RELENZA™

zanamivir 5 mg

Presentation:
Each *Relenza Rotadisk* consists of a circular foil disk with four regularly distributed blisters each containing 5 mg of zanamivir and 20 mg of lactose monohydrate (which contains milk protein). Each *Relenza Rotadisk* is inserted in the accompanying *Diskhaler* device. The medication is then inhaled through the mouth using the *Diskhaler*. Each pack contains 5 Rotadisks.

Indications:
Treatment
Relenza (zanamivir) is indicated for the treatment of infections due to Influenza A and B viruses in adults and children aged 5 years and older. Treatment should commence as soon as possible but no later than forty-eight hours after the onset of the initial symptoms of infection.
Prophylaxis
Vaccination remains the primary method of preventing and controlling influenza.
Relenza is indicated for prophylaxis of influenza A and B in adults and children (5 years) to reduce transmission among individuals in households with an infected person.
Relenza is indicated for prophylaxis of influenza A and B during community outbreaks only in circumstances where such prophylaxis is justified (such as when vaccine that antigenically matches circulating influenza is not available or there is a pandemic).
It is not recommended for routine prophylaxis against influenza infection.
Dosage and Administration:
Treatment of influenza:
The recommended dose of *Relenza* is two oral inhalations (2 x 5 mg) twice daily for five days providing a total daily inhaled dose of 20mg. Treatment should begin as soon as possible after onset of symptoms for maximum benefit, and at the latest should commence within 48 hours of symptom onset. Administration is by oral inhalation.
Prophylaxis of influenza:
The recommended dose of Relenza is two inhalations (2 x 5 mg) once daily, providing a total daily inhaled dose of 10mg, for 10 days. This may be increased up to 28 days if the period of exposure risk extends beyond 10 days.
Relenza Rotadisks are for pulmonary administration by oral inhalation only, using the *Diskhaler* device provided. Patients scheduled to take inhaled drugs, for example fast acting bronchodilators, at the same time as Relenza, should be advised to administer that drug prior to administration of Relenza.
Dosage in Renal Impairment: No alteration of dosage or frequency of administration is required.
Dosage in Hepatic Impairment: There is currently no experience in this patient population. Zanamivir is not hepatically metabolised and no dose modification is required.
Dosage in Elderly Patients: Experience with zanamivir in the elderly (≥65 years) is limited. However based on the pharmacokinetic properties of zanamivir no dose modification is required.
Dosage in Children: No dose modification is required. When zanamivir is prescribed for children, it should be used only under adult supervision.
Contraindications:
The use of *Relenza* is contra-indicated in patients with known hypersensitivity to zanamivir or lactose.
Warnings and Precautions
Influenza infection can be associated with increased airways hyper-responsiveness. There have been very rare reports of patients being treated for influenza who have experienced bronchospasm and/or decline in respiratory function after the use of inhaled zanamivir, some of whom did not have any previous history of respiratory disease. Any such patients should discontinue zanamivir and seek medical evaluation. Patients with underlying respiratory disease should have a fast acting bronchodilator available when taking inhaled zanamivir (see Dosage and Administration).
Zanamivir inhalation powder must not be made into an extemporaneous solution for administration by nebulisation or mechanical ventilation. There have been reports of hospitalised patients with influenza who received a solution made with zanamivir inhalation powder administered by nebulisation or mechanical ventilation, including a fatal case where it was reported that the lactose in this formulation obstructed the proper functioning of the equipment. Zanamivir inhalation powder must only be administered using the device provided.
Influenza can be associated with a variety of neurological and behavioural symptoms. There have been postmarketing reports (mostly from Japan and in paediatric subjects) of seizures, delirium, hallucination and abnormal behaviour in patients with influenza who were receiving neuraminidase inhibitors, including zanamivir. The events were observed mainly early in the illness and often had an abrupt onset and rapid resolution. The contribution of zanamivir to these events has not been established. If neuropsychiatric symptoms occur, the risks and benefits of continuing treatment should be evaluated for each patient.
Interactions
Zanamivir is not protein bound and not hepatically metabolised or modified. Clinically significant drug interactions are unlikely.
Pregnancy and Lactation
Pregnancy
The safe use of zanamivir during pregnancy has not been established.
Reproductive studies performed in rats and rabbits indicated that placental transfer of zanamivir occurs. Studies in rats did not show any evidence of teratogenicity, impairment of fertility or clinically significant impairment of peri or post-natal development of offspring following administration of zanamivir. However, there is no information on placental transfer in humans.
Zanamivir should not be used in pregnancy, especially during the first trimester, unless the possible benefit to the patient is thought to outweigh any possible risk to the foetus.
Lactation
In rats, zanamivir has been shown to be secreted into milk. However, there is no information on secretion into breast milk in humans.
As experience is limited, the use of zanamivir in nursing mothers should be considered only if the possible benefit to the mother is thought to outweigh any possible risk to the infant.
Adverse Reactions
Clinical Trial Data
Zanamivir is well tolerated by the oral inhaled route of administration. In clinical studies, including those studies with high risk patients (the elderly, and patients with certain chronic medical conditions), the adverse events reported were similar in the zanamivir and placebo groups.
Postmarketing Data
The following events have been identified during post-approval use of zanamivir ROTADISK for the treatment of influenza and will be relevant to the ROTACAPS formulation. No postmarketing data has been generated for zanamivir injection; however, the following events may also be relevant to this formulation.
Very common: ≥1/10
Common: ≥1/100 and <1/10
Uncommon: ≥1/1000 and <1/100
Rare: ≥1/10,000 and <1/1000
Very rare: <1/10,000
Immune Systems Disorders:
Very rare: Allergic-type reactions, including anaphylactic and anaphylactoid reactions, facial and oropharyngeal oedema
Nervous systems disorders:
Very rare: Vasovagal-like reactions have been reported in patients with influenza symptoms, such as fever and dehydration, shortly following inhalation of zanamivir.
Respiratory, thoracic and mediastinal disorders:
Very rare: Bronchospasm, dyspnoea
Skin and subcutaneous tissue disorders:
Very rare: Rash, urticaria
Very rare: Severe skin reactions including Erythema Multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis
Overdosage
Symptoms and Signs
Accidental overdose is unlikely with the inhaled formulations due to the physical limitations of the presentation, the route of administration and the low systemic bioavailability (10 to 20 %) of zanamivir. Doses of an investigational (lactose-free) aqueous solution of zanamivir up to 64 mg/day (approximately 3 times the maximum daily recommended dose) have been administered by oral inhalation (by nebuliser) without adverse effects. In clinical trials, systemic exposure by i.v. administration of up to 1200 mg/day for five days showed no adverse effect.
Treatment
As zanamivir has a low molecular weight, low protein binding, and small volume of distribution, it is expected to be removed by hemodialysis. Therefore, this may be considered a management option in the event of symptomatic overdose.
Storage Condition:
Do not store above 30ºC.
Do not use Relenza or the Diskhaler after the expiry date printed on the carton, tube label or Rotadisk.
Do not puncture the blisters before using them in the Relenza Diskhaler device.
Shelf life:
The expiry date is indicated on the packaging.
Manufactured by:
GlaxoSmithKline Australia Pty Ltd*
Boronia, Australia
*Member of the GlaxoSmithKline group of companies.

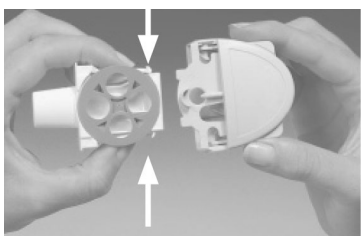
GDS Version Number: 15, **Version Date:** 19 August 2010

Step by step instructions on how to use your Diskhaler device

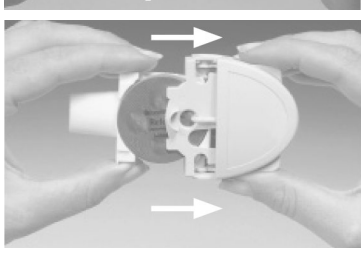
The Relenza powder for inhalation, contained in each Rotadisk blister, is inhaled through the mouth and into the lungs using the Relenza Diskhaler device provided. It is **important** that you follow the instructions provided on how to inhale from the Diskhaler. Before the device can be used, a Relenza Rotadisk needs to be loaded into the Diskhaler.
A Relenza Rotadisk may be kept in the Diskhaler at all times but it is **important** that the blister is only pierced immediately prior to use.
If you have read the instructions and are still not sure how to use the device, speak to your pharmacist who will be able to run through the instructions with you.
The Diskhaler parts and what they do

The Diskhaler has a number of parts:
- The main device body with a hinged lid and piercing needle. Lifting the lid causes the needle to pierce a blister and makes the medicine ready to inhale
- A blue cover which protects the mouthpiece when not in use
- Relenza Rotadisk. Each disk contains 4 blisters of medicine. The Rotadisk fits on to the dark beige wheel inside the inhaler
- The wheel is part of a white sliding tray with finger grips and a mouthpiece

How to load a Rotadisk into the Diskhaler

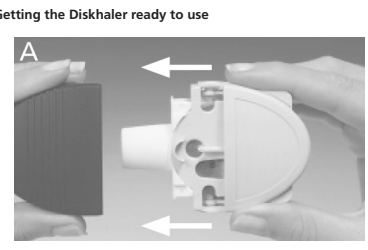


Remove the blue mouthpiece cover and pull the white tray out as far as it will go.
Press the finger grips on either side of the dark beige wheel and gently pull the white tray out of the Diskhaler body.

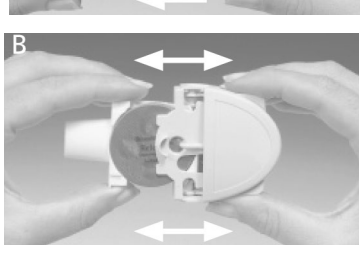


Place a new Relenza Rotadisk onto the wheel, with the embossed side up and push the loaded tray back into the inhaler – holding the device as shown in the picture.
If you do not need to take a dose at the time of loading, put the blue cover back on the Diskhaler until you need to take a dose.
Replace the used disk once you have used all four blisters.

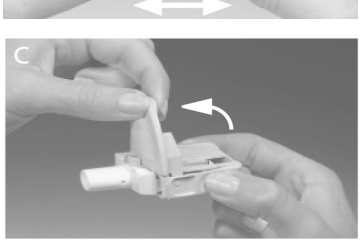
Getting the Diskhaler ready to use



Remove the blue cover and check the mouthpiece is clean, inside and outside.
Check that there is a new blister showing under the needle.



If the blister is punctured, pull the white tray out as far as it will go and then push it back in again. This will turn the wheel and the next blister will appear.
Repeat until a new blister is positioned under the needle.



Lift the lid fully. This will ensure the blister is pierced completely.

Keep your inhaler level (horizontal) until you have inhaled your medicine.
Push the lid back down.
The Diskhaler is now ready to use.

How to inhale your medicine

Breathe out as far as is comfortable, keeping the Diskhaler away from your mouth, and then place the mouthpiece between your teeth. Remember to keep the Diskhaler level.
Close your lips firmly around the mouthpiece – but do not bite it or block the small air holes on either side.
Suck in through your mouth by taking one quick, deep breath in through the mouthpiece. Hold this breath in and remove the Diskhaler from your mouth. Continue to hold your breath for a few seconds or as long as is comfortable.

- To take another dose repeat steps **B** to **E**
- Once you have taken the full dose, always wipe the mouthpiece with a tissue and replace the cover after use. It is important to keep the Diskhaler clean
- Once all the 4 blisters are empty repeat the instructions on 'How to load a Rotadis into the Diskhaler'

THIS IS A MEDICAMENT
Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.

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