1.6.1 Summary of Products Characteristics

1. Name of the Medicinal Product:

Product Name: Kipel – 4 [Montelukast sodium chewable Tablets 4 mg]

2. Qualitative and quantitative composition

Qualitative Declaration:

Name of Ingredients	Specification
Drug Substance	
Montelukast sodium@	Ph.Eur/ USP
Excipients	
Lactose anhydrous (DC grade)#	USP-NF
Mannitol (DC grade)	USP-NF
Hydroxy propyl cellulose	USP-NF
Sodium starch gycollate	USP-NF
Aspartame	USP-NF
Pineapple flavor	IHS
Colloidal silicon dioxide	USP-NF
Magnesium stearate USP-NF	USP-NF

Quantitative Declaration:

Description:

white to off white, Pineapple flavoured, Sweet round shaped biconvex chewable tablets.

Composition:

Ingredients	Specification	mg/tablet	Function of ingredients
Montelukast sodium@	Ph.Eur/ USP	4.20	Active ingredient
Lactose anhydrous (DC grade)#	USP-NF	20.00	Diluent
Mannitol (DC grade)	USP-NF	150.10	Diluent
Hydroxy propyl cellulose	USP-NF	5.00	Binder
Sodium starch gycollate	USP-NF	10.00	Disintegrant
Aspartame	USP-NF	2.00	Sweetening agent
Pineapple flavor	IHS	4.70	Flavoring agent
Colloidal silicon dioxide	USP-NF	2.00	Glident
Magnesium stearate	USP-NF	2.00	Lubricant
Weight of tablet		**200.00**	

USP-NF : United States Pharmacopoeia - National Formulary, USP: United States Pharmacopoeia

IHS: Inhouse Specification.Ph.Eur:European Pharmacopoeia

@ 4.20 mg of Montelukast sodium is eq. to 4.00 mg of Montelukast.

Qty. of montelukast sodium is based on its potency and water content.

$$\text{Actual quantity of Montelukast sodium/tablet} = \frac{100 \times 100 \times 4.20}{\text{Actual Assay Montelukast sodium} \times (100\text{-LOD})}$$

#Quantity of Lactose anhydrous is based on the qty. of Montelukast sodium dispensed.

3. Pharmaceutical Form

Oral Chewable Tablet

4. Clinical Particulars

4.1 Therapeutic Indications

Asthma - Montelukast is indicated for the prophylaxis and chronic treatment of asthma in adults and pediatric patients 12 months of age and older.

Exercise-Induced Bronchoconstriction - Montelukast is indicated for prevention of

exercise-induced bronchoconstriction in patients 15 years of age and older.

Allergic Rhinitis - Montelukast is indicated for the relief of symptoms of allergic rhinitis(seasonal allergic rhinitis in adults and pediatric patients 2 years of age and older, &perennial allergic rhinitis in adults and pediatric patients 6 months of age & older).

4.2 Posology and method of administration

Asthma
Montelukast should be taken once daily in the evening. The following doses are recommended:
For adults and adolescents 15 years of age and older: one 10-mg tablet.

For pediatric patients 6 to 14 years of age: one 5-mg chewable tablet.

For pediatric patients 2 to 5 years of age: one 4-mg chewable tablet

Safety and effectiveness in pediatric patients less than 12 months of age with asthma have not been established.

There have been no clinical trials in patients with asthma to evaluate the relative efficacy of morning versus evening dosing. The pharmacokinetics of montelukast are similar whether dosed in the morning or evening. Efficacy has been demonstrated for asthma when montelukast was administered in the evening without regard to time of food ingestion.

Exercise-Induced Bronchoconstriction (EIB) in Patients 15 Years of Age and Older

For prevention of EIB, a single 10 mg dose of montelukast should be taken at least 2 hours before exercise. An additional dose should not be taken within 24 hours of a previous dose. Patients already taking montelukast daily for another indication (including chronic asthma) should not take an additional dose to prevent EIB. All patients should have available for rescue a short-acting β-agonist. Safety and effectiveness in patients younger than 15 years of age have not been established. Daily administration of montelukast for the chronic treatment of asthma has not been established to prevent acute episodes of EIB.

Allergic Rhinitis
For allergic rhinitis, montelukast should be taken once daily. Efficacy was demonstrated for seasonal allergic rhinitis when montelukast was administered in the morning or the evening without regard to time of food ingestion. The time of administration may be individualized to suit patient needs.

The following doses for the treatment of symptoms of seasonal allergic rhinitis are recommended:

For adults and adolescents 15 years of age and older: one 10-mg tablet.
For pediatric patients 6 to 14 years of age: one 5-mg chewable tablet.
For pediatric patients 2 to 5 years of age: one 4-mg chewable tablet.

Safety and effectiveness in pediatric patients younger than 2 years of age with seasonal allergic rhinitis have not been established.

Asthma and Allergic Rhinitis

Patients with both asthma and allergic rhinitis should take only one montelukast dose daily in the evening.

4.3 Contraindications

Hypersensitivity to any component of this product.

4.4 Special Warnings and Precautions for Use

Not available.

4.5 Drug Interactions

No dose adjustment is needed when montelukast is co-administered with theophylline, prednisone, prednisolone, oral contraceptives, terfenadine, digoxin, warfarin, thyroid hormones, sedative hypnotics, non-steroidal anti-inflammatory agents, benzodiazepines, decongestants, and Cytochrome P450 (CYP) enzyme inducers .

4.6 Pregnancy and Lactation

There are no adequate and well-controlled studies in pregnant women. Montelukast should be used during pregnancy only if clearly needed.

4.7 Effects on Ability to Drive and Use Machines

There is no evidence that Montelukast affects the ability to drive and use machines.

4.8 Undesirable Effects

Common adverse reactions are headache, influenza, abdominal pain, cough, dyspepsia, increase in ALT, asthenia/fatigue, dizziness, fever, gastroenteritis, dental pain, nasal congestion, rash, increase in AST, pyuria.

The following additional adverse reactions have been reported:

Blood and lymphatic system disorders: increased bleeding tendency

Immune system disorders: hypersensitivity reactions including anaphylaxis, very rarely hepatic eosinophilic infiltration

Psychiatric disorders: agitation including aggressive behavior or hostility, anxiousness, depression, dream abnormalities, hallucinations, insomnia, irritability,restlessness, somnambulism, suicidal thinking and behavior (including suicide), tremor.

Nervous system disorders: drowsiness, paraesthesia/hypoesthesia, seizures

Cardiac disorders: palpitations

Respiratory, thoracic and mediastinal disorders: epistaxis

Gastrointestinal disorders: diarrhea, dyspepsia, nausea, very rarely pancreatitis, vomiting

Hepatobiliary disorders: Rare cases of cholestatic hepatitis, hepatocellular liverinjury, and mixed-pattern liver injury have been reported in patients treated with montelukast. Most of these occurred in combination with other confounding factors such as use of other medications, or when montelukast was administered to patients who had underlying potential for liver disease such as alcohol use or other forms of hepatitis.

Skin and subcutaneous tissue disorders: angioedema, bruising, erythema nodosum, pruritus, urticaria.

Musculoskeletal and connective tissue disorders: arthralgia, myalgia including muscle cramps.

General disorders and administration site conditions: edema

In rare cases, patients with asthma on therapy with 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 events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association between montelukast and these underlying conditions has not been established.

4.9 Overdose

No specific information is available on the treatment of overdosage with montelukast. 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.

5. Pharmacological properties

5.1 Pharmacodynamic Properties

Mechanism of action:

The cysteinyl leukotrienes (LTC4, LTD4, and LTE4) are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils. These eicosanoids 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 airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process. 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 that binds with high affinity and selectivity to the CysLT1 receptor (in preference to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or β-adrenergic receptor). Montelukast inhibits physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity. Montelukast causes inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD4 in asthmatics.

5.2 Pharmacokinetic Properties

Absorption
For the 5-mg chewable tablet, the mean Cmax is achieved in 2 to 2.5 hours after administration to adults in the fasted state. The mean oral bioavailability is 73% in the fasted state versus 63% when administered with a standard meal in the morning.

Distribution
Montelukast is more than 99% bound to plasma proteins. The steady state volume of distribution of montelukast averages 8 to 11 liters.

Metabolism
Montelukast is extensively metabolized. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and pediatric patients.

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.

In several studies, the mean plasma half-life of montelukast ranges from 2.7 to 5.5 hours in healthy young adults. The pharmacokinetics of montelukast are nearly linear for oral doses up to 50 mg. During once-daily dosing with 10-mg montelukast, there is little accumulation of the parent drug in plasma (14%).

5.3 Preclinical safety Data

Not available.

6. Pharmaceutical Particulars

6.1 List of Excipients

Lactose anhydrous (DC grade)# , Mannitol (DC grade) , Hydroxy propyl cellulose , Sodium

starch gycollate , Aspartame , Pineapple flavor , Colloidal silicon dioxide , Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

24 months

6.4 Storage

Keep out of reach of children; Protect form light and moisture; Store below 30°C in a dry place.

6.5 Nature and Contents of Container

3 x l0's Tablets in carton

6.6 Special precautions for disposal and other handling

No special requirements for disposal

7. Marketing Authorization Holder:

Mega Lifesciences (Australia) Pty Ltd
Victoria 3810 , Australia

8. Marketing Authorization Numbers:

20/1532/DGCS/PH/2015

9. Date of first authorization / renewal of the authorization:

Date of first authorization: 15-04-2016

10. Date of revision of the text:

11. Dosimetry (If Applicable)

Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals (If Applicable)

Not Applicable