AllerDuo®

1. **Generic Name**

Bilastine

Montelukast

2. **Qualitative and Quantitative composition**

Bilastine…….. 20 mg

Montelukast…….. 10 mg

3. **Dosage form and strength**

Film coated tablets containing 20mg of Bilastine and 10mg of Montelukast.

4. **Clinical particulars**

4.1 Therapeutic indication

AllerDuo is indicated in treatment of allergic rhinitis and Asthma.

4.2 Posology and method of administration

One tablet once a day.

4.3 Contraindication

Hypersensitivity to any component of this product.

4.4 Special warnings and precautions for use

- ALLERDUO TABLETS should not be taken with food or with grapefruit juice or other fruit juices, as this will decrease the effect of bilastine.
- Patients with known aspirin sensitivity should continue avoidance of aspirin or non-steroidal anti inflammatory agents while taking ALLERDUO TABLETS.

- Neuropsychiatric events have been reported with Montelukast. Instruct patients to be alert for neuropsychiatric events.
- Systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, has been reported with montelukast. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy.

4.5 Drug interactions

- Ketoconazole (an antifungal medicine)
- Erythromycin (an antibiotic)
- Diltiazem (to treat angina)
- Cyclosporine (to reduce the activity of your immune system, thus avoiding transplant rejection or reducing disease activity in autoimmune and allergic disorders, such as psoriasis, atopic dermatitis or rheumatoid arthritis)
- Ritonavir (to treat AIDS)
- Rifampicin (an antibiotic)

4.6 Use in special population

- Paediatric: Use in paediatric patients below the age 6 years of age is not recommended since no sufficient data are available.
- Geriatric: No overall clinical differences in safety or effectiveness have been observed between elderly and other adult patients.
- Liver impairment: Use with caution.
- Renal failure: Use with caution.
- Pregnancy and lactation: There are no or limited amount of data from the use in pregnant women and on the effects on fertility. ALLERDUO TABLETS should be administered during pregnancy only if the potential benefit justifies the potential risk to the foetus.

  There are no or limited amount of data from the during breast-feeding, caution should be exercised when ALLERDUO TABLETS is administered to a nursing woman

4.7 Effects on ability to drive and use machine

Patients should be cautioned against engaging in activities requiring complete mental alertness, and motor coordination such as operating machinery until their response to AllerDuo is known.

4.8 Undesirable effects

Most common adverse reactions for Bilastine: Headache, drowsiness, fatigue, Palpitations, Nausea, Diarrhoea, Abdominal pain , Vomiting

Most common adverse reactions for Montelukast: Eosinophilia , Thrombocytopenia , Palpitations , Tachycardia , Vertigo , Ear pain , Tinnitus , Visual impairment , Nausea , Diarrhoea , Abdominal pain , Vomiting , Dyspepsia , Abdominal discomfort , Dry mouth , Constipation , Fatigue , Crying , Malaise , Pyrexia ,Feeling abnormal ,Asthenia, Pain, Chest pain , upper respiratory infection, fever, headache, pharyngitis, cough, otitis media, influenza, rhinorrhea, sinusitis, otitis

4.9 Overdose

There is limited experience of overdose with AllerDuo Tablets. Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

5.1 Mechanism of action

Bilastine

Bilastine is a selective histamine H1 receptor antagonist (Ki = 64nM). During allergic response mast cells undergo degranulation which releases histamine and other substances. By binding to and preventing activation of the H1 receptor, bilastine reduces the development of allergic symptoms due to the release of histamine from mast cells.

Montelukast

The cysteinyl leukotrienes (LTC4, LTD4, LTE4), are potent inflammatory eicosanoids released from various cells including mast cells and eosinophils. These important pro-asthmatic mediators bind to cysteinyl leukotriene (CysLT) receptors. The CysLT type-1 (CysLT1)

receptor is found in the human airway (including airway smooth muscle cells and airway macrophages) and on other proinflammatory cells (including eosinophils and certain myeloid stem cells). CysLTs have been correlated with the pathophysiology of asthma and allergic rhinitis. In asthma, leukotriene-mediated effects include a number of airway actions, including bronchoconstriction, mucous secretion, vascular permeability, and eosinophil recruitment. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both early- and late-phase reactions and are associated with symptoms of allergic rhinitis. Intranasal challenge with CysLTs has been shown to increase nasal airway resistance and symptoms of nasal obstruction. Montelukast has not been assessed in intranasal challenge studies. The clinical relevance of intranasal challenge studies is unknown. Montelukast is an orally active compound that improves parameters of asthmatic inflammation. Based on biochemical and pharmacological bioassays, it binds with high affinity and selectivity to the CysLT1 receptor (in preference to other pharmacologically important airway receptors such as the prostanoid, cholinergic, or β-adrenergic receptor). Montelukast potently inhibits physiologic actions of LTC4, LTD4, and LTE4 at the CysLT1 receptor without any agonist activity.

5.2 Pharmacodynamic properties

Bilastine

Bilastine is an antiallergenic and acts to reduce allergic symptoms such as nasal congestion and urticaria

Montelukast

Montelukast causes inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled L TD4 in asthmatics. Doses as low as 5 mg cause substantial blockage of L TD4-induced bronchoconstriction. In a placebo-controlled, crossover study (n=12).

5.3 Pharmacokinetic properties

Bilastine

- Absorption: Bilastine is rapidly absorbed after oral administration with a time to maximum plasma concentration of around 1.13 hours. No accumulation was observed in subjects treated with bilastine from 20 to 100 mg daily after 14 days. The absolute bioavailability of bilastine is 61%
- Distribution : At therapeutic doses bilastine is 84-90% bound to plasma proteins.
- Metabolism: Bilastine is not significantly metabolized in humans. Bilastine does not induce or inhibit activity of CYP450 isoenzymes in in vitro and in vivo studies. Studies examining hepatic tissues (microsomes and hepatocytes) of human origin using different doses of bilastine demonstrated that there was little to no interaction with CYP isoenzymes.
- Excretion: In a mass balance study performed in healthy volunteers, after administration of a single dose of 20 mg 14C-bilastine, almost 95% of the administered dose was recovered in urine (28.3%) and faeces (66.5%) as unchanged bilastine. The mean elimination half-life calculated in healthy volunteers in the population pharmacokinetic model was 14.5 h.

Montelukast

- Absorption: Montelukast is rapidly absorbed following oral administration. After administration of the 10-mg filmcoated tablet to fasted adults, the mean peak montelukast plasma concentration (Cmax) is achieved in 3 to 4 hours (T max). The mean oral bioavailability is 64%. The oral bioavailability and Cmax are not influenced by a standard meal in the morning.
- Distribution: Montelukast is more than 99% bound to plasma proteins.
- Metabolism: Montelukast is extensively metabolized. In studies with therapeutic doses, plasma concentrations of state in adults and pediatric patients. In vitro studies using human liver microsomes indicate that CYP3A4 and 2C9 are involved in the metabolism of montelukast.
- Elimination: The plasma clearance of montelukast averages 45 mL/min in healthy adults. Following an oral dose of radiolabeled montelukast, 86% of the

radioactivity was recovered in 5-day fecal collections and 0.2% was recovered in urine. During once-daily dosing with 10-mg montelukast, there is little accumulation of the parent drug in plasma (14%).

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Bilastine

Repeated-dose toxicity studies in beagle dogs (52 weeks) and in rats and mice (13 weeks) showed that bilastine at doses up to 2,000 mg/kg/day was not associated with any mortality, ocular effects, or nodules/masses. Likewise, no bilastine-associated neoplastic lesions were observed in rats and mice after 104 weeks of treatment with bilastine at doses up to 2,000 mg/kg/day. In general, bilastine-related clinical signs, body-weight changes, food consumption, clinical chemistry, haematology, and macro- and microscopic findings were of low order and reversible, with effects present only at the highest doses administered. Bilastine (up to 1,000 mg/kg/day) was well tolerated in pregnant/lactating rats and in their offspring and subsequent generations. With respect to effects on embryofoetal development in rabbits, bilastine at 400 mg/kg/day (the highest dose evaluated) was assessed to be the no observed adverse effects level. Overall, bilastine demonstrated a favorable toxicity profile in all animal models investigated and at higher doses than the corresponding recommended daily human dosage.

Montelukast

No mortality occurred following a single oral administration of montelukast sodium at doses up to 5000 mg/kg, in mice and rats, (15 000 mg/m2 and 29 500 mg/m2 in mice and rats, respectively) the maximum dose tested (oral aLD50 >5000 mg/kg). This dose is equivalent to 25 000 times the recommended daily adult human dose (determined using mg/kg/day values)∗ .

7. Description

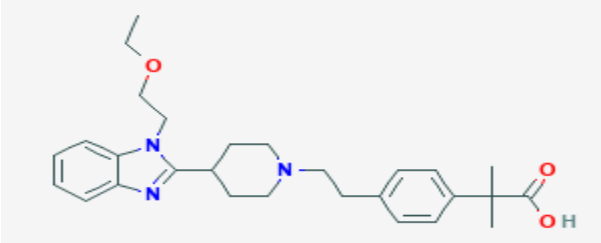
Bilastine

Bilastine belongs to the class of organic compounds known as benzimidazoles. It is considered to be a practically insoluble (in water) and relatively neutral molecule. In humans, bilastine is involved in the bilastine H1-antihistamine action pathway.

Molecular Formula: $C_{28}H_{37}N_3O_3$

Molecular Weight: 463.6 g/mol

Structure:



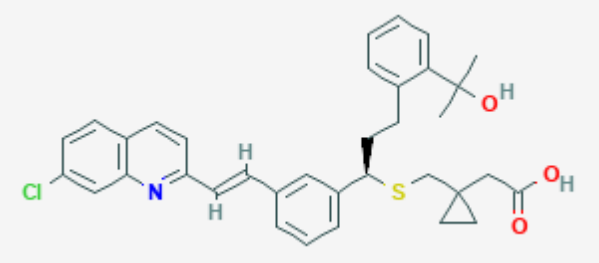
Montelukast

Montelukast is a drug which is used for the treatment of asthma. Montelukast is considered to be a practically insoluble (in water) and relatively neutral molecule. Montelukast has been detected in multiple biofluids, such as urine and blood. Within the cell, montelukast is primarily located in the cytoplasm and membrane (predicted from logP). Montelukast can be converted into montelukast nitrile.

Molecular Formula: $C_{35}H_{36}ClNO_3S$

Molecular Weight: 586.2 g/mol

Structure:



8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life

24 months.

8.3 Packaging Information

ALLERDUO TABLETS is available in pack of 10 tablets.

8.4 Storage and handling instructions

Store in cool and dry place. Keep medicine away from children.

9. Patient Counselling Information

9.1 Adverse Reactions

Refer part 4.8

9.2 Drug Interactions

Refer part 4.5

9.3 Dosage

Refer part 4.2

9.4 Storage

Refer part 8.4

9.5 Risk Factors

Refer part 4.4

9.6 Self-monitoring information

NA

9.7 Information on when to contact a health care provider or seek emergency help

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications

Refer part 4.3

10. Manufactured by Exemed Pharmaceuticals.

11. Details of permission or license number with date

G/25/2011

12. Date of revision: January 2022