BLOKTIENE
Film-Coated Tablet

COMPOSITION

Each film-coated tablet contains montelukast sodium equivalent to 10 mg montelukast

Pharmacodynamic properties

Pharmacotherapeutic group: Leukotriene receptor antagonists
ATC-code: R03D C03

The cysteinyl leukotrienes (LTC_4, LTD_4, LTE_4) 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 ($CysLT_1$) 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 $CysLT_1$ receptor. In clinical studies, montelukast inhibits bronchoconstriction due to inhaled LTD_4 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 paediatric 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.

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 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.

In vitro studies using human liver microsomes indicate that cytochrome P450 3A4, 2A6 and 2C9 are involved in the metabolism of montelukast. Based on further *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.

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).

With high doses of montelukast (20- and 60-fold the recommended adult dose), decrease in plasma theophylline concentration was observed. This effect was not seen at the recommended dose of 10 mg once daily.

THERAPEUTIC INDICATIONS

Bloktiene is indicated in adults for the prophylaxis and chronic treatment of asthma, including the prevention of exercise induced bronchoconstriction.

POSOLOGY AND METHOD OF ADMINISTRATION

Asthma
Montelukast sodium should be taken once daily in the evening (one-10 mg tablet)

Exercise-Induced Bronchoconstriction (EIB)
For prevention of EIB, a single dose (one-10 mg tablet) of Montelukast sodium should be taken at least 2 hours before exercise.
An additional dose of Montelukast sodium should not be taken within 24 hours of previous dose.
Patients already taking Montelukast sodium 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.

Method of administration:
The tablet should be swallowed with a sufficient amount of fluid.

CONTRAINDICATIONS

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

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 doctor's advice as soon as possible if they need more inhalations of short-acting β-agonists than usual.

Montelukast should not be substituded 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 usually, but not always, have been associated with the reduction or withdrawal of oral corticosteroid therapy. The possibility that leukotriene receptor antagonists may be associated with emergence of Churg-Strauss syndrome can neither be excluded nor 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.

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

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

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, caution should be exercised, particularly in children, when montelukast is co-administered with inducers of CYP 3A4, such as phenytoin, phenobarbital and rifampicin.

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.

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 metabolised 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.)

Pregnancy and lactation

Use during pregnancy
Animal studies do not indicate harmful effects with respect to effects on pregnancy or embryonal/foetal development.

Limited data from available pregnancy databases do not suggest a causal relationship between montelukast and malformations (i.e. limb defects) that have been rarely reported in worldwide post marketing experience.

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

Use during lactation
Studies in rats have shown that montelukast is excreted in milk. It is not known if montelukast is excreted in human milk.

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

Effects on ability to drive and use machines

Montelukast is not expected to affect a patient's ability to drive a car or operate machinery. However, in very rare cases, individuals have reported drowsiness or dizziness.

UNDESIRABLE EFFECTS

The following adverse reactions have been reported in post-marketing use of montelukast:
Blood and lymphatic system disorders: increased bleeding tendency
Immune system disorders: hypersensitivity reactions including anaphylaxis, hepatic eosinophilic infiltration
Nervous system disorders: dizziness drowsiness, paraesthesia/hypoesthesia, seizure
Cardiac disorders: palpitations
Respiratory, thoracic and mediastinal disorders: epistaxis
Gastro-intestinal disorders: diarrhea, dry mouth, dyspepsia, nausea, vomiting
Hepatobiliary disorders: elevated levels of serum transaminases (ALT, AST), cholestatic hepatitis
Skin and subcutaneous tissue disorders: angiooedema, bruising, urticaria, pruritus, rash, erythema nodosum
Musculoskeletal and connective tissue disorders: arthralgia, myalgia including muscle cramps
General disorders and administration site conditions: asthenia/fatigue, malaise, oedema, pyrexia . Very rare cases of Churg-Strauss Syndrome (CSS) have been reported during montelukast treatment in asthmatic patients .

OVERDOSE

No specific information is available on the treatment of overdose with 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. 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.

It is not known whether montelukast is dialysable by peritoneal- or haemo-dialysis.

Special precautions for storage

Store in the original package in order to protect from light and moisture.
Shelf Life 36 Months.
Presentation
Bloktiene 10 mg Film-coated tablet
Carton box with 3 blisters containing 10 film-coated tablets
Reg.No.:

HARUS DENGAN RESEP DOKTER

actavis

Manufactured by
Actavis Ltd.
Malta

Imported by
PT Actavis Indonesia
Jakarta - Indonesia

BLOKTIENE 10 mg Tablet
Montelukast

Baca semua leaflet ini dengan seksama sebelum anda atau anak anda mulai minum obat ini karena mengandung informasi penting bagi anda .
• Simpan leaflet ini. Mungkin anda perlu membacanya lagi .
• Jika Anda memiliki pertanyaan lebih lanjut , tanyakan kepada dokter, apoteker atau perawat.
• Obat ini telah diresepkan untuk anda atau anak anda saja. Jangan menyebarkannya ke orang lain. Ini dapat membahayakan mereka, bahkan jika gejala penyakit mereka sama seperti anda atau anak anda.
• Jika anda atau anak anda mendapatkan efek samping, bicarakan dengan dokter, apoteker atau perawat. Termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini .

Apa yang ada dalam leaflet ini :

1 . Apa itu BLOKTIENE dan digunakan untuk apa

BLOKTIENE merupakan obat yang diresepkan yang menghalangi zat didalam tubuh yang disebut leukotrien. Hal ini dapat membantu pencegahan dan pengobatan kronis pada asma, termasuk pencegahan penyempitan saluran napas yang disebabkan oleh olahraga. Montelukast tidak mengandung steroid.

BLOKTIENE digunakan pada orang dewasa untuk:
• membantu pencegahan dan pengobatan kronis pada asma.
• BLOKTIENE juga dapat digunakan untuk mencegah penyempitan saluran napas yang disebabkan oleh olahraga.

2 . Apa yang perlu anda ketahui sebelum anda mengkonsumsi BLOKTIENE

Beritahu dokter anda tentang masalah medis atau alergi yang sekarang atau pernah anda miliki.

Jangan mengkonsumsi BLOKTIENE jika anda
• Alergi terhadap montelukast atau salah satu zat tambahan obat ini.

Peringatan dan perhatian
Bicarakan dengan dokter, apoteker atau perawat anda sebelum mengkonsumsi BLOKTIENE
• Jika asma atau pernapasan anda semakin memburuk, segera beritahu dokter anda.
• BLOKTIENE tidak ditujukan untuk mengobati serangan asma akut. Jika serangan terjadi, ikuti petunjuk dokter yang telah diberikan kepada anda. Bawa selalu obat inhalasi bersama anda.
• Penting bahwa anda mengkonsumsi semua obat asma yang diresepkan oleh dokter Anda.

• Jika anda sedang dalam pengobatan anti-asma , hati-hati jika anda atau dia mengalami kombinasi gejala seperti penyakit seperti flu , kesemutan atau mati rasa pada lengan atau kaki, memburuknya gejala paru-paru, dan/atau ruam, anda harus berkonsultasi dengan dokter anda.
• Anda tidak boleh mengkonsumsi asam asetil salisilat -(aspirin) atau obat anti - inflamasi (juga dikenal sebagai obat anti - inflamasi non-steroid atau NSAID) jika hal tersebut membuat asmanya memburuk.

Obat-obatan lainnya dan montelukast.
Beberapa obat dapat mempengaruhi kerja montelukast , atau montelukast dapat mempengaruhi kerja obat-obat yang lain.
Beritahu dokter atau apoteker anda jika sedang, telah atau akan mengkonsumsi, obat-obatan lainnya, termasuk yang diperoleh tanpa resep .
Beritahu dokter anda jika anda atau anak anda mengkonsumsi obat-obatan berikut sebelum montelukast :
• fenobarbital (digunakan untuk pengobatan epilepsi)
• phenytoin (digunakan untuk pengobatan epilepsi)
• rifampisin (digunakan untuk mengobati tuberkulosis dan beberapa infeksi lainnya)

Montelukast dengan makanan dan minuman
Tablet ini harus dikonsumsi bersamaan dengan air minum secukupnya.

Kehamilan dan menyusui
Penggunaan pada kehamilan
Wanita yang sedang hamil, kemungkinan hamil atau berencana untuk memiliki bayi, mintalah saran dokter anda sebelum mengkonsumsi obat ini. Dokter akan menilai apakah anda dapat mengkonsumsi BLOKTIENE.

Penggunaan pada ibu menyusui
Tidak diketahui apakah BLOKTIENE muncul dalam ASI. Jika anda menyusui atau berniat untuk menyusui, tanyakan kepada dokter Anda sebelum mengkonsumsi obat ini.

Mengemudi dan menggunakan mesin
BLOKTIENE diharapkan tidak mempengaruhi kemampuan anda untuk mengemudikan kendaraan atau mengoperasikan mesin. Namun, pada kasus yang sangat jarang, telah dilaporkan efek samping berupa kantuk dan pusing.

BLOKTIENE tablet salut selaput mengandung laktosa
Jika anda anda mempunyai intoleransi pada beberapa macam gula, hubungi dokter anda sebelum mengkonsumsi obat ini.

3 . Bagaimana cara mengkonsumsi BLOKTIENE
• Anda hanya boleh mengkonsumsi satu tablet sehari sesuai yang diresepkan oleh dokter Anda .
• Ketika anda tidak mengalami gejala asma atau jika mengalami serangan asma akut, montelukast tetap harus dikonsumsi.
• Selalu konsumsi obat ini persis seperti yang telah diberitahu dokter atau apoteker anda. Cek dengan dokter atau apoteker anda jika anda tidak yakin.
• Untuk dikonsumsi melalui mulut.

Untuk dewasa:
Dosis yang dianjurkan adalah satu tablet 10 mg setiap hari pada malam hari. BLOKTIENE 10 mg dapat dikonsumsi dengan atau tanpa makanan.

Jika anda mengkonsumsi BLOKTIENE, pastikan bahwa anda tidak mengkonsumsi produk lain yang mengandung bahan aktif yang sama, montelukast.

Jika anda mengkonsumsi BLOKTIENE lebih banyak dari yang seharusnya
Segera hubungi dokter anda untuk mendapatkan saran.
Tidak ada efek samping yang dilaporkan pada sebagian besar laporan overdosis. Gejala yang paling sering dilaporkan terjadi pada orang dewasa dan anak-anak termasuk sakit perut, kantuk, rasa haus, sakit kepala, muntah, dan hiperaktif.

Jika anda lupa untuk mengkonsumsi BLOKTIENE
Cobalah untuk mengkonsumsi BLOKTIENE seperti yang diresepkan. Namun, jika anda melewatkan dosis, lanjutkan jadwal biasa satu tablet sekali sehari.
Jangan konsumsi dosis ganda untuk menebus dosis yang terlupakan.

Jika Anda berhenti mengkonsumsi BLOKTIENE
BLOKTIENE dapat mengobati asma hanya jika anda terus mengkonsumsinya.
Penting untuk anda untuk tetap mengkonsumsi BLOKTIENE selama diresepkan dokter. Ini akan membantu mengontrol asma anda.
Jika anda memiliki pertanyaan lebih lanjut tentang penggunaan obat ini, tanyakan kepada dokter atau apoteker.

4 . Kemungkinan efek samping
Seperti obat-obatan lainnya, obat ini dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.
Efek samping yang paling sering terkait dengan montelukast setelah obat di pasarkan, berikut telah dilaporkan adalah :

- Peningkatan kecenderungan perdarahan
- Reaksi hipersensitivitas termasuk anafilaksis, infiltrasi *hepatic eosinophilic*.
- Pusing, mengantuk, gelisah/mati rasa, kejang.
- Palpitasi.
- Mimisan.
- Diare, mulut kering, dyspepsia, mual, muntah.
- Peningkatan level serum transaminase (ALT, AST), hepatitis kolestatik.
- Angioedema, memar , gatal, kemerahan disertai gatal, ruam, benjolan merah di bawah kulit, umumnya pada tulang kering (eritema nodosum)
- Nyeri otot atau sendi, kram otot
- Lemah/lelah, merasa tidak enak badan, pembengkakan, demam. Kasus Churg-Strauss Syndrome (CSS) yang sangat jarang telah dilaporkan pada pasien asma selama pengobatan dengan montelukast.

Tanyakan kepada dokter atau apoteker untuk informasi lebih lanjut tentang efek samping. Jika Anda atau anak Anda mendapatkan efek samping, berbicara dengan Anda dokter, apoteker atau perawat . Termasuk efek samping yang tidak tercantum dalam leaflet ini .

5 . Bagaimana cara menyimpan BLOKTIENE
• Jauhkan obat ini dari pandangan dan jangkauan anak-anak .
• Jangan gunakan obat ini setelah tanggal kadaluwarsa yang dinyatakan pada karton dan blister. Tanggal kadaluwarsa mengacu pada hari terakhir dari bulan itu .
• Simpan dalam kemasan asli agar terlindung dari cahaya dan kelembaban.

• Jangan membuang obat-obatan melalui air limbah atau limbah rumah tangga. Tanyakan apoteker Anda bagaimana cara membuang obat-obatan yang tidak Anda gunakan lagi. Langkah-langkah ini akan membantu melindungi lingkungan.

6. Isi paket dan informasi lainnya
Montelukast tablet salut selaput mengandung
• Zat aktif adalah montelukast. Setiap tablet salut selaput mengandung montelukast sodium yang setara dengan 10mg montelukast .
• Bahan lainnya adalah: mikrokristalin selulosa, hidroksipropilselulosa, croscarmellose sodium, laktosa monohidrat, magnesium stearate; *film-coat*: lactose monohydrate, hypromellose 15cP, titanium dioxide, macrogol 4000, iron oxide yellow (E172), iron oxide yellow (E172).

BLOKTIENE 10 mg tablet salut selaput terlihat seperti apa dan isi kemasannya
Tablet selaut selaput
Warna krem, bujur sangkar, tablet cembung ganda dengan M terukir di satu sisi .

Nomor Ijin Edar
DKI

Dipasarkan oleh:
PT. Actavis Indonesia
Jakarta

Diproduksi oleh:
Actavis Ltd
Malta