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

ALLEGRA® M Tablets
Fexofenadine Hydrochloride and Montelukast Tablets

COMPOSITION

ALLEGRA® M Tablets
Each film coated tablet contains:
Fexofenadine hydrochloride I.P. ……... 120 mg
Montelukast Sodium I.P. equivalent to Montelukast …….. 10 mg
Excipients..... q.s.
Colour: Yellow oxide of iron and Titanium Dioxide I.P.

DOSAGE FORM

Film coated tablet

INDICATIONS

ALLEGRA®M tablets are indicated for the treatment of allergic rhinitis in adults only.

DOSAGE AND ADMINISTRATION

Adults: One tablet once daily

USE IN SPECIFIC POPULATIONS

Renal Impairment: There is no data of this combination in renally impaired patients.

Hepatic Impairment: No dosage adjustment is required in case of mild to moderate hepatic insufficiency.

Pregnancy: There are no studies in pregnant women. Allegra® M should be used in pregnancy only if the potential benefit outweighs the potential risk to the foetus.
It may be used during pregnancy only if it is considered to be clearly essential.

Lactation: There are no studies in lactating women. Allegra® M should be used in nursing women only if the potential benefit outweighs the potential risk to the infant.
It may be used in breast-feeding only if it is considered to be clearly essential

Geriatric Use: No dosage adjustment in the elderly is required.

CONTRAINDICATIONS

ALLEGRA® M tablets are contraindicated in patients with a known hypersensitivity to montelukast, fexofenadine or to any of the excipients.

WARNINGS AND PRECAUTIONS

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 beta-agonist should be used. Patients should

seek their doctor's advice as soon as possible if they need more inhalations of short-acting beta-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.

Neuropsychiatric events have been reported in adults, adolescents, and children taking Montelukast (see section Adverse reactions). Patients and physicians should be alerted 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.

This medicinal product contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

INTERACTIONS

Fexofenadine

The coadministration of fexofenadine hydrochloride with erythromycin or ketoconazole resulted in no significant increases in QTc. No differences in adverse effects were reported whether these agents were administered alone or in combination.

Administration of an antacid containing aluminium and magnesium hydroxide gels 15 minutes prior to fexofenadine hydrochloride, caused a reduction in the bioavailability. It is advisable to leave 2-hours between the administration of fexofenadine hydrochloride and aluminium- and magnesium hydroxide-containing antacids.

No interaction between fexofenadine and omeprazole was observed.

Montelukast

Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma. No dose adjustment is needed when montelukast is co-administered with 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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

UNDESIRABLE EFFECTS

Fexofenadine

In placebo-controlled trials involving seasonal allergic rhinitis and chronic idiopathic urticaria patients, adverse events were comparable in fexofenadine- and placebo-treated patients.

The most frequent adverse events reported with fexofenadine include:
>3%: headache,
1-3%: drowsiness, dizziness and nausea.

Events that have been reported during controlled trials involving seasonal allergic rhinitis and chronic idiopathic urticaria patients with incidences less than 1% and similar to placebo and have been reported rarely during postmarketing surveillance include: fatigue, insomnia, nervousness, and sleep disorders or paroniria. In rare cases, rash, urticaria, pruritus and hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnea, flushing and systemic anaphylaxis have been reported.

Adverse events reported in placebo-controlled chronic idiopathic urticaria studies were similar to those reported in placebo-controlled seasonal allergic rhinitis studies. In placebo-controlled trials involving pediatric seasonal allergic rhinitis patients (6-11 years of age), adverse events were similar to those observed in trials involving seasonal allergic rhinitis patients 12 years and older. In controlled clinical trials involving pediatric

patients 6 months to 5 years of age, there were no unexpected adverse events in patients treated with fexofenadine hydrochloride.

Montelukast
The following adverse reactions have been reported in postmarketing use:

System Organ Class	Adverse Reaction	Frequency Category
Infections and infestations	upper respiratory infection[1]	Very Common
Blood and lymphatic system disorders	increased bleeding tendency	Rare
	Thrombocytopenia	Very Rare
Immune system disorder	hypersensitivity reactions including anaphylaxis	Uncommon
	hepatic eosinophilic infiltration	Very Rare
Psychiatric disorders	dream abnormalities including nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behaviour or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor[2])	Uncommon
	disturbance in attention, memory impairment, tic	Rare
	hallucinations, disorientation, suicidal thinking and behaviour (suicidality)	Very Rare
	Obsessive-compulsive symptoms[1], dysphemia[1]	Not Known
Nervous system disorder	dizziness, drowsiness paresthesia/hypoesthesia, seizure	Uncommon
Cardiac disorders	palpitations	Rare
Respiratory, thoracic and mediastinal disorders	epistaxis	Uncommon
	Churg-Strauss Syndrome (CSS) (see section Warnings and Precautions), pulmonary eosinophilia	Very Rare
Gastrointestinal disorders	Diarrhoea[3], nausea[3], vomiting[3]	Common
	dry mouth, dyspepsia	Uncommon
Hepatobiliary disorders	elevated levels of serum transaminases (ALT, AST)	Common
	Hepatitis (including cholestatic, hepatocellular, and mixed-pattern liver injury).	Very Rare
Skin and subcutaneous tissue disorders	Rash[3]	Common
	bruising, urticaria, pruritus	Uncommon
	angioedema	Rare
	erythema nodosum, erythema multiforme	Very Rare
Musculoskeletal and connective tissue disorders	arthralgia, myalgia including muscle cramps	Uncommon
Renal and urinary disorders	Enuresis in children	Uncommon
General disorders and administration site conditions	Pyrexia[3]	Common
	asthenia/fatigue, malaise, oedema,	Uncommon

Frequency category: Defined for each adverse reaction by the incidence reported in the clinical trials data base: Very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000).

[1] This adverse experience, reported as very common in the patients who received montelukast, was also reported as very common in the patients who received placebo in clinical trials.
[2] Frequency category: Rare.
[3] This adverse experience, reported as common in the patients who received montelukast, was also reported as common in the patients who received placebo in clinical trials.

OVERDOSAGE

There is no data reported on the overdosage of this combination since launch in 2012. However, overdosage has been reported with individual molecules.

Fexofenadine

Human Experience:
Most reports of fexofenadine hydrochloride overdose contain limited information. However, dizziness, drowsiness, and dry mouth have been reported. Single doses up to 800 mg and doses up to 690 mg BID for 1 month or 240 mg QD for 1 year were studied in healthy subjects without the development of clinically significant adverse events as compared to placebo. The maximum tolerated dose of fexofenadine was not established.

Management:
Consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended. Hemodialysis did not effectively remove fexofenadine from blood.

Montelukast

In chronic asthma studies, montelukast has been administered at doses up to 200 mg/day to 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 1000 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 haemo-dialysis.

MANUFACTURED BY:
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Source:

- Fexofenadine: CCDS V6 dated 14th May 2020
- Montelukast: CCDS v1 dated 04th Feb 2021

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