For the use of a Registered Medical Practitioner only

1. Generic Name

Bilastine 20mg and Montelukast 10mg Tablets

Bilazest™-M

2. Qualitative and Quantitative Composition

Each film coated tablet contains:

Bilastine I.P..……...…….……. 20 mg

Montelukast sodium I.P.

equivalent to Montelukast.……..……. 10 mg

colours: Ferric oxide USP-NF Red, Ferric oxide USP-NF Yellow, Titanium dioxide I.P.

3. Dosage Form & Strength

Film-coated tablets

4. Clinical Particulars

4.1 Therapeutic Indications

Indicated for the treatment of allergic rhinitis in adults.

4.2 Posology and Method of administration

One tablet (20 mg Bilastine and 10 mg Montelukast) once daily.

Method of administration

Orally

4.3 Contraindications

Hypersensitivity to the bilastine or montelukast or to any of the excipients.

4.4 Special warnings and precautions for use

Bilastine

Paediatric population

Efficacy and safety of bilastine in children under 2 years of age have not been established and there is little clinical experience in children aged 2 to 5 years, therefore bilastine should not be used in these age groups.

In patients with moderate or severe renal impairment coadministration of bilastine with P-glycoprotein inhibitors, such as e.g, ketoconazole, erythromycin, cyclosporine, ritonavir or diltiazem, may increase plasmatic levels of bilastine and therefore increase the risk of adverse effects of bilastine. Therefore, coadministration of bilastine and P-glycoprotein inhibitors should be avoided in patients with moderate or severe renal impairment.

Montelukast

Patients should be advised never to use oral montelukast to treat acute asthma attacks and to keep their usual appropriate rescue medication for this purpose readily available. If an acute attack occurs, a short-acting inhaled β-agonist should be used. Patients should seek their doctors' advice as soon as possible if they need more inhalations of short-acting β-agonists than usual.

Montelukast should not be substituted abruptly for inhaled or oral corticosteroids.

There are no data demonstrating that oral corticosteroids can be reduced when montelukast is given concomitantly.

In rare cases, patients on therapy with anti-asthma agents including montelukast may present with systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition which is often treated with systemic corticosteroid therapy. These cases have been sometimes associated with the reduction or withdrawal of oral corticosteroid therapy. Although a causal relationship with leukotriene receptor antagonism has not been established, physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. Patients who develop these symptoms should be reassessed and their treatment regimens evaluated.

Treatment with montelukast does not alter the need for patients with aspirin-sensitive asthma to avoid taking aspirin and other non-steroidal anti-inflammatory drugs.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Neuropsychiatric events have been reported in adults, adolescents, and children taking montelukast. Patients and physicians should be alert for neuropsychiatric events. Patients and/or caregivers should be instructed to notify their physician if these changes occur. Prescribers should carefully evaluate the risks and benefits of continuing treatment with montelukast if such events occur.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults and are summarised below.

Interaction with food

Food significantly reduces the oral bioavailability of bilastine by 30%.

Interaction with grapefruit juice

Concomitant intake of bilastine 20 mg and grapefruit juice decreased bilastine bioavailability by 30%. This effect may also apply to other fruit juices. The degree of bioavailability decrease may vary between producers and fruits. The mechanism for this interaction is an inhibition of OATP1A2, an uptake transporter for which bilastine is a substrate. Medicinal products that are substrates or inhibitors of OATP1A2, such as ritonavir or rifampicin, may likewise have the potential to decrease plasma concentrations of bilastine.

Interaction with ketoconazole or erythromycin

Concomitant intake of bilastine 20 mg o.d. and ketoconazole 400 mg o.d. or erythromycin 500 mg t.i.d. increased bilastine AUC 2-fold and Cmax 2-3 fold. These changes can be explained by interaction with intestinal efflux transporters, since bilastine is substrate for P-gp and not metabolised. These changes do not appear to affect the safety profile of bilastine and ketoconazole or erythromycin, respectively. Other medicinal products that are substrates or inhibitors of P-gp, such as cyclosporine, may likewise have the potential to increase plasma concentrations of bilastine.

Interaction with diltiazem

Concomitant intake of bilastine 20 mg o.d. and diltiazem 60 mg o.d. increased C_{max} of bilastine by 50%. This effect can be explained by interaction with intestinal efflux transporters, and does not appear to affect the safety profile of bilastine.

Interaction with alcohol

The psychomotor performance after concomitant intake of alcohol and 20 mg bilastine o.d. was similar to that observed after intake of alcohol and placebo.

Interaction with lorazepam

Concomitant intake of bilastine 20 mg o.d. and lorazepam 3 mg o.d. for 8 days did not potentiate the depressant CNS effects of lorazepam.

Paediatric population

Interaction studies have only been performed in adults. As there is no clinical experience regarding the interaction of bilastine with other medicinal products, food or fruit juices in children, the results obtained in adult interactions studies should be at present taken into consideration when prescribing bilastine to children. There are no clinical data in children to state whether changes to the AUC or C_{max} due to interactions affect the safety profile of bilastine.

Montelukast

Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma. In drug-interactions studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following medicinal products:

theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/norethindrone 35/1), terfenadine, digoxin and warfarin. The area under the plasma concentration curve (AUC) for montelukast was decreased approximately 40% in subjects with co-administration of phenobarbital. Since montelukast is metabolised by CYP 3A4, 2C8, and 2C9, caution should be exercised, particularly in children, when montelukast is co-administered with inducers of CYP 3A4, 2C8, and 2C9, such as phenytoin, phenobarbital and rifampicin.

In vitro studies have shown that montelukast is a potent inhibitor of CYP 2C8. However, data from a clinical drug-drug interaction study involving montelukast and rosiglitazone (a probe

substrate representative of medicinal products primarily metabolized by CYP 2C8) demonstrated that montelukast does not inhibit CYP 2C8 in vivo. Therefore, montelukast is not anticipated to markedly alter the metabolism of medicinal products metabolised by this enzyme (e.g., paclitaxel, rosiglitazone, and repaglinide).

In vitro studies have shown that montelukast is a substrate of CYP 2C8, and to a less significant extent, of 2C9, and 3A4. In a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) gemfibrozil increased the systemic exposure of montelukast by 4.4-fold. No routine dosage adjustment of montelukast is required upon co-administration with gemfibrozil or other potent inhibitors of CYP 2C8, but the physician should be aware of the potential for an increase in adverse reactions.

Based on *in vitro* data, clinically important drug interactions with less potent inhibitors of CYP 2C8 (e.g., trimethoprim) are not anticipated. Co-administration of montelukast with itraconazole, a strong inhibitor of CYP 3A4, resulted in no significant increase in the systemic exposure of montelukast.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

Bilastine

There are no or limited amount of data from the use of bilastine in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity, parturition or postnatal development.

Montelukast

Animal studies do not indicate harmful effects with respect to effects on pregnancy or embryonal/foetal development. Limited data from available pregnancy databases do not suggest a causal relationship between montelukast and malformations (i.e. limb defects) that have been rarely reported in worldwide post-marketing experience.

As a precautionary measure, it is preferable to avoid the use of Bilastine + Montelukast combination tablets during pregnancy.

Breast-feeding

Bilastine

The excretion of bilastine in milk has not been studied in humans. Available pharmacokinetic data in animals have shown excretion of bilastine in milk.

Montelukast

Studies in rats have shown that montelukast is excreted in milk. It is unknown whether montelukast/metabolites are excreted in human milk.

A decision on whether to continue/discontinue breast-feeding or to discontinue/abstain from bilastine + montelukast combination therapy must be made taking into account the benefit of breast-feeding for the child and the benefit of therapy for the mother.

Fertility

There are no or limited amount of clinical data. A study in rats did not indicate any negative effect on fertility with bilastine.

4.7 Effects on ability to drive and use machines

Bilastine

A study performed in adults to assess the effects of bilastine on the ability to drive demonstrated that treatment with 20 mg did not affect the driving performance. However, as the individual response to the medicinal product may vary, patients should be advised not to drive or use machines until they have established their own response to bilastine.

Montelukast

Montelukast has no or negligible influence on the ability to drive and use machines. However, individuals have reported drowsiness or dizziness.

4.8 Undesirable Effects

Bilastine

The incidence of adverse events in adult and adolescent patients suffering from allergic rhino conjunctivitis or chronic idiopathic urticaria treated with 20 mg bilastine in clinical trials was comparable with the incidence in patients receiving placebo (12.7% versus 12.8%).

In adult and adolescent patients

Infections and infestations

Uncommon: Oral herpes

Metabolism and nutrition disorders

Uncommon: Increased appetite

Psychiatric disorders

Uncommon: Anxiety, Insomnia

Nervous system disorders

Common: Somnolence, Headache

Uncommon: Dizziness

Ear and labyrinth disorders

Uncommon: Tinnitus, Vertigo

Cardiac disorders

Uncommon: Right bundle branch block, Sinus arrhythmia, Electrocardiogram QT prolonged, Other ECG abnormalities

Respiratory, thoracic and mediastinal disorders

Uncommon: Dyspnoea, Nasal discomfort, Nasal dryness

Gastrointestinal disorders

Uncommon: Upper abdominal pain, Abdominal pain, Nausea, Stomach discomfort, Diarrhoea, Dry mouth, Dyspepsia, Gastritis

Skin and subcutaneous tissue disorders

Uncommon: Pruritus

General disorders and administration site conditions

Uncommon: Fatigue, Thirst, Improved pre-existing condition, Pyrexia, Asthenia

Investigations

Uncommon: Increased gamma-glutamyltransferase, Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood creatinine increased, Blood triglycerides increased, Increased weight

In Paediatric Population

Infections and infestations

Common: Rhinitis

Nervous system disorders

Common: Headache

Uncommon: Dizziness, Loss of consciousness

Eye disorders

Common: Allergic conjunctivitis

Uncommon: Eye irritation

Gastrointestinal disorders

Common: Abdominal pain / Upper abdominal pain

Uncommon: Diarrhoea, Nausea, Lip swelling

Skin and subcutaneous tissue disorders

Uncommon: Eczema, Urticaria

General disorders and administration site conditions

Uncommon: Fatigue

Montelukast

Infections and infestations

Very Common: upper respiratory infection

Blood and lymphatic system disorders

Rare: increased bleeding tendency

Very Rare: thrombocytopenia

Immune system disorders

Uncommon: hypersensitivity reactions including anaphylaxis

Very Rare: hepatic eosinophilic infiltration

Psychiatric disorders

Uncommon: dream abnormalities including nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behaviour or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor)

Rare: disturbance in attention, memory impairment, tic

Very Rare: hallucinations, disorientation, suicidal thinking and behaviour (suicidality), obsessive-compulsive symptoms, dysphemia

Nervous system disorders

Uncommon: dizziness, drowsiness, paraesthesia/hypoesthesia, seizure

Cardiac disorders

Rare: palpitations

Respiratory, thoracic and mediastinal disorders

Uncommon: epistaxis

Very Rare: Churg-Strauss Syndrome (CSS)

Very Rare: pulmonary eosinophilia

Gastro-intestinal disorders

Common: diarrhoea, nausea, vomiting

Uncommon: dry mouth, dyspepsia

Hepatobiliary disorders

Common: elevated levels of serum transaminases (ALT, AST)

Very Rare: hepatitis (including cholestatic, hepatocellular, and mixed-pattern liver injury)

Skin and subcutaneous tissue disorders

Common: rash

Uncommon: bruising, urticaria, pruritus

Rare: angioedema

Very Rare: erythema nodosum, erythema multiforme

Musculoskeletal and connective tissue disorders

Uncommon: arthralgia, myalgia including muscle cramps

Renal and urinary disorders

Uncommon: enuresis in children

General disorders and administration site conditions

Uncommon: asthenia/fatigue, malaise, oedema

Reporting of suspected adverse reactions

Health care professionals, patients/consumers are advised to closely monitor the possibility of the above ADRs associated with the use of the above drugs. If such reactions are encountered, please report to the Hetero either by filling of Suspect Adverse Drug Reactions Reporting Form (**form.heteroworld.com**) or by **Hetero Helpline No.180-020-01303**.

4.9 Overdose

Bilastine

Information regarding acute overdose of bilastine is retrieved from the experience of clinical trials conducted during the development and the post-marketing surveillance. In clinical trials, after administration of bilastine at doses 10 to 11 times the therapeutic dose (220 mg as single dose; or 200 mg/day for 7 days) to 26 adult healthy volunteer's frequency of treatment emergent adverse events was two times higher than with placebo. The adverse reactions most frequently reported were dizziness, headache and nausea. No serious adverse events and no significant prolongation in the QTc interval were reported. The information collected in the post-marketing surveillance is consistent with that reported in clinical trials.

Critical evaluation of bilastine's multiple dose (100 mg x 4 days) effect on ventricular repolarization by a “thorough QT/QTc cross-over study” involving 30 healthy adult volunteers did not show significant QTc prolongation.

There are no data for overdose in children.

In the event of overdose symptomatic and supportive treatment is recommended.

There is no known specific antidote to bilastine.

Montelukast

In chronic asthma studies, montelukast has been administered at doses up to 200 mg/day to adult patients for 22 weeks and in short term studies, up to 900 mg/day to patients for approximately one week without clinically important adverse experiences.

There have been reports of acute overdose in post-marketing experience and clinical studies with montelukast. These include reports in adults and children with a dose as high as 1,000 mg (approximately 61 mg/kg in a 42-month old child). The clinical and laboratory findings observed were consistent with the safety profile in adults and paediatric patients. There were no adverse experiences in the majority of overdose reports.

Symptoms of overdose

The most frequently occurring adverse experiences were consistent with the safety profile of montelukast and included abdominal pain, somnolence, thirst, headache, vomiting, and psychomotor hyperactivity.

Management of overdose

No specific information is available on the treatment of overdose with montelukast. It is not known whether montelukast is dialysable by peritoneal- or haemodialysis.

5. Pharmacological Properties

5.1 Mechanism of action

Bilastine

Bilastine is a non-sedating, long-acting histamine antagonist with selective peripheral H1 receptor antagonist affinity and no affinity for muscarinic receptors.

Bilastine inhibited histamine-induced wheal and flare skin reactions for 24 hours following single doses.

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 pro-inflammatory 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 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.

5.2 Pharmacodynamic properties

Bilastine

In clinical trials performed in adult and adolescent patients with allergic rhinoconjunctivitis (seasonal and perennial), bilastine 20 mg, administered once daily for 14-28 days, was effective in relieving symptoms such as sneezing, nasal discharge, nasal itching, nasal congestion, ocular itching, tearing and ocular redness. Bilastine effectively controlled symptoms for 24 hours.

No clinically relevant prolongation of QTc interval or any other cardiovascular effect has been observed in the clinical trials performed with bilastine, even at doses of 200 mg daily (10 times the clinical dose) for 7 days in 9 subjects, or even when coadministered with P-gp inhibitors, such as ketoconazole (24 subjects) and erythromycin (24 subjects). Additionally a thorough QT study including 30 volunteers has been performed.

In controlled clinical trials at the recommended dose of 20 mg once daily, the CNS safety profile of bilastine was similar to placebo and the incidence of somnolence was not statistically different from placebo. Bilastine at doses of up to 40 mg q.d. did not affect

psychomotor performance in clinical trials and did not affect driving performance in a standard driving test.

Elderly patients (≥ 65 years) included in phase II and III studies showed no difference in efficacy or safety with respect to younger patients. A post-authorization study in 146 elderly patients showed no differences in the safety profile with respect to the adult population.

Montelukast

Montelukast is an orally active compound which binds with high affinity and selectivity to the CysLT1 receptor. In clinical studies, montelukast inhibits bronchoconstriction due to inhaled LTD4 at doses as low as 5 mg. Bronchodilation was observed within 2 hours of oral administration. The bronchodilation effect caused by a β-agonist was additive to that caused by montelukast. Treatment with montelukast inhibited both early- and late-phase bronchoconstriction due to antigen challenge. Montelukast, compared with placebo, decreased peripheral blood eosinophils in adult and paediatric patients. In a separate study, treatment with montelukast significantly decreased eosinophils in the airways (as measured in sputum) and in peripheral blood while improving clinical asthma control.

5.3 Pharmacokinetic properties

Absorption

Bilastine

Bilastine is rapidly absorbed after oral administration with a time to maximum plasma concentration of around 1.3 hours. No accumulation was observed. The mean value of bilastine oral bioavailability is 61%.

Montelukast

Montelukast is rapidly absorbed following oral administration. For the 10 mg film-coated tablet, the mean peak plasma concentration (C_{max}) is achieved 3 hours (T_{max}) after administration in adults in the fasted state. The mean oral bioavailability is 64%. The oral bioavailability and C_{max} are not influenced by a standard meal. Safety and efficacy were demonstrated in clinical trials where the 10 mg film-coated tablet was administered without regard to the timing of food ingestion.

For the 5 mg chewable tablet, the C_{max} is achieved in 2 hours after administration in adults in the fasted state. The mean oral bioavailability is 73% and is decreased to 63% by a standard meal.

Distribution

Bilastine

In vitro and *in vivo* studies have shown that bilastine is a substrate of P-gp and OATP. Bilastine does not appear to be a substrate of the transporter BCRP or renal transporters OCT2, OAT1 and OAT3. Based on *in vitro* studies, bilastine is not expected to inhibit the following transporters in the systemic circulation: P-gp, MRP2, BCRP, BSEP, OATP1B1, OATP1B3, OATP2B1, OAT1, OAT3, OCT1, OCT2, and NTCP, since only mild inhibition was detected for P-gp, OATP2B1 and OCT1, with an estimated IC50 ≥ 300 μM, much higher than the calculated clinical plasma Cmax and therefore these interactions will not be clinically relevant. However, based on these results inhibition by bilastine of transporters present in the intestinal mucosa, e.g. P-gp, cannot be excluded.

At therapeutic doses bilastine is 84-90% bound to plasma proteins.

Montelukast

Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8-11 litres. Studies in rats with radiolabelled montelukast indicate minimal distribution across the blood-brain barrier. In addition, concentrations of radiolabelled material at 24 hours post-dose were minimal in all other tissues.

Metabolism

Bilastine

Bilastine did not induce or inhibit activity of CYP450 isoenzymes in *in vitro* studies.

Montelukast

Montelukast is extensively metabolised. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and children.

Cytochrome P450 2C8 is the major enzyme in the metabolism of montelukast. Additionally, CYP 3A4 and 2C9 may have a minor contribution, although itraconazole, an inhibitor of CYP 3A4, was shown not to change pharmacokinetic variables of montelukast in healthy subjects that received 10 mg montelukast daily. Based on in vitro results in human liver microsomes, therapeutic plasma concentrations of montelukast do not inhibit cytochromes P450 3A4, 2C9, 1A2, 2A6, 2C19, or 2D6. The contribution of metabolites to the therapeutic effect of montelukast is minimal.

Excretion

Bilastine

In a mass balance study performed in healthy adult 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, confirming that bilastine is not significantly metabolized in humans. The mean elimination half-life calculated in healthy volunteers was 14.5 h.

Linearity

Bilastine presents linear pharmacokinetics in the dose range studied (5 to 220 mg), with a low interindividual variability.

Montelukast

The plasma clearance of montelukast averages 45 ml/min in healthy adults. Following an oral dose of radiolabelled montelukast, 86% of the radioactivity was recovered in 5-day faecal collections and <0.2% was recovered in urine. Coupled with estimates of montelukast oral bioavailability, this indicates that montelukast and its metabolites are excreted almost exclusively via the bile.

6. Nonclinical Properties

6.1 Animal Toxicology or Pharmacology

Bilastine

Non-clinical data with bilastine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

In reproduction toxicity studies effects of bilastine on the foetus (pre-and post-implantation loss in rats and incomplete ossification of cranial bones, sternebrae and limbs in rabbits) were only observed at maternal toxic doses. The exposure levels at the NOAELs are sufficiently in excess (> 30 fold) to the human exposure at the recommended therapeutic dose.

In a lactation study, bilastine was identified in the milk of nursing rats administered a single oral dose (20 mg/kg). Concentrations of bilastine in milk were about half of those in maternal plasma. The relevance of those results for humans is unknown.

In a fertility study in rats, bilastine administered orally up to 1000 mg/kg/day did not induce any effect on female and male reproductive organs. Mating, fertility and pregnancy indices were not affected.

As seen in a distribution study in rats with determination of drug concentrations by autoradiography, bilastine does not accumulate in the CNS.

Montelukast

In animal toxicity studies, minor serum biochemical alterations in ALT, glucose, phosphorus and triglycerides were observed which were transient in nature. The signs of toxicity in animals were increased excretion of saliva, gastrointestinal symptoms, loose stools and ion imbalance. These occurred at dosages which provided >17-fold the systemic exposure seen at the clinical dosage. In monkeys, the adverse effects appeared at doses from 150 mg/kg/day (>232-fold the systemic exposure seen at the clinical dose). In animal studies, montelukast did not affect fertility or reproductive performance at systemic exposure exceeding the clinical systemic exposure by greater than 24-fold. A slight decrease in pup body weight was noted in the female fertility study in rats at 200 mg/kg/day (>69-fold the clinical systemic exposure). In studies in rabbits, a higher incidence of incomplete ossification, compared with concurrent control animals, was seen at systemic exposure >24-fold the clinical systemic exposure seen at the clinical dose. No abnormalities were seen in rats. Montelukast has been shown to cross the placental barrier and is excreted in breast milk of animals.

No deaths occurred following a single oral administration of montelukast sodium at doses up to 5,000 mg/kg in mice and rats (15,000 mg/m2 and 30,000 mg/m2 in mice and rats, respectively), the maximum dose tested. This dose is equivalent to 25,000 times the recommended daily adult human dose (based on an adult patient weight of 50 kg).

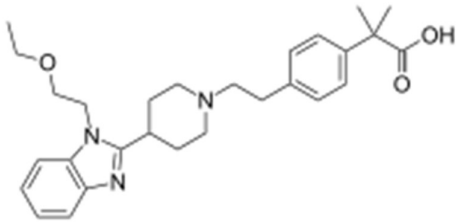
Montelukast was determined not to be phototoxic in mice for UVA, UVB or visible light spectra at doses up to 500 mg/kg/day (approximately >200-fold based on systemic exposure).

Montelukast was neither mutagenic in in vitro and in vivo tests nor tumorigenic in rodent species.

7. Description

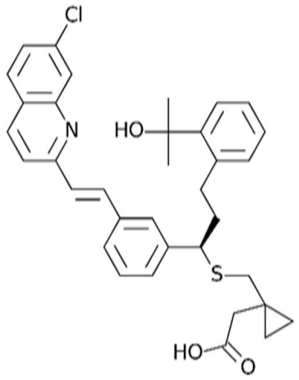
Bilastine

Bilastine is a second generation H1-antihistamine, indicated for the treatment of allergic rhinitis and chronic urticaria. Bilastine is known chemically as 2-[4-(2-{4-[1-(2-ethoxyethyl)-1h-benzimidazol-2-yl] piperidin-1-yl} ethyl) phenyl]-2-methylpropanoic acid; 2-[4-[2-[4-[1-(2-ethoxyethyl) benzimidazol-2-yl] piperidin-1-yl] ethyl] phenyl]-2-methylpropanoic acid. Its empirical formula is $C_{28}H_{37}N_3O_3$ and the molecular weight is 463.61168 g/mol. The chemical structure is:



Montelukast

Montelukast is a leukotriene receptor antagonist which inhibits physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity. Montelukast is chemically known as [R-(E)]-1-[[[1-[3-[2-(7-chloro-2-quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropane acetic acid. Its empirical formula is $C_{35}H_{35}ClNO_3S$ and the molecular weight is 586.183. The chemical structure is:



8. Pharmaceutical Particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Refer pack

8.3 Packing Information

Each alu-alu blister contains 10 Tablets.

8.4 Storage and handling instructions

Store at a temperature not exceeding 30ºC. Protect from moisture.

9. Patient Counselling Information

Talk to your doctor or pharmacist before using this medicine if you have moderate or severe renal impairment and in addition you are taking other medicines.

Children

Do not give this medicine to children under 12 years of age.

Do not exceed the recommended dose. If symptoms persist, consult your doctor.

Other medicines and bilastine

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

In particular, please discuss with your doctor if you are taking any of the following medicines:

- 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)

Bilastine with food, drink and alcohol

These tablets should not be taken with food or with grapefruit juice or other fruit juices, as this will decrease the effect of bilastine. To avoid this, you can:

- take the tablet and wait for one hour before taking food or fruit juice or
- if you have taken food or fruit juice, wait for two hours before taking the tablet.
- Bilastine, at the recommended dose (20 mg), does not increase the drowsiness produced by alcohol.

Pregnancy, breast-feeding and fertility

There are no or limited amount of data from the use of bilastine in pregnant women and during breast-feeding and on the effects on fertility.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Ask your doctor or pharmacist for advice before taking any medicine.

If you are breast-feeding or plan to breast-feed. It is not known this medicine passes into your breast milk. Talk to your healthcare provider before you take.

Do not take this medicine if you are allergic to any of its ingredients.

Before taking this medicine, tell your healthcare provider if you:

- Are allergic to aspirin

- Have phenylketonuria.
- Have any other medical conditions

Take montelukast 1 time each day, at about the same time each day

10. Details of Manufacturer

Manufactured by:

Hetero Labs Limited (Unit I),

Village: Kalyanpur, Chakkan Road,

Tehsil: Baddi , Dist: Solan,

Himachal Pradesh - 173205.

Marketed by:

Abbott Healthcare Pvt. Ltd.

Angel Space, Bldg. D-4, Gala No. 1 to 3 &

11 to 13 Ground Floor, 101 to 106 &

111 to 116 First Floor, 201 to 206 &

211 to 216 2nd Floor, Pimplas, Dist. Thane, Bhiwandi - 421 302,

Maharashtra, India.

TM- Trademark of Abbott Healthcare Pvt. Ltd.

11. Details of permission or licence number with date

Mfg. License No. MNB/06/328 dated 25/04/2024

12. Date of revision

Version 4.0, dated 22-Oct-25