Tiovair®
(Tiotropium)

Highnoon

COMPOSITION
Tiovair Rotacap: Each capsule contains:
Tiotropium (as Bromide Monohydrate) 18mcg

DESCRIPTION
It is a synthetic, non-chiral, quaternary ammonium compound. It is sparingly soluble in water and soluble in methanol. The dry powder formulation within the Tiovair capsule is intended for oral inhalation only. The drug substance, tiotropium monohydrate, is an anticholinergic with specificity for muscarinic receptors.

MECHANISM OF ACTION
Tiotropium is a long-acting, antimuscarinic agent, which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors, M1 to M5. By binding to the muscarinic receptors in the bronchial smooth musculature, tiotropium inhibits the cholinergic (bronchoconstrictive) effects of acetylcholine, released from parasympathetic nerve endings. The long duration is probably due to the very slow dissociation from M3 receptor, exhibiting a significantly longer dissociation half-life than ipratropium.

PHARMACOKINETIC
After inhalation some tiotropium is absorbed from the lungs, with majority deposited in the gastrointestinal tract. In healthy subjects a systemic bioavailability of about 24% is reported after dry powder inhalation, and about 33% after inhalation of the solution. Tiotropium is about 72% bound to plasma protein. It is excreted largely unchanged in the urine, although it may undergo some metabolism by non-enzymatic cleavage and by the cytochrome P 450 isoenzymes, CYP2D6 and CYP3A4. The terminal elimination half-life is between 25 and 45 hours in COPD patients and 34 to 44 hours in asthma patients.

INDICATIONS
Tiotropium is indicated:
- For the long-term, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.
- To reduce exacerbations in COPD patients.
- Management of asthma

It is not suitable for the initial treatment of acute bronchospasm.

DOSAGE AND ADMINISTRATION
Capsules are intended for use through Revolizer or Rotaflo only and are not to be swallowed. The recommended dosage of tiotropium is inhalation of one rotacap once daily. Tiotropium should only be inhaled with the Revolizer or Rotaflo device. The recommended dose should not be exceeded. Tiotropium rotacaps must not be swallowed.

CONTRAINDICATIONS
Tiotropium inhalation powder is contraindicated in patients with hypersensitivity to tiotropium, atropine or its derivatives, e.g. ipratropium or oxitropium or to the excipient lactose monohydrate.

WARNINGS AND PRECAUTIONS
- Tiotropium should not be used for the initial treatment of acute episodes of bronchospasm, i.e. rescue therapy.
- Immediate hypersensitivity reactions including urticaria, angioedema (including swelling of the lips, tongue, or throat), rash, bronchospasm, anaphylaxis, or itching may occur after administration of tiotropium inhalation powder.
- As with other anticholinergic drugs, tiotropium should be used with caution in patients with narrow-angle glaucoma, prostatic hyperplasia or bladder-neck obstruction.
- Inhaled medicines may cause inhalation-induced bronchospasm. Patients should be cautioned to avoid getting the drug powder into their eyes. This should be advised that it may result in precipitation or worsening of narrow-angle glaucoma, eye pain or discomfort, temporary blurring of vision, visual halos or coloured images in association with red eyes from conjunctival and corneal congestion. Patients should stop using tiotropium and consult a physician immediately when signs and symptoms of narrow-angle glaucoma appear. Dry mouth, which has been observed with anti-cholinergic treatment, in the long term may be associated with dental caries. Tiotropium may not be used more frequently than once daily.
- Patients with moderate to severe renal impairment treated with Tiotropium; their (creatinine clearance 50m/L or less) should be monitored closely as tiotropium is mainly excreted by the kidneys.

ADVERSE EFFECTS
The reported adverse events are; systemic anticholinergic effects include dry month, dry throat, increased heart rate, blurred vision, glaucoma, urinary difficulty, urinary retention, constipation, upper airway irritant phenomena, an increased incidence of dry mouth and constipation.

The additional reported adverse events are; diarrhoea, hypertension, tonsillitis, abdominal pain, insomnia, angioedema, dehydration, arthralgia, muscle spasms, pain in extremity, chest pain, hepatic function abnormal, liver function test abnormal, atrial fibrillation, tachycardia, glossitis, stomatitis, urticarial, pharyngitis, cough, sinusitis, rhinitis, palpitations, oropharyngeal candidiasis, dizziness, headache, taste disorders, epistaxis, dysphonia, pruritus, rash, dysphagia, gingivitis, nausea, intestinal obstruction including ileus paralytic, joint swelling, dysuria, laryngitis, angioedema, dry skin, skin infection, increase risk of stroke, subacute cutaneous erythematosus, photosensitive lichenoid, acute porphyria, and skin ulcer.

DRUG INTERACTIONS
- Tiotropium has been used concomitantly with short-acting and long-acting sympathomimetic (beta-agonists) bronchodilator, methylxanthines, oral and inhaled steroids, antihistamine, mucolytic, leukotriene modifiers, cromones, and anti-IgF treatment without increase in adverse reactions.
- There is a potential for an additive interaction with concomitantly used anticholinergic medications. Therefore, avoid coadministered of Tiotropium with other anticholinergic-containing drugs as this may lead to an increase in anticholinergic adverse effects.

USE IN SPECIFIC POPULATIONS
Pregnancy
There are no adequate and well controlled studies of Tiovair in pregnant women. Administration of Tiovair in pregnant woman should only be considered if the potential benefit justifies the potential risk to the foetus.

Lactation
Clinical data from nursing women exposed to tiotropium are not available. It is not known that the tiotropium is excreted in human milk, but because many drugs are excreted in human milk, so caution should be exercised if Tiovair is administered to a nursing woman.

Geriatric patients can use tiotropium at the recommended dose.

OVERDOSE
High doses of tiotropium may lead to anticholinergic signs and symptoms.

However, there were no systemic anticholinergic adverse effects following a single inhaled dose of up to 340 microgram tiotropium in healthy volunteers. Additionally, no relevant adverse effects, beyond dry mouth, were observed following 7-day dosing of up to 170 microgram tiotropium in healthy volunteers. In a multiple dose study in COPD patients with a maximum daily dose of 43 microgram tiotropium over four weeks no significant undesirable effects have been observed.

Acute intoxication by inadvertent oral ingestion of tiotropium capsules is unlikely due to low oral bioavailability.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

ROTACAPS ARE INTENDED FOR USE THROUGH ROTAFLO OR REVOLIZER ONLY AND ARE NOT TO BE SWALLOWED.

PRESENTATION
Tiovair Rotacaps: Alu. Alu. Blister Pack of 3 x 10's.

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(ٹائیوٹروپیئم)

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by
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