_{50} is 114 mg/kg. Depending upon the species and the dosage, the toxic signs included decreased activity followed by hyperpnea and salivation, which proceeded to ataxia, and finally, prostration or convulsions before death. Animals which survived the toxic dose had uneventful recoveries.

Subchronic Toxicity

Orciprenaline sulfate has been studied for various periods in rats, dogs and monkeys. In rats given up to 25 times (4.5, 13.5, 40.5 mg/kg/day) the recommended maximum human dose orally for 3 months, there were only increases in the weights of the hearts and livers. In dogs given orciprenaline sulfate for 3 months in doses of 6.25, 25 and 100 mg/kg/day, there were no dose–related toxic effects, although one dog in each of the three drug level groups died following the first dose. In monkeys, doses of orciprenaline sulfate of 10, 30 and 100 mg/kg/day for six months had no demonstrable toxic effects and all the animals survived.

Inhalation Toxicity

Hemorrhages occurred in the myocardium and bladder mucosa of 2 of 6 dogs that received 0.5-0.6 mg of orciprenaline sulfate aerosol/kg/day for 3 months. Three of 6 dogs that received a single dose of 11 to 13 mg of drug per kg had endocardial and/or renal hemorrhages; one of these also had a small hemorrhage in the circle of Willis. Petechial hemorrhages were observed in the coronary groove and auricles of a dog that died, and suspicious macroscopic lesions occurred in the hearts of 6 other dogs that received doses of orciprenaline sulfate aerosol ranging from 125 to 455 mg/kg.

Questionable macroscopic lesions also occurred in kidneys and hearts of monkeys given 250-750 mg/kg. However, isoproterenol also causes myocardial hemorrhages and infarcts in dogs and rats. Subcutaneous doses as small as 2.5 and 0.8 mg/kg produced these effects in dogs and rats respectively; minimal hemorrhage–producing doses were not investigated in the canine experiment.

Carcinogenicity

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential.

Teratogenicity

The teratogenicity of orciprenaline sulfate has been studied in rabbits, rats, mice and monkeys. In rabbits and rats, the drug was given orally and parenterally; in mice it was given only parenterally; in monkeys it was given only orally. The results of these studies indicate that orciprenaline sulfate has no appreciable teratogenic effects even at dosages considerably higher than the recommended human dose. At extremely high dosage levels in the rabbit, all sympathomimetic amines studied (ephedrine, isoproterenol, orciprenaline sulfate, and phenylephrine) caused abnormalities such as limb flexures, agenesis of digits, hydrocephalus, agenesis of mouth, cleft palate and polycystic liver, in a proportion of the test animals. At the high dosage levels used in these studies, there was a decreased conception rate suggesting maternal toxicity. There was also suggestive evidence that the pregnant rabbit was more susceptible to the toxic effects which occur at extremely high dosage levels, than non–pregnant animals.

17 SUPPORTING PRODUCT MONOGRAPHS

ORCIPRENALINE (Orciprenaline sulfate syrup 2 mg/ml and oral) Product Monograph APOTEX INC. Date of Revision: September 17, 2021, Control Number: 251291.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]ORCIPRENALINE

Orciprenaline Sulfate Syrup

Read this carefully before you start taking **ORCIPRENALINE** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ORCIPRENALINE**.

What is ORCIPRENALINE used for?

ORCIPRENALINE syrup used in adults and children (4 years of age or older) to treat symptoms from the following lung problems:

- bronchial asthma (widespread narrowing of the airways in the lungs);
- chronic bronchitis (consistent irritation or inflammation of the air tubes in the lungs);
- pulmonary emphysema (airflow blockage in the lungs);
- bronchospasm (reduced airflow from the tightening of the lung muscles) in sarcoidosis (growth of inflammatory cells in the lungs), silicosis (lung inflammation from breathing in silica), lung cancer, or tuberculosis (TB -infection caused by bacteria).

How does ORCIPRENALINE work?

ORCIPRENALINE belongs to a group of medicines called bronchodilators. It relaxes the muscles in the walls of the small air passages in the lungs. This helps to open up the airways so that you can breathe more easily by reducing the frequency and severity of your:

- involuntary lung contraction episodes (bronchospastic attacks), and
- lung problem symptoms (e.g., wheezing, chest congestion and shortness of breath).

What are the ingredients in ORCIPRENALINE?

Medicinal ingredient: Orciprenaline sulfate
Non-medicinal ingredients: Artificial grape flavour, edetate disodium, glycerin, hydroxyethyl cellulose, methylparaben, propylparaben, purified water, and sorbitol.

ORCIPRENALINE comes in the following dosage forms:

Syrup: 2 mg/mL

Do not use ORCIPRENALINE if:

- you are allergic to orciprenaline sulfate or any of the other ingredients in the ORCIPRENALINE.
- you are allergic to a type of medications known as sympathomimetic amines (e.g., epinephrine, norepinephrine, ephedrine, etc.).
- you have heart problems.
- you have hypertrophic obstructive cardiomyopathy (the muscular wall between the two bottom chambers of the heart is thicker than normal and blocks blood flow out of the heart).
- you have abnormal heart rhythms (arrhythmias).
- you are pregnant and are at risk for premature labour or miscarriage.
- you are taking medications known as beta blockers (e.g., propranolol).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ORCIPRENALINE. Talk about any health conditions or problems you may have, including if you:

- are taking anti inflammatory medications,
- have heart problems or blood problems (e.g., arrhythmias, myocardial infarction, heart disorders, and high blood pressure),
- have diabetes,
- have glaucoma,
- have high thyroid hormone levels (hyperthyroidism),
- have phaeochromocytoma (a noncancerous tumor that develops in the adrenal gland),
- are pregnant or planning to become pregnant,
- have asthma,
- are taking medications known as xanthine derivatives, steroids, and diuretics (water pills),
- are breastfeeding or planning to breastfeed. It is not known if ORCIPRENALINE can pass into breast milk.

Other warnings you should know about:

Serious hypokalemia (low levels of potassium in the blood): Treatment with ORCIPRENALINE can cause serious hypokalemia if you have asthma. The risk is higher if you are also taking xanthine derivatives, steroids, and diuretics (water pills). Ask your healthcare professional if you are unsure. Your healthcare professional will monitor your potassium levels in these situations. However, if you notice an acute or rapidly worsening shortness of breath (dyspnea), you should tell your healthcare professional right away.

If your ORCIPRENALINE treatment does not improve your condition or if your condition gets worse, you should also tell your healthcare professional. A new treatment plan may be necessary.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.
The following may interact with ORCIPRENALINE:

- medications known as sympathomimetic agents (e.g., epinephrine).
- antidepressant medications known as monoamine oxidase inhibitors and tricyclic antidepressants (used to treat depression).
- inhaled anaesthetics known as halogenated hydrocarbon anaesthetics (e.g., halothane, trichloroethylene and enflurane).
- medications known as beta blockers (used to reduce blood pressure).
- anti-inflammatory medications known as corticosteroids.
- medications that belong to a group called methylxanthines.
- medications known as diuretics or the water pill (used to increase the amount of water released in your urine, and reduce blood pressure).

If you are unsure, ask your healthcare professional.

How to take ORCIPRENALINE:

- Take ORCIPRENALINE orally and exactly as prescribed by your doctor.
- The syrup should be measured using a teaspoon to ensure the appropriate dose.

Usual dose:
Your doctor will tell you how much and how often to take the syrup each day. This will depend on your condition, other medications you are taking, and how you respond to the treatment. The usual doses are as follows:

- **Adults (18 years of age and older):** Two teaspoons (10 mL) of syrup (20 mg) three or four times a day.
- **Adolescents (12 to 17 years of age):** Two teaspoons (10 mL) of syrup (20 mg) three times a day.
- **Children (4 to 11 years of age):** One teaspoon (5 mL) of syrup (10 mg) three times a day.

Overdose:

The symptoms of an overdose can include any of the side effects listed. The most common side

effects of an overdose include:

- high or low blood pressure,
- irregular or rapid heartbeats,
- chest pain,
- trembling,
- flushing of the face.

If an overdose occurs, your healthcare professional will stop your treatment and an appropriate intervention may be considered.

If you think you, or a person you are caring for, have taken too much ORCIPRENALINE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take your dose, take it as soon as you remember. But if it is almost time for your next dose, do not take the missed dose. Instead, take the next scheduled dose. Do not try to make up for the missed dose by taking two doses at the same time.

What are possible side effects from using ORCIPRENALINE?

These are not all the possible side effects you may have when taking ORCIPRENALINE. If you experience any side effects not listed here, tell your healthcare professional.
Side effects may include:

- nervousness,
- shaking,
- sweating,
- muscle weakness or pain,
- psychological changes.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Arrhythmia (abnormal heart rhythms): rapid, slow or irregular heartbeat		√	
RARE			
Hypertension or hypotension (high or low blood pressure):		√	

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
headache, fatigue, vision problems, dizziness, lightheadedness, shortness of breath, fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations, nausea, or vomiting			
Heart problems: irregular heartbeat, changes in the rhythm or rate of the heartbeat, chest pain, chest discomfort, high blood pressure, shortness of breath, fainting, swelling of the legs, ankles and feet, or weakness		√	
Allergic reactions: swelling of the eyelids, face, lips, tongue or throat, accompanied by difficulty in breathing, speaking or swallowing, wheezing, drop in blood pressure, feeling sick to your stomach and throwing up, hives, or rash			√
UNKNOWN FREQUENCY			
Hypokalemia (low potassium levels in the blood): muscle weakness and spasms, cramping, constipation, feeling of skipped heart beats or palpitations, fatigue, tingling, or numbness		√	
Bronchospasm (tightening of muscles in the lung)**:** shortness of breath, chest tightness, wheezing, or coughing			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad

enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store ORCIPRENALINE at room temperature (15°C to 30°C) Protect from light.

Keep out of reach and sight of children.

If you want more information about ORCIPRENALINE:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html). Find the Patient Medication Information on the manufacturer's website (https://www.aapharma.ca/en/), or by calling 1-877-998-9097.

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