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เอกสารกำกับยาภาษาอังกฤษ

(เหมือนกันทุกขนาดบรรจุ)

MONKAST

Montelukast film-coated tablet

1. Name of the medicinal product

MONKAST-5 film-coated tablet

MONKAST-10 film-coated tablet

2. Qualitative and quantitative composition

MONKAST-5

Each film-coated tablet contains montelukast sodium, which is equivalent to 5 mg montelukast.

MONKAST-10

Each film-coated tablet contains montelukast sodium, which is equivalent to 10 mg montelukast.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet

MONKAST-5: Orange, round, biconvex film coated tablet and plain on both sides.

MONKAST-10: Light orange, round, biconvex film coated tablet, with engraved “10” on one side and plain on the other.

4. Clinical Particulars

4.1 Therapeutic indications [1.1], [2.1]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (1) Therapeutic indications.)

(Reference 2: Product Circular of Singulair®, Thailand, Update January 2019. Topic (1) Indications.)

Montelukast is indicated in the treatment of asthma as add-on therapy in those patients with mild to moderate persistent asthma who are inadequately controlled on inhaled corticosteroids and in whom “as-needed” short acting beta-agonists provide inadequate clinical control of asthma. In those asthmatic patients in whom Montelukast is indicated in asthma, Montelukast can also provide symptomatic relief of seasonal allergic rhinitis.

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Montelukast is also indicated in the prophylaxis of asthma in which the predominant component is exercise-induced bronchoconstriction.

4.2 Posology and method of administration [1.2], [2.2]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (2) Posology and method of administration.)

(Reference 2: Product Circular of Singulair®, Thailand, Update January 2019. Topic (2) Dosage and administration.)

Posology

The recommended dose for adults and adolescents 15 years of age and older with asthma, or with asthma and concomitant seasonal allergic rhinitis, is one 10 mg tablet daily to be taken in the evening.

The recommended dose for pediatric patients 6 to 14 years of age with asthma, or with asthma and concomitant seasonal allergic rhinitis, is one 5 mg tablet daily to be taken in the evening.

Special populations

Elderly

No dose adjustment is necessary for elderly patients.

Renal impairment

No dose adjustment is necessary in patients with renal insufficiency.

Hepatic impairment

No dose adjustment is necessary in patients with mild-to-moderate hepatic impairment.

Therapy with Montelukast in relation to other treatments for asthma

Montelukast can be added to a patient's existing treatment regimen. Inhaled corticosteroids: Treatment with Montelukast can be used as add-on therapy in patients when inhaled corticosteroids plus “as needed” short acting β-agonists provide inadequate clinical control. Montelukast should not be abruptly substituted for inhaled corticosteroids (see section 4.4).

Method of administration

Oral use. MONKAST-10 and MONKAST-5 can be taken with or without food.

4.3 Contraindication [1.3], [2.3]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (3) Contraindication)

(Reference 2: Product Circular of Singulair®, Thailand, Update January 2019. Topic (3) Contraindications)

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warning and precautions for use [1.4]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (4) Special warnings and precautions for use.)

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 (see section 4.8). 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 Interactions with other medicinal products and other forms of interactions [1.5]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (5) Interactions with other medicinal products and other forms of interactions.)

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 metabolized 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 metabolized 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.

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4.6 Fertility, pregnancy and lactation [1.6], [3.6]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (6) Fertility, pregnancy and lactation.)

(Reference 3: AHFS Drug Information 2018 p. 2919 Topic (6) Leukotriene Modifiers/ Montelukast Sodium/ Cautions/ Pregnancy, Fertility, and Lactation)

Pregnancy

Animal studies do not indicate harmful effects with respect to effects on pregnancy or embryonal/fetal development. Available data from published prospective and retrospective cohort studies with montelukast use in pregnant women evaluating major birth defects have not established a drug-associated risk. Available studies have methodologic limitations, including small sample size, in some cases retrospective data collection, and inconsistent comparator groups.

Montelukast may be used during pregnancy only if it is considered to be clearly essential.

Breast-feeding

Studies in rats have shown that montelukast is excreted in milk (see section 5.3). It is unknown whether montelukast/metabolites are excreted in human milk.

Montelukast may be used in breast-feeding only if it is considered to be clearly essential.

Fertility

Reproduction studies in female rats using oral montelukast doses up to 100 mg/kg (estimated exposure approximately 20 times the AUC for adults at the maximum recommended daily oral dose) have not revealed evidence of impaired fertility, oral doses of 200 mg/kg (estimated exposure 70 times the AUC for adults at the maximum recommended daily oral dose) have been associated with reduced fertility and fecundity indices. Reproduction studies in male rates using oral montelukast doses up to 800 mg/kg (estimated exposure approximately 160 times the AUC for adults at the maximum recommended daily oral dose) have not revealed evidence of impaired fertility.

4.7 Effects on ability to drive and use machines [1.7]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (7) Effects on ability to drive and use machines.)

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

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4.8 Undesirable effects [1.8]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (8) Undesirable effects.)

Montelukast has been evaluated in clinical studies as follows:

• 10 mg film-coated tablets in approximately 4,000 adult and adolescent asthmatic patients 15 years of age and older.

• 10 mg film-coated tablets in approximately 400 adult and adolescent asthmatic patients with seasonal allergic rhinitis 15 years of age and older.

• 5 mg chewable tablets in approximately 1,750 pediatric asthmatic patients 6 to 14 years of age.

The following drug-related adverse reactions in clinical studies were reported commonly (≥1/100 to <1/10) in asthmatic patients treated with montelukast and at a greater incidence than in patients treated with placebo:

Body System Class	Adult and Adolescent Patients 15 years and older (two 12-week studies; n=795)	Pediatric Patients 6 to 14 years old (one 8-week study; n=201) (two 56-week studies; n=615)
Nervous system disorders	headache	headache
Gastro-intestinal disorders	Abdominal pain	

With prolonged treatment in clinical trials with a limited number of patients for up to 2 years for adults, and up to 12 months for pediatric patients 6 to 14 years of age, the safety profile did not change.

Tabulated list of Adverse Reactions

Adverse reactions reported in post-marketing use are listed, by System Organ Class and specific Adverse Reactions, in the table below. Frequency Categories were estimated based on relevant clinical trials.

System Organ Class	**Adverse Reactions**	**Frequency Category***
Infections and infestations	upper respiratory infection†	Very Common
Blood and lymphatic system disorders	increased bleeding tendency	Rare
	thrombocytopenia	Very Rare
Immune system disorders	hypersensitivity reactions including anaphylaxis	Uncommon
	hepatic eosinophilic infiltration	Very Rare

Psychiatric disorders	dream abnormalities including nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behavior or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor[§])	Uncommon
	disturbance in attention, memory impairment, tic	Rare
	hallucinations, disorientation, suicidal thinking and behavior (suicidality), obsessive-compulsive symptoms, dysphemia	Very Rare
Nervous system disorders	dizziness, drowsiness, paraesthesia/hypoesthesia, seizure	Uncommon
Cardiac disorders	palpitations	Rare
Respiratory, thoracic and mediastinal disorders	epistaxis	Uncommon
	Churg-Strauss Syndrome (CSS) (see section 4.4)	Very Rare
	pulmonary eosinophilia	Very Rare
Gastro-intestinal disorders	diarrhea‡, nausea‡, vomiting[‡]	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[‡]	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[‡]	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).

†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.

‡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.

§ Frequency Category: Rare

4.9 Overdose [1.9]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (9) Overdose.)

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 pediatric 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 hemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties [1.10]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (10) Pharmacodynamic properties.)

Pharmacotherapeutic group: Leukotriene receptor antagonist

ATC-code: R03D C03

Mechanism of action

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.

Pharmacodynamic effects

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 pediatric 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.

Clinical efficacy and safety

In studies in adults, montelukast, 10 mg once daily, compared with placebo, demonstrated significant improvements in morning FEV1 (10.4% vs 2.7% change from baseline), AM peak expiratory flow rate (PEFR) (24.5 L/min vs 3.3 L/min change from baseline), and significant decrease in total β-agonist use (-26.1% vs -4.6% change from baseline). Improvement in patient-reported daytime and nighttime asthma symptoms scores was significantly better than placebo.

Studies in adults demonstrated the ability of montelukast to add to the clinical effect of inhaled corticosteroid (% change from baseline for inhaled beclomethasone plus montelukast vs beclomethasone, respectively for FEV1: 5.43% vs 1.04%; β-agonist use: -8.70% vs 2.64%). Compared with inhaled beclomethasone (200 μg twice daily with a spacer device),

montelukast demonstrated a more rapid initial response, although over the 12-week study, beclomethasone provided a greater average treatment effect (% change from baseline for montelukast vs beclomethasone, respectively for FEV1: 7.49% vs 13.3%; β-agonist use: -28.28% vs -43.89%). However, compared with beclomethasone, a high percentage of patients treated with montelukast achieved similar clinical responses (e.g., 50% of patients treated with beclomethasone achieved an improvement in FEV1 of approximately 11% or more over baseline while approximately 42% of patients treated with montelukast achieved the same response).

A clinical study was conducted to evaluate montelukast for the symptomatic treatment of seasonal allergic rhinitis in adult and adolescent asthmatic patients 15 years of age and older with concomitant seasonal allergic rhinitis. In this study, montelukast 10 mg tablets administered once daily demonstrated a statistically significant improvement in the Daily Rhinitis Symptoms score, compared with placebo. The Daily Rhinitis Symptoms score is the average of the Daytime Nasal Symptoms score (mean of nasal congestion, rhinorrhea, sneezing, nasal itching) and the Nighttime Symptoms score (mean of nasal congestion upon awakening, difficulty going to sleep, and nighttime awakenings scores). Global evaluations of allergic rhinitis by patients and physicians were significantly improved, compared with placebo. The evaluation of asthma efficacy was not a primary objective in this study.

In an 8-week study in pediatric patients 6 to 14 years of age, montelukast 5 mg once daily, compared with placebo, significantly improved respiratory function (FEV1 8.71% vs 4.16% change from baseline; AM PEFR 27.9 L/min vs 17.8 L/min change from baseline) and decreased “as-needed” β-agonist use (-11.7% vs +8.2% change from baseline).

Significant reduction of exercise-induced bronchoconstriction (EIB) was demonstrated in a 12-week study in adults (maximal fall in FEV1 22.33% for montelukast vs 32.40% for placebo; time to recovery to within 5% of baseline FEV1 44.22 min vs 60.64 min). This effect was consistent throughout the 12-week study period. Reduction in EIB was also demonstrated in a short term study in pediatric patients (maximal fall in FEV1 18.27% vs 26.11%; time to recovery to within 5% of baseline FEV1 17.76 min vs 27.98 min). The effect in both studies was demonstrated at the end of the once-daily dosing interval.

In aspirin-sensitive asthmatic patients receiving concomitant inhaled and/or oral corticosteroids, treatment with montelukast, compared with placebo, resulted in significant improvement in asthma control (FEV1 8.55% vs -1.74% change from baseline and decrease in total β-agonist use -27.78% vs 2.09% change from baseline).

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5.2 Pharmacokinetic properties [1.11]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (11) Pharmacokinetic properties.)

Absorption

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

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

Biotransformation

Montelukast is extensively metabolized. 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 radiolabeled montelukast, 86% of the radioactivity was recovered in 5-day fecal 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.

Characteristics in Patients

No dosage adjustment is necessary for the elderly or mild to moderate hepatic insufficiency. Studies in patients with renal impairment have not been undertaken. Because montelukast and its metabolites are eliminated by the biliary route, no dose adjustment is anticipated to be necessary in patients with renal impairment. There are no data on the pharmacokinetics of montelukast in patients with severe hepatic insufficiency (Child-Pugh score >9).

5.3 Preclinical safety data [1.12]

(Reference 1: SmPC of Singulair®, Update 27 March 2020. Topic (12) Preclinical safety data.)

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.

6. Pharmaceutical particulars

6.1 List of excipients

MONKAST-5, MONKAST-10

Croscarmellose sodium, Lactose monohydrate, Microcrystalline cellulose PH101, Hydroxy propyl cellulose, Isopropyl alcohol, Microcrystalline cellulose PH 102, Magnesium stearate, Opadry® AMB II white, Purified Water, Red iron oxide, Yellow iron oxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Not applicable

6.5 Nature and contents of container

MONKAST-5

Film-coated tablets with packed in aluminium-aluminium, amber PVC-aluminium and opaque white PVC-aluminium blister pack of 10 and 14 tablets packed in paper box of 1, 2, 3, 10 and 50 packs

MONKAST-10

Film-coated tablets with packed in aluminium-aluminium, amber PVC-aluminium and opaque white PVC-aluminium blister pack of 10 and 14 tablets packed in paper box of 1, 2, 3, 10 and 50 packs

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7. Manufacturer

Millimed Co., Ltd. (Branch)

174 Moo 8, Pha Ngam, Wiang Chai, Chiang Rai, 57210, Thailand

Tel +66 2945 9555

8. Marketing authorization number(s)

MONKAST-5

XXXXXXXX

MONKAST-10

XXXXXXXX

9. Date of first authorization/renewal of the authorization

XX.XX.XX

10. Date of revision of the text

09 Febuary 2022