For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

MASTOWELL M

1. Generic Name

Montelukast and Bilastine Tablet (10 mg + 20 mg)

2. Qualitative and quantitative composition

Each film coated bilayrered tablet contains:

Montelukast sodium IP eq. to
Montelukast…….10 mg

Bilastine ……. 20 mg

Excipients…… q.s

Colour: Erythrosine Lake (In Montelukast Layer)

The excipients used are Microcrystalline cellulose, Lactose, Polyvinyl pyrilidone, Starch, Sodium Starch Gloycolate, Colloidal Silicon Dioxide, Magnesium Stearate, Talcum, Cross Carmilos Sodium, Hydroxy Propyl Methyl Cellulose, Methyl Paraben, Propyl Paraben, Erythrosine Lake.

3. Dosage form and strength

Dosage form: Film coated bilayrered tablet

Strength: Montelukast 10 mg + Bilastine 20 mg

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

For the treatment of allergic rhinitis in adults.

4.2 Posology and Method of Administration

The recommended dose is one tablet once daily for the relief of symptoms of allergic rhinitis in adults.

The tablet should be taken one hour before or two hours after intake of food or fruit juice.

Duration of treatment

For allergic rhinitis the treatment should be limited to the period of exposure to allergens. For seasonal allergic rhinitis treatment could be discontinued after the symptoms have resolved and reinitiated upon their reappearance. In perennial allergic rhinitis continued treatment may be proposed to the patients during the allergen exposure periods.

Special populations

Elderly

No dosage adjustments are required in elderly patients.

Renal impairment

No dosage adjustment is required in adult patients with renal impairment.

Hepatic impairment

No dosage adjustment is required in adult patients with hepatic impairment.

Method of administration

Oral use.

The tablet is to be swallowed with water. It is recommended to take the daily dose in one single intake

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special Warnings and Precautions for Use

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**.**

Bilastine

In patients with moderate or severe renal impairment co-administration 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.

4.5 Drugs Interactions

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.

Bilastin

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 C_{max} 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.

4.6 Use in Special Populations (Such as Pregnant Women, Lactating Women, Paediatric Patients, Geriatric Patients Etc.)

There are no sufficient and well controlled studies on montelukast and bilastine combination in pregnant women and nursing mothers. Therefore the montelukast and bilastine combination may be used during pregnancy and lactation only if it is considered to be clearly essential.

4.7 Effects On Ability to Drive and Use Machines

Montelukast/bilastine combination has no or negligible influence on the ability to drive and use of machine. 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 this combination.

4.8 Undesirable Effects

The below adverse effects were determined based on data from the Montelukast and/or Bilastine clinical studies and post-marketing use.

Blood and lymphatic system disorders

Increased bleeding tendency, thrombocytopenia

Infections and infestations

Upper respiratory infection, oral herpes

Immune system disorder

Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, rash, localized oedema/local swelling, and erythema), Hepatic eosinophilic infiltration

Metabolism and nutrition disorders

lncreased appetite

Psychiatric disorders

Dream abnormalities including nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behaviour or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor), disturbance in attention, memory impairment, tic, hallucinations, disorientation, suicidal thinking and behaviour (suicidality), Dysphemia

Ear and labyrinth disorders

Tinnitus, vertigo

Cardiac disorders

Right bundle branch block, sinus arrhythmia, other ECG abnormal/ties, electrocardiogram QT prolonged, tachycardia, palpitation.

Nervous system disorders

Somnolence, headache, dizziness, drowsiness paraesthesia/hypoesthesia, seizure

Respiratory, thoracic and mediastinal disorders

Dyspnea, nasal discomfort, nasal dryness, epistaxis, churg-Strauss Syndrome (CSS), pulmonary eosinophilia

Gastrointestinal disorders

Upper abdominal pain, nausea, vomiting, stomach discomfort, diarrhea, dry mouth, dyspepsia and gastritis

Hepatobiliary disorders

Hepatitis (including cholestatic, hepatocellular, and mixed-pattern liver injury).

Skin and subcutaneous tissue disorders

Pruritus, rash, bruising, urticaria, pruritus, angioedema, erythema nodosum, erythema multiforme.

Musculoskeletal and connective tissue disorders

Arthralgia, myalgia including muscle cramps

General disorders and administration site conditions

Fatigue, thirst, improved pre-existing condition, malaise, oedema pyrexia and asthenia/fatigue.

Investigations

Uncommon: Increased gamma-glutamyl transferase, alanine aminotransferase increased, aspartate aminotransferase increased, blood creatinine increased, blood triglycerides increased and increased weight

4.9 Overdose

Montelukast

In chronic asthma reported 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.

Bilastine

Information regarding acute overdose of bilastine is retrieved from the experience of reported 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.

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

There is no known specific antidote to bilastine.

5. Pharmacological properties

5.1 Mechanism of Action

Montelukast

Montelukast is an orally active compound which binds with high affinity and selectivity to the CysLT1 receptor.

Bilastine

Bilastine is an antihistamine; its principal effects are mediated via selective inhibition of peripheral H1 receptors. The anti-histaminic activity of bilastine has been documented in a variety of animal and human models. It shows moderate 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 of high affinity for histamine H,-receptors and no affinity for muscarinic, serotonergic, dopaminergic and noradrenergic receptors. Bilastine has been demonstrated to have limited distribution to the brain following oral administration.

5.2 Pharmacodynamic Properties

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. 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.

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

5.3 Pharmacokinetic Properties

Montelukast

Absorption

Montelukast is rapidly absorbed following oral administration. For the 10 mg film-coated tablet, the mean peak plasma concentration (Cmax) is achieved 3 hours (Tmax) after administration in adults in the fasted state. The mean oral bioavailability is 64%. The oral bioavailability and Cmax 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 Cmax 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

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.

Biotransformation

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.

Elimination

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.

Bilastine

Absorption

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%.

Distribution

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 $\geq$ 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.

Biotransformation

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

Elimination

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.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

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, gastro-intestinal 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 (>69fold 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 5000 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.

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.

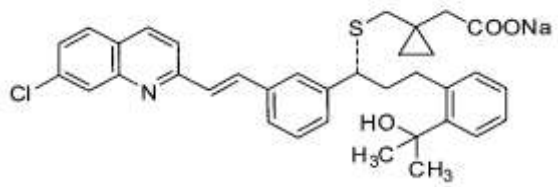
In a lactation study, bilastine was identified in the milk of nursing rats administered a single oral dose (20 mg/kg). Concentrations of bilastine in milk were about half of those in maternal plasma. The relevance of those results for humans is unknown.

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.

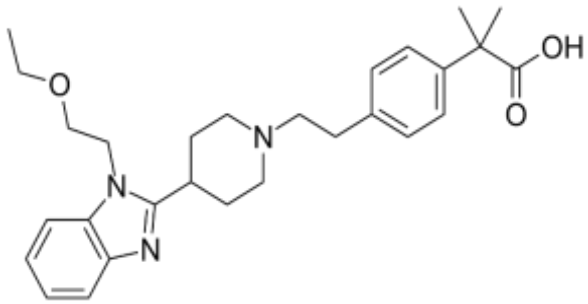
As seen in a distribution study in rats with determination of drug concentrations by autoradiography, bilastine does not accumulate in the CNS.

7. DESCRIPTION

Montelukast Sodium is monosodium salt of 1-[[[(1R)-1-[3-[(1E)-2(7-chloro-2-quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl] thio] methyl] cyclopropaneacetic acid. The empirical formula is $C_{35}H_{35}ClNNaO_3S$ and its molecular weight is 608.2 g/mol. The chemical structure of Montelukast is:



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-methylpropionic acid. The empirical formula is $C_{28}H_{37}N_3O_3$ and its molecular weight is 463.622 g/mol. The chemical structure of Bilastine is:



MASTOWELL M is one side pink & other side white coloured, round, biconvex, bilayered, film coated tablets, plain on both side. The excipients used are Microcrystalline cellulose, Lactose, Polyvinyl pyrilidone, Starch, Sodium Starch Gloycolate, Colloidal Silicon Dioxide, Magnesium Stearate, Talcum, Cross Carmilos Sodium, Hydroxy Propyl Methyl Cellulose, Methyl Paraben, Propyl Paraben, Erythrosine Lake.

8. Pharmaceutical Particulars

8.1 Incompatibilities

None

8.2 Shelf-life

Do not use later than date of expiry

8.3 Packaging information

MASTOWELL M is packed in Alu-Alu blister Pack of 10 tablets.

8.4 Storage and Handing Instructions

Store at a temperature not exceeding 30ºC, protect from light and moisture.

Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

Package leaflet: Information for the user

MASTOWELL M

Read all of this leaflet carefully before you start taking this medicine.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.

• If any of the side effects gets troublesome or serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist. **In this leaflet:**

9.1. What MASTOWELL M is and what it is used for

9.2. Before you take MASTOWELL M

9.3. How to take MASTOWELL M

9.4. Possible side effects

9.5. How to store MASTOWELL M

9.6. Contents of the pack and other information

9.1. WHAT MASTOWELL M IS AND WHAT IT IS USED FOR

MASTOWELL M contains the active substance montelukast which is a leukotriene receptor antagonist that blocks substances called leukotrienes, and bilastine which is an antihistamine. MASTOWELL M is used to relieve the symptoms of allergic rhinitis (sneezing, itchy, runny, blocked-up nose and red and watery eyes).

9.2. BEFORE YOU TAKE MASTOWELL M

Do not take MASTOWELL M

if you are allergic to Montelukast /bilastine or any of the other ingredients of this medicine.

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

Other medicines and MASTOWELL M

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)

•Phenobarbital (used for treatment of epilepsy)

•Phenytoin (used for treatment of epilepsy)

•Rifampicin (used to treat tuberculosis and some other infections)

•Gemfibrozil (used for treatment of high lipid levels in plasma)

MASTOWELL M 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.

Pregnancy, breast-feeding and fertility

There are no or limited amount of data from the use of MASTOWELL M in pregnant women and during breast-feeding.

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.

Driving and using machines

MASTOWELL M has no or negligible influence on the ability to drive and use of machine. However the response from each patient to the medicine may be different. Therefore you should check how this medicine affects you, before driving or operating machinery.

9.3. HOW TO TAKE MASTOWELL M

Always take this medicine exactly as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose in adults is one tablet once a day.

•The tablet is for oral use.

•The tablet must be taken one hour before or two hours after intake of food or fruit juice.

•Swallow your tablet with a glass of water.

Regarding the duration of treatment, your physician will determine the type of disease you are suffering from and will determine for how long you should take MASTOWELL M.

If you take more MASTOWELL M than you should

If you, or anyone else, have taken too many MASTOWELL M tablets, contact your doctor or pharmacist immediately or go to the emergency department of your nearest hospital. Please remember to take this medicine pack or this leaflet with you.

If you forget to take MASTOWELL M

Do not take a double dose to make up for a forgotten dose.

If you forget to take your dose on time, take it as soon as possible, and then go back to your regular dosing schedule.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side effects that may be experienced in adults and adolescents are:

- rash
- headache
- drowsiness
- fever
- diarrhoea, nausea, vomiting
- elevated liver enzyme
- behaviour and mood related changes: dream abnormalities, including nightmares, trouble sleeping, sleepwalking, irritability, feeling anxious, restlessness
- dizziness, drowsiness, pins and needles/numbness
- nosebleed
- dry mouth, indigestion
- bruising, itching, hives
- joint or muscle pain, muscle cramps

- bedwetting in children
- weakness/tiredness, feeling unwell, swelling
- abnormal ECG heart tracing
- stomach pain
- increased appetite
- irregular heartbeat
- increased weight
- dry or uncomfortable nose
- belly pain
- gastritis (inflammation of the stomach wall)
- vertigo (a feeling of dizziness or spinning)
- thirst
- dyspnoea (difficulty in breathing)
- indigestion
- cold sores (oral herpes)
- tinnitus (ringing in the ears)
- difficulty in sleeping
- blood tests which show changes in the way kidney is working
- blood fats increased
- palpitations (feeling your heart beat)
- tachycardia (fast heart beat)
- allergic reactions the signs of which may include difficulty in breathing, dizziness, collapsing or losing consciousness, swelling of your face, lips, tongue or throat, and/or swelling and redness of the skin. If you notice any of these serious side effects, stop taking the medicine and seek urgent medical advice straight away.
- behaviour and mood related changes: disturbance in attention, memory impairment, uncontrolled muscle movements
- tender red lumps under the skin, most commonly on your shins (erythema nodosum)
- behaviour and mood related changes: obsessive-compulsive symptoms, stuttering

9.5. HOW TO STORE MASTOWELL M

Store at a temperature not exceeding 30ºC, protect from light and moisture.

Keep out of reach of children

9.6. CONTENTS OF THE PACK AND OTHER INFORMATION

What MASTOWELL M contains

The active substance are montelukast and bilastine. Each tablet contains montelukast 10mg and bilastine 20 mg.

The excipients used are Microcrystalline cellulose, Lactose, Polyvinyl pyrilidone, Starch, Sodium Starch Gloycolate, Colloidal Silicon Dioxide, Magnesium Stearate, Talcum, Cross Carmilos Sodium, Hydroxy Propyl Methyl Cellulose, Methyl Paraben, Propyl Paraben, Erythrosine Lake.

10. DETAILS OF MANUFACTURER

Synokem Pharmaceuticals Ltd

Plot No. 56-57, Sector 6A, I. I. E (SIDCUL), Ranipur (BHEL),

Haridwar – 249403(Uttarakhand).

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Mfg Licence No.: 27/UA/2018 issued on 12.03.2020

12. DATE OF REVISION

Not Applicable

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/ MASTOWELL M 10,20 mg/AUG-20/01/PI