Optra® HFA

[Ipratropium bromide]
CFC Free Inhaler 20mcg

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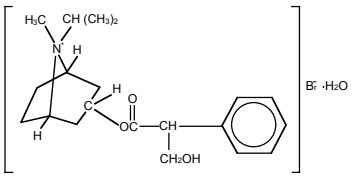
DESCRIPTION
OPTRA HFA (Ipratropium bromide) Inhaler is a pressurized metered dose inhaler that delivers 20mcg ipratropium bromide per actuation into the mouth piece of a specially designed actuator. OPTRA HFA (Ipratropium bromide) contains HFA 134a as propellant and does not contain any chlorofluorocarbons. Ipratropium bromide is a synthetic quaternary ammonium compound, chemically related to atropine. It is chemically described as (1R,3r,5S,8r)-3-[[(2RS)-3-Hydroxy-2-phenylpropanoyl]oxy]-8-methyl-8-(1-methylethyl)- 8-azoniabicyclo[3.2.1]octane bromide monohydrate. Its molecular formula is $C_{20}H_{30}BrNO_3.H_2O$ and the structural formula is:



Ipratropium bromide

QUALITATIVE & QUANTITATIVE COMPOSITION
OPTRA HFA (Ipratropium bromide) Inhaler is available for administration as:

OPTRA HFA Inhaler 20mcg
Each metered dose contains:
Ipratropium bromide BP…20mcg
(as monohydrate)

CLINICAL PHARMACOLOGY
Mechanism of Action
Ipratropium bromide is an anticholinergic (parasympatholytic) agent it appears to inhibits the vagally mediated reflexes by antagonising the action of acetylcholine, the transmitter agent released from the vagus nerve. Anticholinergics prevent the increase in intracellular concentration of Ca^{++} which is caused by interaction of acetylcholine with the muscarinic receptor on bronchial smooth muscle.
The bronchodilation following inhalation of ipratropium bromide is induced by local drug concentrations sufficient for anticholinergic efficacy at the bronchial smooth muscle and not by systemic concentrations.

Pharmacokinetics
Absorption
Ipratropium bromide is absorbed quickly after oral inhalation from a pressurized metered dose inhaler. Following inhalation about 10% to 30% of a dose is deposited in the lungs where it exerts its therapeutic effect. Mean plasma concentrations (C_{max}) is reached within 5 minutes after inhalation. Time courses of bronchodilation and systemic pharmacokinetics do not run in parallel. The total systemic bioavailability of inhaled dose of Ipratropium bromide is estimated to be in the range of 7% to 28%.

Distribution
Ipratropium bromide is minimally bound (less than 20%) to plasma protein. The quarternary amine of the ipratropium ion does not cross the blood-brain barrier.

Metabolism
After inhalation about 77% of the systemically available dose is metabolized by ester hydrolysis (41%) and conjugation (36%).

Excretion
The elimination half-life is about 2 hours after inhalation. After inhalation 4.4% to 13.1% of ipratropium bromide from a metered dose inhaler is excreted as unchanged compound in urine.

THERAPEUTIC INDICATIONS
OPTRA HFA (Ipratropium bromide) Inhaler is indicated as:
- Bronchodilator for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.
- Adjunct to $beta_2$-agonists in the management of acute severe asthma.

DOSAGE AND ADMINISTRATION
Adults (including the elderly):
Usually 1 or 2 inhalations three or four times daily, although some patients may need up to 4 inhalations at a time to obtain maximum benefit during early treatment. Patients may take additional inhalations as required, however, the total number of inhalations should not exceed 12 in 24 hours.

Children:
Between 6-12 years: Usually 1 or 2 inhalations, three times daily.
Under 6 years: Usually 1 inhalation, three times daily. In order to ensure that the inhaler is used correctly, administration should be supervised by an adult. The recommended dose should not be exceeded.

If therapy does not produce a significant improvement, if the patient's condition gets worse or if a reduced response to treatment becomes apparent, medical advice must be sought. In the case of acute or rapidly worsening dyspnea (difficulty in breathing) a doctor should be consulted immediately.

Administration:
The correct administration of ipratropium bromide from the inhaler is essential for successful therapy. The canister should be pressed twice to release two metered doses into the air before the inhaler is used for the first time, or when the inhaler has not been used for 3 days or more, to ensure that the inhaler is working properly and that it is ready for use.

ADVERSE REACTIONS
Following adverse reactions have been reported with the use of ipratropium bromide:

Common: Headache, dizziness, cough, throat irritation, nausea, dryness of mouth and gastrointestinal motility disorder.

Uncommon: Blurred vision, mydriasis, intraocular pressure increased, eye pain, halo vision, conjunctival hyperemia, corneal oedema, glaucoma, anaphylactic reaction, hypersensitivity, angioedema of tongue, lips & face, palpitations, supraventricular tachycardia, bronchospasm, paradoxical bronchospasm, laryngospasm, pharyngeal oedema, dry throat, diarrhea, constipation, vomiting, stomatitis, rash, pruritus and urinary retention.

Rare: Accommodation disorder, atrial fibrillation, heart rate increased and urticaria.

CONTRAINDICATIONS
Ipratropium bromide is contraindicated in patients with:
- Hypersensitivity to Ipratropium bromide or to any excipeint of the product.
- Hypersensitivity to atropine or its derivatives.

PRECAUTIONS
Use For Maintenance Treatment Only
Ipratropium bromide is a bronchodilator for the maintenance treatment of bronchospasm associated with COPD and is not indicated for the initial treatment of acute episodes of bronchospasm where rescue therapy is required for rapid response.

Ocular Effects
Ipratropium bromide is an anticholinergic and its use may increase intraocular pressure. This may result in precipitation or worsening of narrow-angle glaucoma. Therefore, it should

be used with caution in patients with narrow-angle glaucoma. Patients should avoid spraying ipratropium bromide inhaler into the eye.

Paradoxical Bronchospasm
Ipratropium bromide can produce paradoxical bronchospasm that can be life threatening. If this occurs, treatment with ipratropium bromide should be stopped and other treatments considered.

Hypersensitivity Reactions, Including Anaphylaxis
Hypersensitivity reactions including urticaria, angioedema, rash, bronchospasm, anaphylaxis and oropharyngeal edema, may occur after the administration of ipratropium bromide. If such a reaction occurs, therapy with ipratropium bromide should be stopped at once and alternative treatment should be considered.

Urinary Retention
Ipratropium bromide may cause urinary retention. Therefore, caution is advised when administering ipratropium bromide to patients with prostatic hyperplasia or bladder-neck obstruction.

Cystic fibrosis
Patients with cystic fibrosis may be prone to gastrointestinal motility disturbances, ipratropium bromide should be used with caution in these patients.

Pregnancy
There are no adequate and well-controlled studies of ipratropium bromide in pregnant women. Ipratropium bromide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether ipratropium bromide is excreted into human milk. Caution should be exercised when ipratropium bromide is administered to a nursing mother.

DRUG INTERACTIONS
- Administration of ipratropium bromide with beta-adrenergics and xanthine preparations may intensify the bronchodilator effect.
- Co-administration of ipratropium bromide with other anticholinergic drugs should be avoided, as this may lead to an increase in anticholinergic adverse effects.

OVERDOSAGE
No symptoms specific to overdosage have been encountered. Minor systemic manifestations of anticholinergic action, including dry mouth, visual accommodation disturbances and tachycardia may occur.

STORAGE
Store below 30°C.
Protect from direct sunlight, heat and frost.

As with most inhaled medications in aerosol canisters, the therapeutic effect of this medication may decrease when the canister is cold.
The canister should not be broken, punctured or burnt, even when apparently empty.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
OPTRA HFA (Ipratropium bromide) Inhaler 20mcg is available as metered dose Inhaler with specially designed actuator. Each canister provides 200 inhalations.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
Jewim Pharmaceutical (Shandong) Co. Ltd.
Taian High-Tech Industrial Development Zone
Shandong, China.

Manufactured for:
Getz pharma (PVT) LIMITED
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