LEUKOTRIENE RECEPTOR ANTAGONIST -  
ANTI-BRONCHIAL ASTHMA DRUG -  
KIPRES® Chewable Tablets 5mg  
< The Japanese Pharmacopoeia Montelukast sodium chewable tablets>  

Storage  
Store in a tight and light-resistant container and at room temperature.  

Expiration date  
Indicated on package (Use up as soon as possible after opening the seal, even if it is before expiration date.)  

Cautions  
See “PRECAUTIONS FOR HANDLING”  

CONTRAINDICATIONS  
(This product is contraindicated in the following patients.)  
Patients who are hypersensitive to any component of KIPRES  

DESCRIPTION  
Product description  
<table>
<thead>
<tr>
<th>Active ingredient</th>
<th>Montelukast 5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>: The Japanese Pharmacopoeia (JP)</td>
<td></td>
</tr>
<tr>
<td>Inactive ingredient</td>
<td>D-mannitol, crystalline cellulose, red ferric oxide, hydroxypropyl cellulose, croscarmellose sodium, magnesium stearate, aspartame (L-phenylalanine compound), flavor</td>
</tr>
<tr>
<td>Dosage form</td>
<td>Uncoated compressed chewable tablets</td>
</tr>
<tr>
<td>Color</td>
<td>pink</td>
</tr>
<tr>
<td>Appearance</td>
<td>Diameter 9.5 mm, Thickness 4.4 mm, Weight About 300mg</td>
</tr>
<tr>
<td>Identification code</td>
<td>KP-371</td>
</tr>
</tbody>
</table>

INDICATIONS  
Bronchial asthma  

DOSAGE AND ADMINISTRATION  
The usual dosage for pediatric patients 6 years of age and older is 5 mg as montelukast orally administered once daily at bedtime.  

PRECAUTIONS FOR DOSAGE AND ADMINISTRATION  
(1) KIPRES should be taken after dissolving it in the mouth or after crushing it with the teeth.  
(2) Since the montelukast chewable tablet is not biologically equivalent to the montelukast film-coated tablet, and since the bioavailability of the montelukast chewable tablet is higher compared to the montelukast film-coated tablet [1], the montelukast chewable 5-mg tablet and the montelukast film-coated 5-mg tablet should not be substituted with each other.  

PRECAUTIONS  
1. Important Precautions  
1) Pediatric patients and their guardians or appropriate substitutive persons should be informed that KIPRES should be taken continuously not only during periods of worsening asthma, but also while asthma is controlled.  
2) Because KIPRES differs from bronchial dilators, steroids, etc., it is not a drug to relieve existing asthma attacks. This fact must be fully explained to pediatric patients and their guardians or appropriate substitutive persons.  
3) If a major attack is observed when administering KIPRES to a bronchial asthma patient, a bronchial dilator or steroid must be administered.
4) If the patient is receiving long-term steroid treatment and the plan is to reduce the amount of steroids by administering KIPRES, this should be accomplished gradually under strict supervision.

5) If the patient has been able to reduce the amount of steroid support by administering KIPRES, be cautious about the possibility of reoccurrence of the original symptoms.

6) Psychiatric symptoms including depression, suicidal ideation, suicide and aggressive behavior have been reported although a causal relationship with this drug is not clear. Therefore, the patient's condition should be sufficiently observed. (See the "Other Precautions" subsection)

7) There are reports that Churg-Strauss syndrome-like angitis have occurred during use of leukotriene antagonists, which includes KIPRES. These symptoms are mainly produced when reducing or suspending the use of oral steroids. When using KIPRES, be cautious about eosinophil count and angitiic symptoms (numbness, weakness of limbs, pyrexia, arthralgia, and infiltration of the lung, etc.)

8) When the efficacy of KIPRES is not observed, therapy with KIPRES should not be continued randomly for a long-term period.

2. Drug Interactions

This drug is mainly metabolized by the drug metabolizing enzymes cytochromes P450 (CYP) 2C8/2C9 and 3A4. [See the "PHARMACOKINETICS" section.]

[Careful coadministration (This drug should be coadministered with caution.)]

<table>
<thead>
<tr>
<th>Drug</th>
<th>Signs, symptoms and treatment</th>
<th>Mechanism and risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>The action of this drug may be reduced.</td>
<td>Phenobarbital induces CYP3A4, thereby promoting the metabolism of this drug.[See the &quot;PHARMACOKINETICS&quot; section.]</td>
</tr>
</tbody>
</table>

3. Adverse Reactions

Pediatric ≥6 years of age (Domestic Clinical Studies Results)

In clinical studies conducted in Japan, 2 cases of adverse reactions were reported in 2 (2.1%) out of 96 patients. The adverse reactions were urticaria-like rash, dizziness in 1 case each respectively.(At approval)

In the specific drug-use-results survey conducted in Japan, 9 cases (including abnormal laboratory test values) of adverse reactions were observed in 8 patients out of 1,194 patients evaluated for safety(0.7%). The adverse reactions were nausea in 2 cases(0.2%), vomiting, headache, tic, eczema, erythema multiforme, urticaria, flushing in 1 case each respectively(0.1%).

In the post-marketing clinical studies2(3) conducted in Japan, 12 cases (including abnormal laboratory test values) of adverse reactions were observed in 9 patients out of 134 patients evaluated for safety(6.7%). The adverse reactions were protein urine present in 2 cases (1.5%), nausea, headache, menstrual disorder, affectability, white blood cell count increased, protein total increased, blood bilirubin increased, blood creatine phosphokinase increased, blood urea increased, urobilinogen urine increased in 1 case each respectively(0.7%).(At the end of reexamination)

[Overseas Clinical Studies Results, Reference]

In long-term clinical studies conducted overseas in pediatric patients with bronchial asthma 4), 13 adverse reactions were reported in 10 (5.8%) of 172 patients. The most frequently reported adverse reactions observed were headache (3 events, 1.7%), dyspepsia (2 events, 1.2%), and flatulence (2 events, 1.2%). Also, the abnormality in laboratory test findings observed was "increased total bilirubin" in 1 case.

Adult (Domestic Clinical Studies Results, Reference)

In clinical studies conducted in Japan, 66 adverse reactions were reported in 46 (8.8%) of 522 patients. The most frequently reported adverse reactions observed were diarrhea (9 events, 1.7%), abdominal pain (7 events, 1.3%), nausea (6 events, 1.1%), heart burn (5 events, 1.0%) and headache (5 events, 1.0%). Also, 80 abnormalities in laboratory test findings were observed in 49 patients of 507 patients and the most frequently reported abnormalities were increased ALT (GPT) (14 events in 505 patients), increased γ-GTP (9 events in 463 patients) and increased alkaline phosphatase (8 events in 476 patients).

1) Clinically significant adverse reactions

(1) Anaphylaxis (frequency unknown)

Since anaphylaxis may occur, close observation should be maintained. If symptoms appear, this drug should be discontinued immediately and appropriate measures should be taken.

(2) Angioedema (frequency unknown)

Since angioedema may occur, close observation should be maintained. If symptoms appear, this drug should be discontinued immediately and appropriate measures should be taken.

(3) Fulminant hepatitis (frequency unknown), hepatitis (frequency unknown), hepatic dysfunction (0.01%), jaundice (frequency unknown)

Since fulminant hepatitis, hepatitis, hepatic dysfunction and jaundice may occur, close observation should be maintained. If abnormalities are observed, this drug should be discontinued and appropriate measures should be taken.

(4) Toxic epidermal necrolysis (TEN) (frequency unknown), oculomucocutaneous syndrome (Stevens-Johnson syndrome) (frequency unknown), erythema multiforme (0.01%)
Since toxic epidermal necrolysis, oculomucocutaneous syndrome and erythema multiforme may occur, close observation should be maintained. If abnormalities are observed, this drug should be discontinued and appropriate measures should be taken.

(5) **Thrombocytopenia** (frequency unknown)

Thrombocytopenia (initial symptoms: bleeding tendency such as purpura, nose bleeding and gingival bleeding) may occur. Therefore, if such a symptom as this occurs, this drug should be discontinued and appropriate measures should be taken.

### 2) Other adverse reactions

If the following symptoms or abnormalities appear, appropriate measures such as discontinuation of therapy should be considered.

<table>
<thead>
<tr>
<th>Incidence</th>
<th>0.1% - &lt;1%</th>
<th>&lt;0.1%</th>
<th>Incidence unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypersensitivity</strong></td>
<td>Rash, pruritus</td>
<td>Urticaria,</td>
<td>Hepatic eosinophilic infiltration</td>
</tr>
<tr>
<td><strong>Psychiatric and nervous system</strong></td>
<td>Headache, somnolence,</td>
<td>Restlessness,</td>
<td>Dream abnormalities, irritability, seizure, agitation, tremor, somnambulism, disorientation, mental concentration decreased, memory impairment, delirium</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
<td>Pulmonary eosinophilia</td>
</tr>
<tr>
<td><strong>Gastrointestinal system</strong></td>
<td>Diarrhea, abdominal pain, epigastric discomfort, nausea</td>
<td>Heartburn, vomiting, constipation, stomatitis</td>
<td>Dyspepsia</td>
</tr>
<tr>
<td><strong>Hepatic</strong></td>
<td>Hepatic function abnormal, increased AST (GOT), increased ALT (GPT), increased alkaline phosphatase, increased</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The adverse reaction frequency was calculated based on clinical studies, post-marketing surveys (drug-use-results survey, specific drug-use-results survey, and postmarketing clinical studies) of Tablets, Chewable Tablets and Fine Granules conducted in Japan.

### 4. Use during Pregnancy, Delivery or Lactation

1) KIPRES should be administered to pregnant women or women suspected of being pregnant only when it is judged that the benefits from the treatment exceed the possible risks.  
[The safety of KIPRES in pregnant women has not been established. During worldwide marketing experience, congenital limb malformations have been reported in the offspring of women being treated with KIPRES during pregnancy. Most of these women were also taking other asthma medications during their pregnancy. A causal relationship between these events and KIPRES has not been established.]

2) Caution should be used in the administration of KIPRES to nursing mothers.
[In animal studies (rats), it has been reported that KIPRES is secreted into breast milk.]

### 5. Pediatric Use

1) For pediatrics ≥1 year and <6 years of age, montelukast fine granules 4-mg should be administered once daily at bedtime.
2) The safety of montelukast formulations in babies under 1 year of age, newborns and premature babies has not been fully established.

[ Due to lack of domestic experience with montelukast formulations ]

6. Precautions concerning Use

1) At the time of delivery: When drugs packed in a PTP sheet are used, patients should be instructed to take the drugs out of the sheet. [It has been reported that when patients mis-swallowed drugs with a PTP sheet (after failing to take the drugs out of the sheet), a hard, sharply angled edge of the sheet struck to the esophageal mucosa. Furthermore, if perforation occurred, serious complications, such as mediastinitis were reported.]

2) KIPRES may be taken with or without food.

7. Other Precautions

The result of a pooled analysis of 41 placebo-controlled clinical studies indicated that while suicidal ideation was observed in one out of 9,929 patients in the montelukast group, no suicidal ideation was observed in 7,780 patients in the placebo group. Also, the result of a separate pooled analysis of 46 placebo-controlled clinical studies indicated that behavior-related adverse experiences (including insomnia and irritability) were observed in 319 (2.73%) out of 11,673 patients in the montelukast group and 200 (2.27%) out of 8,827 patients in the placebo group. No statistically significant difference was observed between them.

PHARMACOKINETICS

1. Blood Concentrations

1) Pediatrics

When one montelukast chewable tablet 5-mg was orally given after meal once daily to pediatric patients with mild-to-moderate bronchial asthma for 7 consecutive days, the Cmax on Day 1 (630 ng/mL) was achieved in 3.1 hours after administration and in 4.3 hours after administration on Day 7(628 ng/mL). The plasma concentrations declined with an apparent half-life (t1/2) of approximately 4 hours on both Day 1 and Day 7(Figure 1). The AUC0-24h on the 1st and 7th day were 4170 ng · hr/mL and 4910 ng · hr/mL, respectively. These results suggest that, as with adults, there is little accumulation of montelukast in the plasma (Table 1). 2)

2) Adults [For reference]

(1) Results of Domestic Clinical Studies

Following a single oral dose of montelukast film-coated tablets 10-mg to 8 healthy adults in the fasted state, the peak plasma concentration (Cmax, 526 ng/mL) of montelukast was reached in 3.9 hours (Tmax), and plasma concentrations declined with a t1/2 of 4.6 hours. The AUC0-∞ was 3,840 ng · hr/mL. 5)

(2) Results of Clinically Studies Conducted Overseas

Tmax was delayed from 2.3 ± 0.9 hours to 4.0 ± 1.9 hours following administration of montelukast chewable tablets 5-mg after meal to healthy adults compared to administration in the fasted state. Also, Cmax decreased by 48% from 488 ± 66 ng/mL to 256 ± 82 ng/mL and AUC0-∞ decreased by 13% from 2,730 ± 743 ng · hr/mL to 2,386 ± 498 ng · hr/mL. 9)

Following a single oral dose of montelukast film-coated tablets 10-mg to the healthy elderly (65 to 73 years of age), the Cmax (495 ng/mL) was achieved in 2.8 hours, and plasma concentrations declined with a t1/2 of 6.6 hours. The AUC0-∞ in the elderly (3423.2 ± 1,344.7 ng · hr/mL) was not significantly different.
3. Metabolism

Kyorin Pharmaceutical Co., Ltd.

Following a single oral dose of montelukast film-coated tablets 10-mg to patients with mild-to-moderate hepatic insufficiency and clinical evidence of cirrhosis, the Cmax (313 ng/mL) was achieved in 4.0 hours, and plasma concentrations declined with a t1/2 of 8.6 hours. The t1/2 of the patients was slightly longer compared with 4.7 hours in healthy adults, and the AUC increased by 41% from 2,248.7 ± 812.1 ng · hr/mL to 3,167.2 ± 1,305.5 ng · hr/mL. Listed below are the pharmacokinetic parameters following administration of montelukast chewable tablets 5-mg and montelukast film-coated tablets 10-mg to healthy adults (Table 2). 12)

Table 2 Pharmacokinetic Parameters in Healthy Adults.

<table>
<thead>
<tr>
<th>Dose and Formulation</th>
<th>Tmax (hr)</th>
<th>Cmax (ng/mL)</th>
<th>t1/2 (hr)</th>
<th>AUC0→∞ (ng·hr/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg CT</td>
<td>2.0±0.3</td>
<td>493.7±83.1</td>
<td>4.8±0.3</td>
<td>2938.8±583.1</td>
</tr>
<tr>
<td>10 mg FCT</td>
<td>4.0±1.4</td>
<td>333.4±109.6</td>
<td>4.6±0.6</td>
<td>2447.6±779.0</td>
</tr>
</tbody>
</table>

CT: Montelukast chewable tablets, FCT: Montelukast film-coated tablets

Following administration of montelukast chewable tablets 5-mg and montelukast film-coated tablets 10-mg to healthy adults, bioavailabilities were approximately 73% and approximately 64%, respectively. 13)

2. Distribution

The binding of montelukast with human plasma proteins was 99.6%. Montelukast was more than 99% bound to both albumin and α1-acid glycoproteins at physiological concentrations. 14)

3. Metabolism

The main metabolites of montelukast in human are side chain methyl hydroxylated metabolites and benzylc methylene hydroxylated metabolites. Cytochromes P450 (CYP) molecular species CYP2C8/2C9 and 3A4 are involved in the formation of these metabolites, and CYP2C8 is the main enzyme in the metabolism of montelukast. It has been confirmed that side chain methyl hydroxylated metabolites are further metabolized oxidatively to carboxylic acid metabolites. Based on further in vitro results, therapeutic plasma concentrations of montelukast do not inhibit CYP3A4, 2C9, 1A2, 2A6, 2C19, or 2D6. 15)–18)

Also, other in vitro studies have shown that montelukast is an inhibitor of CYP2C8. However, data from an overseas clinical drug-drug interaction study involving montelukast and a representative drug primarily metabolized by CYP2C8 (rosiglitazone) demonstrated that montelukast does not inhibit CYP2C8 in vivo. 19) Therefore montelukast is not anticipated to alter the metabolism of drugs metabolized by this enzyme (e.g. paclitaxel.)

4. Excretion

1) Results of Domestic Clinical Studies

Following single 400-mg oral administration of montelukast capsules to healthy adults, unchanged drug was not detected in the urine. 20)

2) Results of Clinical Studies Conducted Overseas (Reference)

During the 5 days after single oral administration of 102 mg of radiolabeled montelukast capsules to healthy adults, 86 % of the radioactivity was recovered in feces and 0.1 % in urine. 20)

5. Coadministration with other agents (Results of Clinical Studies Conducted Overseas, Reference)

1) Phenobarbital 21)

When 100 mg phenobarbital (repeated administration for 14 days) was administered to healthy adults and then montelukast film-coated tablets 10 mg (single administration) was orally coadministered, the AUC0→∞ of montelukast was reduced by approximately 40%.

2) Theophylline 22)

When a high oral dose of montelukast capsules (200 mg qd repeated administration for 6 weeks or 200 mg tid repeated administration for 8 days) was coadministered with an oral dose of theophylline (250 mg single administration) to healthy adults or coadministered with an intravenous dose of theophylline (5 mg/kg single administration), a decrease in plasma concentrations of theophylline was observed. Theophylline plasma concentrations did not change when an oral 10-mg dose of montelukast film-coated tablets (repeated administration for 10 days) was coadministered with an intravenous dose of 5 mg/kg theophylline (single administration).

3) Prednisone, Prednisolone

Following oral coadministration of 200 mg montelukast capsules (repeated administration for 6 weeks) with 20 mg prednisone (single administration) to healthy adults, the AUC0→∞ of prednisone was significantly lowered compared with placebo group. However, the AUC0→∞ of prednisone was not changed between before and after the administration of 200 mg montelukast capsules within the same subjects. The pharmacokinetics of the active metabolite prednisolone was not changed.

Coadministration of 200 mg montelukast capsules (repeated administration for 6 weeks) with 20 mg intravenous prednisolone (single administration) to healthy adults had no effect on the pharmacokinetics of either prednisone or prednisolone.

4) Oral contraceptives 23) (ethinyl estradiol/norethindrone 35 μg/1 mg)

Following oral coadministration of 100 mg montelukast capsules (repeated administration for 8 days) with oral contraceptives (ethinyl estradiol/norethindrone 35 μg/1 mg single administration) to healthy adults, the pharmacokinetics of either ethinyl estradiol or norethindrone was not affected.
5) Digoxin

Following oral coadministration of montelukast film-coated tablets 10 mg (repeated administration for 7 days) with 0.5 mg digoxin (single administration) to healthy adults, the pharmacokinetics of immunoactive digoxin was not affected.

6) Warfarin

Following oral coadministration of montelukast film-coated tablets 10 mg (repeated administration for 7 days) with 30 mg warfarin (single administration) to healthy adults, the plasma total drug concentrations of warfarin were not affected. Also, no effect on prothrombin time of warfarin was observed.

(Note) The approved dosage of KIPRES is 5 mg in pediatrics 6 to 14 years of age.

CLINICAL STUDIES

1. Pediatrics

1) Domestic Clinical Studies Results

(1) The efficacy rate (a rate corresponding to greater than and equal to moderate improvement classified according to the general improvement) of KIPRES was 60.9% (123/202 patients) in pediatric patients 6 to 14 years of age with bronchial asthma.

(2) In a double-blind, comparative Phase IV clinical study in pediatric patients 6 to 14 years of age with bronchial asthma, the peak flow improvement (A.M.) at Week 2 for KIPRES (5 mg/day) and the comparator, ketotifen (dry syrup: 6 years of age; 1.2 mg/day, ≥7 years of age; 2 mg/day), were 13.4±3.1 L/min and 3.6±3.1 L/min (LS mean±SE), respectively.

2) Overseas Clinical Studies Results

In placebo-controlled double-blind clinical studies conducted overseas in 196 pediatric patients with bronchial asthma, treatment with KIPRES resulted in a 8.7% increase in forced expiratory volume in 1 second.

2. Adults [For reference]

1) In clinical studies including a double-blind comparative study conducted in Japan, the efficacy of KIPRES was 55.6% (145/261 patients) for definitive general improvement in adult patients with bronchial asthma.

2) In double-blind, comparative Phase III clinical studies in patients with bronchial asthma, the efficacy rate for KIPRES in final general improvement is 58.5% (83/142 patients) and that for pranlukast hydrate (450 mg) is 46.0% (63/137 patients). The non-inferiority (non-inferiority margin Δ=10%) of KIPRES to pranlukast were demonstrated.

3) In clinical studies conducted in Japan, the tolerability of KIPRES has been shown to be up to 400 mg/day in healthy adults. 

(Note) The approved dosage of KIPRES is 5 mg in pediatrics 6 to 14 years of age.

PHARMACOLOGY

Mechanism of Action

Montelukast binds with high selectivity to type 1 cysteinyl leukotriene (CysLT₁) receptors, thereby inhibiting the pathophysiologic actions (bronchoconstriction, vascular permeability, and mucus secretion) of the pro-inflammatory mediators LTD₄ and LTE₄. Due to this mechanism of action, montelukast significantly improves parameters of asthmatic inflammation contributing to its anti-asthmatic effect.

1. LT Receptor Antagonism (Receptor Binding Studies)

In receptor binding studies using membranes isolated from guinea pig lung, U937 and THP-1 cells, the binding of LTD₄ to receptors was shown to be strongly inhibited by KIPRES and this inhibition was not affected by the presence of blood ingredients. On the other hand, a weak receptor antagonism against LTC₄ and LTB₄ was observed.

2. Inhibitory Effect on Bronchoconstriction (Isolated Tissues and Animal Studies)

The LTD₄-induced contractions were competitively inhibited by KIPRES in isolated guinea pig trachea. KIPRES was also shown to have a potent, continuous inhibitory action against LTD₄-induced bronchoconstriction reactions in guinea pigs and squirrel monkeys. On the other hand, KIPRES did not block contraction of isolated tissues induced by LTC₄ (in the absence of LTC₄ metabolism). Also, there was also no inhibition of bronchoconstriction in guinea pigs induced by histamine, arachidonic acid, serotonin and acetylcholine.

3. Inhibitory Effect on Antigen-Induced Bronchoconstriction

KIPRES inhibited antigen-induced bronchoconstriction reactions in sensitized inbred asthmaic rats, guinea pigs and squirrel monkeys when administered intravenously or orally. In overseas clinical studies, KIPRES inhibited early and late-phase bronchoconstriction due to antigen challenge by 75% and 57%, respectively.

4. Inhibitory Effect on Immediate and Delayed Bronchoconstriction Reactions

KIPRES inhibited antigen-induced immediate and delayed bronchoconstriction reactions in sensitized squirrel monkeys when administered orally.

5. Inhibitory Effect on Anaphylactic Shock

KIPRES partly inhibited anaphylactic shock induced by egg albumin in sensitized guinea pigs.

6. Improvement of Pulmonary Function

KIPRES improved the forced expiratory volume in 1 second and peak expiratory flow in patients with mild-to-moderate chronic bronchial asthma.
7. Effect on Eosinophils

KIPRES significantly reduced the sputum eosinophil to total leukocyte ratio in patients with mild-to-moderate chronic bronchial asthma, compared with placebo. 31) Similarly, KIPRES significantly reduced the peripheral blood eosinophil to total leukocyte ratio in adults 30) and pediatric patients. 32), 33)

PHYSICOCHEMISTRY

Nonproprietary name:
Montelukast Sodium (JAN)

Chemical name:
Monosodium (1R)-1-{3-[(1E)-2-(7-chloroquinolin-2-yl)ethenyl]phenyl}-3-[(1-hydroxy-1-methylethyl)phenyl]propyl)sulfanyl]methyl)cyclopropyl)acetate

Molecular formula: C35H35ClNNaO3S
Molecular weight: 608.17

Structural formula:

\[
\begin{align*}
\text{N} & \quad \text{H} \\
\text{S} & \quad \text{CO}_2\text{Na} \\
\text{Cl} & \quad \text{OH} \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

Description:
Montelukast Sodium occurs as a white to pale yellow-white powder.
It is very soluble in methanol and in ethanol (99,5), and freely soluble in water.
It is hygroscopic.
It turns yellow on exposure to light.
It shows a crystal polymorphism.

Partition coefficient:
Log Kow=2.3±0.2 in 1-octanol/phosphate buffered system (pH7)

PRECAUTIONS FOR HANDLING

Storage conditions: Protect from moisture after opening the seal.

PACKAGING

KIPRES Chewable Tablets 5 mg:
- PTP pack: 28 tablets (14 tablets × 2)
- 100 tablets (10 tablets × 10)
- 140 tablets (14 tablets × 10)

REFERENCES

9) Food effects of montelukast chewable tablets 5mg (In-house data)
11) Pharmacokinetics of montelukast in patients with hepatic insufficiency (In-house data)
12) Pharmacokinetics of montelukast in healthy adults (In-house data)
13) Bioavailability of montelukast (In-house data)
14) Binding of montelukast with proteins (In-house data)
29) Inhibitory effects of montelukast on anaphylactic shock (In-house data)

REQUEST FOR LITERATURE SHOULD BE MADE TO:
A request for in-house data mentioned in the References can also be made to the following.
Kyorin Pharmaceutical Co., Ltd. Drug Information Center
6, Kanda surugadai 4-chome, Chiyoda-ku, Tokyo 101-8311, Japan
TEL: 0120-409-341 (Toll-free)
9:00 to 17:30 (Monday through Friday exclusive of national holidays)

Manufactured and marketed by:
Kyorin Pharmaceutical Co., Ltd.
6, Kanda surugadai 4-chome, Chiyoda-ku, Tokyo 101-8311, Japan