SCHEDULING STATUS **S3**

PROPRIETARY NAME (AND DOSAGE FORM):
MONTEFLO 4 (Chewable Tablets)
MONTEFLO 5 (Chewable Tablets)
MONTEFLO 10 (Tablets)

COMPOSITION
MONTEFLO 4: Each chewable tablet contains montelukast sodium equivalent to 4 mg montelukast.
MONTEFLO 5: Each chewable tablet contains montelukast sodium equivalent to 5 mg montelukast.
MONTEFLO 4 and **MONTEFLO** 5 also contain the following inactive ingredients: Mannitol, cellulose microcrystalline, croscarmellose sodium, aspartame, cherry flavour, ferric oxide red, magnesium stearate.
MONTEFLO 10: Each tablet contains montelukast sodium equivalent to 10 mg montelukast.
MONTEFLO 10 also contains the following inactive ingredients: Mannitol, cellulose microcrystalline, croscarmellose sodium, aspartame, cherry flavour, ferric oxide red and ferric oxide yellow, magnesium stearate.

PHARMACOLOGICAL CLASSIFICATION
A.10.2.2 Other anti-asthmatics, Leukotriene receptor antagonist

PHARMACOLOGICAL ACTION
Pharmacodynamics:
Montelukast causes potent inhibition of airway cysteinyl leukotriene receptors.
The cysteinyl leukotrienes (LTC_4, LTD_4, LTE_4) are potent inflammatory eicosanoids which are 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. In asthma, leukotriene-mediated effects include a number of airway actions, including bronchoconstriction, mucus secretion, vascular permeability, and eosinophil recruitment. Montelukast binds with high affinity and selectivity to the $CysLT_1$ receptor. Montelukast inhibits physiological actions of LTC_4, LTD_4, and LTE_4 at the $CysLT_1$ receptor without agonist activity. Doses as low as 5 mg cause substantial blockage of LTD_4 induced bronchoconstriction.

PHARMACOKINETICS:
Absorption
Montelukast is rapidly absorbed following oral administration. The mean peak plasma concentration (C_{max}) for the 4 mg chewable tablet is achieved 2 hours after administration in paediatric patients 2 to 5 years of age in the fasted state. Safety and efficacy were demonstrated in clinical studies where the 4 mg chewable tablet was administered without regard to the timing of food ingestion. The mean peak plasma concentration (C_{max}) for the 5 mg chewable tablet is achieved 2 hours after administration in adults in the fasted state. The mean oral bioavailability is 73 %.Food does not have a clinically important influence with chronic administration. The mean peak plasma concentration (C_{max}), for the 10 mg tablet is achieved 3 hours (T_{max}), after administration in adults in the fasted state. The mean oral bioavailability is 64 %. A standard meal does not influence the oral bioavailability and C_{max}.
Distribution
Binding is more than 99 % to plasma proteins. The steady-state volume of distribution of montelukast averages 8 to 11 litres.
Metabolism
Montelukast is extensively metabolised in the liver.
In vitro studies using human liver microsomes indicate that cytochrome P450 3A4 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.
Elimination
Elimination data are not available for children 2 to 5 years of age. However, 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 faecal collections and less than 0,2 % was recovered in urine. Coupled with estimates of montelukast oral bioavailability, this indicates montelukast and its metabolites are excreted almost exclusively *via* the bile. The mean plasma half-life of montelukast ranged from 2,7 to 5,5 hours in healthy young adults. Montelukast pharmacokinetics are nearly linear for oral doses up to 50 mg. No difference in pharmacokinetics was noted between dosing in the morning or in the evening. During once daily dosing there is little accumulation of the parent compound in plasma (approximately 14 %).
Hepatic insufficiency
Patients with mild-to-moderate hepatic insufficiency and clinical evidence of cirrhosis had evidence of decreased metabolism of montelukast resulting in approximately 41 % higher mean montelukast area under the plasma concentration curve (AUC) following a single 10 mg dose. The elimination of montelukast is slightly prolonged compared with that in healthy subjects (mean half-life, 7,4 hours). No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency. There are no clinical data in patients with severe hepatic insufficiency (Child-Pugh score greater than 9). The pharmacokinetic profile and the oral bioavailability of a single 10 mg oral dose of montelukast are similar in elderly and younger adults. The plasma half-life of montelukast is slightly longer in the elderly. No dosage adjustment in the elderly is required.

INDICATIONS
MONTEFLO tablets are indicated for prophylaxis and chronic treatment of atopic asthma.
MONTEFLO 4 chewable tablets are indicated for paediatric patients 2 to 5 years of age.
MONTEFLO 5 chewable tablets are indicated for paediatric patients over 6 years of age.
MONTEFLO 10 tablets are indicated in adults and children 15 years of age and older.

CONTRA-INDICATIONS
Hypersensitivity to any components of this product. Pregnancy and lactation
• **MONTEFLO** 5 and 10 should not be used in children under the age of 6 years, as safety and efficacy have not been demonstrated.
• **MONTEFLO** 4 should not be used in children under the age of 2 years, as safety and efficacy have not been demonstrated.
• **MONTEFLO** 10 should not be used in children under the age of 15 years, as safety and efficacy have not been demonstrated.

WARNINGS AND SPECIAL PRECAUTIONS
General The efficacy of oral **MONTEFLO** for the treatment of acute asthma attacks has not been established. **MONTEFLO** should not be used as monotherapy for the treatment and management of exercise induced bronchospasm. Patients who have exacerbations of asthma after exercise should continue to use their usual regimen of inhaled beta-agonists as prophylaxis and have available for rescue a short-acting inhaled beta-agonist. **MONTEFLO** is not indicated for use in the reversal of bronchospasm in acute asthma attacks, including status asthmaticus. Patients should be advised to have appropriate rescue medication available. Therapy with **MONTEFLO** can be continued during acute exacerbations of asthma. While the dose of inhaled corticosteroid may be reduced gradually under medical supervision, **MONTEFLO** should not be abruptly substituted for inhaled or oral corticosteroids. Patients with known aspirin sensitivity should continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking **MONTEFLO**. Although **MONTEFLO** is effective in improving airway function in asthmatics with documented aspirin sensitivity, it has not been shown to reduce bronchoconstrictor response to aspirin and other non-steroidal anti-inflammatory drugs in aspirin-sensitive asthmatic patients.
Renal Insufficiency Since montelukast and its metabolites are not excreted in the urine, the pharmacokinetics of montelukast were not evaluated in patients with renal insufficiency. No dosage adjustment is recommended in these patients.
Use in Elderly There are no age-related differences in the efficacy or safety profiles of **MONTEFLO**.
Eosinophilic Conditions
Patients on therapy with **MONTEFLO** 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. Doctors should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications and/or neuropathy presenting in their patients. **MONTEFLO** should be withdrawn in these patients (see **SIDE EFFECTS**).
Neuropsychiatric events
Neuropsychiatric events have been reported in some patients taking **MONTEFLO**. These include agitation, aggression, anxiousness, dream abnormalities, hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behaviour (including suicide), and tremor. Patients and healthcare professionals should be aware of the potential for neuropsychiatric events. Patients should be instructed to inform their healthcare professionals if these events occur. Healthcare professionals should carefully evaluate the risks and benefits of continuing treatment with **MONTEFLO** if such events occur.
Hepatic function impairment The metabolism of montelukast may be decreased in patients with mild to moderate hepatic function and impairment and clinical evidence of cirrhosis. The half-life may be slightly prolonged; however, dosage adjustment is not necessary. Data are not available in patients with severe hepatic function impairment. Due to the side effects such as dizziness or drowsiness, caution should be taken when driving and operating heavy machinery. Patients should therefore be advised not to drive or operate machinery until their individual susceptibility is known.
Information for patients:
Patients should be advised to take **MONTEFLO** daily as prescribed, even when they are asymptomatic, as well as during periods of worsening asthma, and to contact their doctor if their asthma is not well-controlled.
Patients should be advised that **MONTEFLO** is not for the treatment of acute asthma attacks.
They should have appropriate short-acting inhaled beta-agonist medication available to treat asthma exacerbations.
Patients should be advised that, while using **MONTEFLO**, medical attention should be sought if short-acting inhaled bronchodilators are needed more often than usual, or if more than the maximum number of inhalations of short-acting bronchodilator treatment prescribed for a 24-hour period are needed. Patients receiving **MONTEFLO** should be instructed not to decrease the dose or stop taking any other anti-asthma medicine unless instructed to do so by their doctor. **MONTEFLO** should not be used as monotherapy for the management and treatment of exercise induced bronchospasm. Patients who have exacerbations of asthma after exercise should be instructed to continue to use their usual regimen of inhaled beta-agonists as prophylaxis, unless otherwise instructed by their doctor. All patients should have a short-acting inhaled beta-agonist available for rescue treatment. Patients with known aspirin sensitivity should be advised to continue avoidance of aspirin or non steroidal anti-inflammatory agents while taking **MONTEFLO**. Although **MONTEFLO** is effective in improving airway function in asthmatics, it has not been shown to reduce the bronchoconstrictor response to aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) in aspirin-sensitive asthmatic patients.
MONTEFLO 4 and 5 mg chewable tablets and 10 mg tablets:
Phenylketonuric patients should be informed that **MONTEFLO** 4 and 5 mg chewable tablets and 10 mg tablets contain aspartame which has a phenylalanine component.

INTERACTIONS
MONTEFLO may be administered together with other therapies used in the prophylaxis and chronic treatment of asthma. In medicine interaction studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following medicines: theophylline, prednisone, prednisolone, oral contraceptives (ethinyloestradiol-norethindrone 35/1), digoxin and warfarin. The area under the plasma concentration-time curve (AUC) for montelukast was decreased approximately 40 % in subjects with co-administration of phenobarbital. No dosage adjustment for **MONTEFLO** is recommended. However, clinical monitoring is recommended when potent hepatic enzyme inducers: phenytoin, phenobarbital or rifampicin are given with **MONTEFLO**.

PREGNANCY AND LACTATION
The safety of this medicine in pregnancy and lactating women has not been established and therefore the use thereof during pregnancy and lactation is not recommended. It is not known if **MONTEFLO** is excreted in human milk.

DOSAGE AND DIRECTIONS FOR USE
MONTEFLO should be taken once daily in the evening.
MONTEFLO 4 chewable tablets *Paediatric patients 2 to 5 years of Age with Atopic Asthma:* The dosage for paediatric patients 2 to 5 years of age is one 4 mg chewable tablet daily to be taken at bedtime.
MONTEFLO 5 chewable tablets *Paediatric patients 6 to 14 years of age with Atopic Asthma:* The dosage for paediatric patients 6 to 14 years of age is one 5 mg chewable tablet daily.
MONTEFLO 10 tablets *Adults and Children 15 years of Age and Older with Atopic Asthma:* The dosage for adults 15 years of age and older is one 10 mg tablet daily.
General Recommendations: A therapeutic effect of **MONTEFLO** on parameters of asthma control occurs within one day.
MONTEFLO can be taken with or without food. Patients are advised to continue taking **MONTEFLO** while their asthma is controlled, as well as during periods of worsening asthma. No dosage adjustment is necessary for the elderly, for patients with renal insufficiency, or mild to moderate hepatic impairment, or for patients of either gender. **MONTEFLO** can be added to a patient's existing treatment regimen.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS
Side-effects:
Metabolic and nutritional disorders:
Frequent: Thirst
Nervous system disorders:
Frequent: Headache, dizziness
Frequency not known: Drowsiness, paraesthesia/hypoesthesia, seizure
Gastrointestinal disorders:
Frequent: Abdominal pain, diarrhoea, dyspepsia, gastroenteritis, pain (dental)
Frequency not known: Dry mouth, nausea, vomiting
Infections and infestations:
Frequency not known: Upper respiratory infection, varicella, gastroenteritis
Blood and lymphatic system disorders:
Frequency not known: Increased bleeding tendency, agranulocytosis
Immune system disorders:
Frequency not known: Hypersensitivity reactions including anaphylaxis, hepatic eosinophilic infiltration, angioedema
Psychiatric disorders:
Frequent: insomnia
Frequency not known: Abnormal dreams, hallucinations, agitation including aggressive behaviour, anxiety, depression, irritability, restlessness, suicidal thinking and behaviour (suicidality), tremor
Cardiac disorders:
Frequency not known: Palpitations
Respiratory, thoracic and mediastinal disorders:
Frequent: Congestion (nasal), cough, influenza
Frequency not known: Epistaxis
Hepatobiliary disorders:
Frequent: Elevated levels of serum transaminases (ALT, AST)
Frequency not known: hepatitis (including cholestatic, hepatocellular and mixed-pattern liver injury
Skin and subcutaneous tissue disorders:
Frequent: Rash
Frequency not known: Bruising, erythema nodosum, pruritus, urticaria, eczema
Musculoskeletal and connective tissue disorders:
Arthralgia, myalgia (including muscle cramps)
General disorders and administration site conditions:
Frequent: Asthenia (fatigue), malaise, pyrexia

Patients on therapy with **MONTEFLO** 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. Medical doctors should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. **MONTEFLO** should be withdrawn in these patients (see **WARNINGS AND SPECIAL PRECAUTIONS**, Eosinophilic Conditions).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
No specific information is available on the treatment of overdosage with **MONTEFLO**. In chronic asthma studies **MONTEFLO** 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 were no adverse experiences reported in the majority of overdosage reports. The most frequent adverse experiences observed were thirst, somnolence, mydriasis, hyperkinesias and abdominal pain. It is not known whether montelukast is dialysable by peritoneal or haemodialysis.

IDENTIFICATION
MONTEFLO 4: Pink coloured, oval biconvex "shaped", uncoated chewable tablet with a breakline on both sides. The breakline is for appearance only and not to halve the dose.
MONTEFLO 5: Pink coloured, round biconvex "shaped", uncoated chewable tablet with a breakline on both sides. The breakline is for appearance only and not to halve the dose.
MONTEFLO 10: Brown coloured, round biconvex "shaped", uncoated tablet with a breakline on both sides. The breakline is for appearance only and not to halve the dose.

PRESENTATION
MONTEFLO 4, 5 and 10 are available in silver coloured CFBAlu/Alu blister packs of 10 tablets, 30 tablets per pack.

STORAGE INSTRUCTIONS
Store at or below 25 ºC. Protect from light and moisture. Keep the blisters in the outer carton until required for use. KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER
MONTEFLO 4: 44/10.2.2/0257
MONTEFLO 5: 44/10.2.2/0262
MONTEFLO 10: 44/10.2.2/0286

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
Trinity Pharma (Pty) Limited, Oval Business Park, Wanderers Building, Unit 1B, Office A, Cnr Sloane and Meadowbrook Close, Bryanston, 2194

DATE OF PUBLICATION OF THE PACKAGE INSERT
July 2012

SKEDULERINGSTATUS: **S3**

HANDELSNAAM (EN DOSEERVORM):
MONTEFLO 4 (koutablette)
MONTEFLO 5 (koutablette)
MONTEFLO 10 (tablette)

SAMESTELLING:
MONTEFLO 4: Elke koutablet bevat 4 mg montelukast (as montelukast natrium).
MONTEFLO 5: Elke koutablet bevat 5 mg montelukast (as montelukast natrium).
MONTEFLO 4 & **5** bevat ook die volgende onaktiewe bestanddele:
Mannitol, mikrokristallyne sellulose, natriumkroskarmellose, aspartaam, kersiegeursel, rooi ysteroksied, magnesiumstearaat.

MONTEFLO 10: Elke tablet bevat 10 mg montelukast (as montelukast natrium).
MONTEFLO 10 bevat ook die volgende onaktiewe bestanddele:
Mannitol, mikrokristallyne sellulose, natriumkroskarmellose, aspartaam, kersiegeursel, rooi ysteroksied en geel ysteroksied, magnesiumstearaat .

FARMAKOLOGIESE KLASSIFIKASIE:
A. 10.2.2 Ander anti-asmatiese middels, Leukotriene reseptorantagoniste

FARMAKOLOGIESE WERKING:
Farmakodinamika:
Montelukast veroorsaak kragtige inhibering van die sisteïen leukotriene reseptore in die lugweg.
Die sisteïen leukotriene (LTC_4, LTD_4, LTE_4) is kragtige inflammatoriese eikosanoïede wat deur verskeie selle, insluitend masselle en eosinofiele, vrygestel word. Hierdie belangrike pro-asmatiese fassiliteerders bind aan sisteïen leukotriene (CysL T) reseptore. Die CysL T tipe-1 ($CysLT_1$) reseptor word in die menslike lugweë (insluitend die gladdespier en makrofages) asook op ander pro-inflammatoriese selle (insluitend eosinofiele en sekere miëloïede stamselle) aangetref. Binding van sisteïen leukotriene aan leukotriene reseptore hou verband met die patofisiologie van asma, insluitend brongokonstriksie, mukus sekresie, vaskulêre deurlaatbaarheid en eosinofiel aanvulling. Montelukast bind met hoë affiniteit en selektiwiteit aan die $CysLT_1$ reseptor. Montelukast inhibeer die fisiologiese uitwerking van LTC4, LTD4 en LTE4 by die CysLT1 reseptore, sonder enige aktiwiteit as agonis. Doserings so laag as 5 mg veroorsaak aansienlike blokkering van LTD4-geïnduseerde brongokonstriksie.

FARMAKOKINETIKA:
Absorpsie:
Montelukast word vinnig geabsorbeer na mondelikse toediening. Die gemiddelde piek-plasmakonsentrasie (C_{max}) vir die 4 mg koutablet word 2 uur na toediening in pediatriese pasiënte, tussen die ouderdom van 2 tot 5 jaar, tydens vastende toestand bereik. Veiligheid en effektiwiteit is in kliniese studies, waar die 4 mg koutablet toegedien is sonder dat die tyd van voedselinname in ag geneem is, bewys.
Die gemiddelde piek-plasmakonsentrasie (C_{max}) vir die 5 mg koutablet word 2 uur na toediening in volwassenes tydens vastende toestand bereik. Die gemiddelde orale biobeskikbaarheid is 73 %. Voedsel het nie `n klinies belangrike invloed gedurende kroniese behandeling nie. Die gemiddelde piek-plasmakonsentrasie (C_{max}) vir die 10 mg tablet word 3 uur (T_{max}) na toediening in volwassenes tydens vastende toestand bereik. Die gemiddelde orale biobeskikbaarheid is 64 %. Die piek-plasmakonsentrasie na toediening word nie deur die innname van `n standaard maaltyd beïnvloed nie.
Verspreiding:
Montelukast is meer as 99 % gebind aan plasmaproteïne. Die gelyke volume van verspreiding van motelukast is gemiddeld 6 tot 11 liter.
Metabolisme:
Montelukast word uitsluitlik in die lewer gemetaboliseer.
In vitro studies met menslewer mikrosome dui daarop dat sitochroom P450 3A4 en 2C9 tydens die metabolisme van montelukast betrokke is. Verdere *in vitro* studies op menslewer mikrosome het bewys dat plasmakonsentrasies van montelukast nie sitochroom P450, 3A4, 2C9, 1A2, 2A6, 2C19 of 2D6 inhibeer nie.
Uitskeiding:
Data met betrekking tot die uitskeiding van montelukast is nie in kinders tussen die ouderdom van 2 en 5 jaar beskikbaar nie. In gesonde volwassenes is die verwydering van montelukast in plasma gemiddeld 45 ml/min. Na 'n mondelikse dosering van radio-aktief gemerkte montelukast, word 86 % van die radio-aktiwiteit in 5 dae se fekale kolleksies herwin en minder as 0,2 % word in uriene herwin. Daar kan dus, gepaardgaande met beraminge van montelukast se orale biobeskikbaarheid, tot die gevolgtrekking gekom word dat montelukast en sy metaboliete uitsluitlik deur gal uitgeskei word. Die gemiddelde plasma half-leeftyd van montelukast wissel tussen 2,7 tot 5,5 uur in gesonde, jong volwassenes. Montelukast farmakokinetika is by mondelikse doserings tot en met 50 mg feitlik lineêr. Daar is geen verskil in die farmakokinetika tussen doserings wat in die oggend of aand geneem word nie. Tydens eenmalige doserings is daar byna geen opeenhoping van die eenvoudigste vorm van montelukast in plasma (ongeveer 14 %) nie.
Lewerinkorting:
Tydens `n enkeldosering van 10 mg montelukast mag pasiënte met ligte tot matige lewerinkorting, asook diegene met kliniese tekens van sirrose, `n afname in metabolisme toon wat dienooreenkomstig tot `n hoër area onder plasmakonsentrasie kurwe (AOK) van 41 % tot gevolg mag hê. Die uitskeiding van montelukast is effens verleng in vergelyking met die van gesonde volwassenes (gemiddelde half-leeftyd van 7,4 uur). Geen dosis-aanpassing word in pasiënte met ligte tot matige lewerinkorting benodig nie. Geen kliniese data is in pasiënte met erge lewerinkorting (Child-Pugh telling > 9) beskikbaar nie. Die farmakokinetika en orale biobeskikbaarheid van `n enkeldosering van 10 mg van montelukast is soortgelyk in bejaardes sowel as jonger volwassenes. Die plasma half-leeftyd duur effens langer in bejaardes, maar geen dosis-aanpassing is nodig nie.

INDIKASIES:
MONTEFLO tablette word aangedui vir profilakse en kroniese behandeling van atopiese asma.
MONTEFLO 4 koutablette word aangedui by pediatriese pasiënte 2 tot 5 jaar oud.
MONTEFLO 5 koutablette word aangedui by pediatriese pasiënte ouer as 6 jaar.
MONTEFLO 10 tablette word aangedui by volwassenes en kinders van 15 jaar en ouer.

KONTRA-INDIKASIES:
Hipersensitiwiteit vir enige bestanddele teenwoordig in hierdie produk.
Swangerskap en laktasie.
• **MONTEFLO 5** en **10** moet nie by kinders jonger as 6 jaar gebruik word nie, aangesien veiligheid en doeltreffendheid nie bewys is nie.
• **MONTEFLO 4** moet nie by kinders jonger as 2 jaar gebruik word nie, aangesien veiligheid en doeltreffendheid nie bewys is nie.
• **MONTEFLO 10** moet nie by kinders jonger as 15 jaar gebruik word nie, aangesien veiligheid en doeltreffendheid nie bewys is nie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
Algemeen:
Die doeltreffendheid van mondelikse **MONTEFLO** vir die behandeling van akute asma-aanvalle is nog nie vasgestel nie. **MONTEFLO** moet nie as monoterapie vir die behandeling en bestuur van oefeningsgeïnduseerde brongospasma gebruik word nie. Pasiënte wat opflikkerings van asma na oefening ervaar, moet voortgaan om hul normale behandelinsroetine te volg. Die gebruik van inhalasie beta-agoniste as profilakse moet voortgaan tesame met `n kortwerkende inhalasie beta-agonis vir noodgevalle. **MONTEFLO** word nie vir die behandeling van brongospasma tydens akute asma-aanvalle, insluitend status asthmaticus, aangedui nie. Pasiënte moet aangeraai word om geskikte noodmedikasie byderhand te hê. Behandeling met **MONTEFLO** kan gedurende akute opflikkerings van asma voorgesit word. **MONTEFLO** moet nie skielik met inhalasie of mondelikse kortikosteroïedes vervang word nie. Die dosis van die kortikosteroïed kan geleidelik onder mediese toesig verminder word. Terwyl **MONTEFLO** geneem word moet pasiënte met bekende sensitiwiteit steeds voortgaan om aspirien of Nie-steroïed Anti-inflammatoriese Middels (NSAIMs) te vermy. Daar is nie bevind dat **MONTEFLO**, wat effektief is vir die verbetering van lugwegfunksie, die brongokonstriksie-respons op aspirien of ander NSAIMs, in die geval van aspirien sensitiewe asma pasiënte, verkort nie.
Inkorting van nierfunksie:
Geen dosis-aanpassings word aanbeveel in pasiënte met nierinkorting nie, aangesien montelukast en sy metaboliete nie in die uriene uitgeskei word nie. Die evaluering van montelukast farmakokinetika is nie in pasiënte met nierinkorting bestudeer nie.
Gebruik by Bejaardes:
Daar is geen ouderdomsverwante verskille in die doeltreffendheids– of veiligheidsprofiele van **MONTEFLO** nie.
Eosinofiele toestande:
Sistemiese eosinofilie mag in pasiënte wat **MONTEFLO** neem voorkom. Soms kan dit met die kliniese eienskappe van vaskulitis, in ooreenstemming met Churg-Strauss-Sindroom, `n toestand wat dikwels met sistemiese kortikosteroïedes behandel word, presenteer. Hierdie voorvalle kom gewoonlik, maar nie altyd nie, in assosiasie met die vermindering van mondelikse kortikosteroïed behandeling voor. Daar word aanbeveel dat dokters op die uitkyk vir tekens van eosinofilie, vaskulitis-uitslag, agteruitgang van pulmonêre simptome, hartkomplikasies en/of neuropatie moet wees. **MONTEFLO** moet by hierdie pasiënte onttrek word (sien NEWE-EFFEKTE).
Neuropsigiatriese voorvalle:
Neuropsigiatriese voorvalle is in sommige pasiënte wat **MONTEFLO** neem, aangemeld. Hierdie sluit opgewondenheid, aggressie, angstigheid, droomabnormaliteite, hallusinasies, depressie, slaaploosheid, prikkelbaarheid, rusteloosheid, selfmoordgedagtes en -gedrag (insluitende selfmoord) en tremor in. Pasiënte en professionele gesondheidsorgkundiges moet van die moontlikheid van neuropsigiatriese voorvalle bewus wees. Pasiënte moet ingelig word om hul gesondheidsorgkundige in kennis te stel indien hierdie voorvalle voorkom. Indien sulke voorvalle voorkom moet gesondheidsorgkundiges met oorsig die risiko's en voordele van voorgesette behandeling met **MONTEFLO** oorweeg.
Inkorting van lewerfunksie:
Die metabolisme van montelukast kan in pasiënte met ligte tot matige lewerfunksie inkorting en kliniese tekens van sirrose, afneem. Die halfleeftyd kan effens langer wees, nogtans is dosisaanpassing nie nodig nie. Geen data is beskikbaar vir pasiënte met ernstige lewerfunksie inkorting nie. Weens newe-effekte soos duiseligheid en lomerigheid wat mag voorkom tydens die gebruik van **MONTEFLO**, moet die bestuur en hantering van swaar masjinerie met omsigtigheid hanteer word.

Pasiënte moet bewus gemaak word om nie te bestuur of met swaar masjinerie te werk nie, totdat hul weet watter individuele uitwerking **MONTEFLO** op hul het.
Inligting vir pasiënte:
Pasiënte moet aangeraai word om **MONTEFLO** op `n daaglikse basis soos voorgeskryf, te neem. Dit geld selfs indien hul asimptomaties is of ten tye van verslegtende asma. Pasiënte moet aangeraai word om hul geneesheer te kontak indien hul asma nie goed onder beheer is nie. Pasiënte moet ingelig word dat **MONTEFLO** nie geskik is vir die behandeling van akute asma-aanvalle nie. Hulle moet geskikte kortwerkende inhalasie beta-agoniste medikasie beskikbaar hê om opflikkerings van asma te behandel. Pasiënte moet aangeraai word om terwyl hulle **MONTEFLO** gebruik, mediese aandag te kry indien kortwerkende inhalasie brongodilators meer dikwels as gewoonlik gebruik word, of indien meer as die maksimum aanbevole dosis van kortwerkende inhalasie brongodilators binne `n tydperk van 24-uur benodig word. Pasiënte wat **MONTEFLO** gebruik moet aangeraai word om nie hul dosis te verminder of om die gebruik van ander asma middels te staak nie, tensy dit so deur hul geneesheer aanbeveel word. **MONTEFLO** moet nie as monoterapie vir die bestuur en behandeling van oefeningsgeïnduseerde brongospasma gebruik word nie. Pasiënte wat opflikkerings van asma na oefening ervaar, moet voortgaan om hul normale roetine te volg deur die gebruik van inhalasie beta-agoniste as profilakse te gebruik en `n kortwerkende inhalasie beta-agonis vir noodgevalle byderhand te hou. Pasiënte met bekende aspirien-sensitiwiteit moet steeds, terwyl **MONTEFLO** geneem word, voortgaan om aspirien of Nie-steroïed Anti-inflammatoriese Middels (NSAIMs) te vermy. Daar is nie bevind dat **MONTEFLO**, wat effektief is vir die verbetering van lugwegfunksie, die brongokonstriksie-respons op aspirien of ander NSAIMs in aspirien sensitiewe asma pasiënte verkort nie.

MONTEFLO 4 en **5** mg koutablette en **10** mg tablette:
Pasiënte met fenielketonurie moet ingelig word dat **MONTEFLO 4** & **5** koutablette en **MONTEFLO 10** tablette aspartaam, wat `n bron van fenielalanien is, bevat.

INTERAKSIES:
MONTEFLO kan gesamentlik met ander middels gebruik wat word vir die voorkoming en chroniese behandeling van asma, toegedien word. Navorsingstudies het bevind dat die aanbevole kliniese dosis van montelukast geen klinies belangrike effekte op die farmakokinetika van die volgende middels gehad het nie: teofillien, prednisoon, prednisoloon, orale voorbehoedmiddels (etinielestradiol-noretindroon 35/1), digoksien en warfarien. Gesamentlike gebruik van montelukast met fenobarbital lei tot `n afname van ongeveer 40 % in die area onder die kurwe (AOK). Geen dosisaanpassing vir **MONTEFLO** word aanbeveel nie. Monitering word egter tydens die gesamentlike gebruik van **MONTEFLO** en kragtige hepatiese ensieminhibeerders soos fenitoïen, fenobarbital of rifampisien, aanbeveel.

SWANGERSKAP EN LAKTASIE:
Die veiligheid van **MONTEFLO** tydens swangerskap en laktasie is nie bepaal nie. **MONTEFLO** moet dus nie gedurende swangerskap en laktasie gebruik word nie. Dit is nie bekend of montelukast in borsmelk uitgeskei word nie.

DOSIS EN GEBRUIKSAANWYSINGS:
MONTEFLO moet een maal per dag in die aand geneem word.
MONTEFLO 4 koutablette:
Pediatriese pasiënte 2 tot 5 jaar oud met Atopiese Asma:
Die dosering vir pediatriese pasiënte 2 tot 5 jaar oud is een 4 mg koutablet per dag tydens slaaptyd
MONTEFLO 5 koubare tablette:
Pediatriese pasiënte 6 tot 14 jaar oud met Atopiese Asma:
Die dosering vir pediatriese pasiënte 6 tot 14 jaar oud is een 5 mg koutablet per dag.
MONTEFLO 10 tablette:
Volwassenes en kinders 15 jaar oud en ouer met Atopiese Asma:
Die dosering vir kinders en volwassenes 15 jaar oud en ouer is een 10 mg tablet per dag.
Algemene Aanbevelings:
`n Terapeutiese effek (gebasseer op parameters van asmakontrole) kan tydens die gebruik van **MONTEFLO**, binne een dag ervaar word. **MONTEFLO** kan met of sonder voedsel geneem word. Pasiënte moet aangeraai word om aan te hou om **MONTEFLO** elke dag te neem, selfs terwyl hul asma onder beheer is, asook ten tye van verslegtende asma. Geen dosisaanpassing is nie nodig vir bejaardes, pasiënte met nierinkorting, ligte tot matige lewerinkorting of pasiënte van `n bepaalde geslag nie. **MONTEFLO** kan by 'n pasiënt se bestaande behandelingstrategie bygevoeg word.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREëLS:
Newe-effekte:
Metaboliese en voedingsafwykings:
Dikwels: Dors
Senuweestelselafwykings:
Dikwels: Hoofpyn, duiseligheid
Frekwensie onbekend: Lomerigheid, parestesie/hipo-estesie, stuipe
Gastroïntestinale afwykings:
Dikwels: Abdominale pyn, diarree, dispepsie, gastroënteritis , tandpyn
Frekwensie onbekend: Droë mond, naarheid, braking
Infeksies en infestasies:
Frekwensie onbekend: Boonste lugweginfeksie, varisella, gastroënteritis
Bloed- en limfatiese stelselafwykings:
Frekwensie onbekend: Verhoogde bloedingstendens, agranulositose
Immuunstelselafwykings:
Frekwensie onbekend: Hipersensitiwiteitsreaksies insluitende anafilakse, hepatiese eosinofiliese infiltrasie, angio-edeem
Psigiatriese afwykings:
Dikwels: Slaaploosheid
Frekwensie onbekend: Abnormale drome, hallusinasies, opgewondenheid insluitende aggressiewe gedrag, angstigheid, depressie, prikkelbaarheid, rusteloosheid, selfmoordgedagtes en –gedrag (insluitend selfmoord), tremor
Kardiale afwykings:
Frekwensie onbekend: Hartkloppings
Respiratoriese, torakale en mediastinale afwykings:
Dikwels: Neuskongestie, hoes, griep
Frekwensie onbekend: Epistaksis
Hepato-biliêre afwykings:
Dikwels: Verhoogde vlakke van serumtransaminase (ALT, AST)
Frekwensie onbekend: Hepatitis (insluitend cholestatiese, hepatosellulêre asook gemengde patroon lewerbeskadiging)
Vel- en subkutaneuse weefselafwykings:
Dikwels: Uitslag
Frekwensie onbekend: Kneus, erythema nodosum, pruritus, urtikarie, ekseem
Muskuloskeletale en bindweefselafwykings:
Artralgie, mialgie (insluitende spierkrampe)
Algemene afwykings en toedieningsitus toestande:
Dikwels: Astenie (uitputting), malaise, koors

Sistemiese eosinofilie mag in pasiënte wat **MONTEFLO** neem voorkom. Soms kan dit met die kliniese eienskappe van vaskulitis, in ooreenstemming met Churg-Strauss-Sindroom, `n toestand wat dikwels met sistemiese kortikosteroïedes behandel word, presenteer. Hierdie voorvalle kom gewoonlik, maar nie altyd nie, in assosiasie met die vermindering van mondelikse kortikosteroïed behandeling voor. Daar word aanbeveel dat dokters op die uitkyk vir tekens van eosinofilie, vaskulitis-uitslag, agteruitgang van pulmonêre simptome, hartkomplikasies en/of neuropatie moet wees. **MONTEFLO** moet by hierdie pasiënte onttrek word (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREëLS, Eosinofiliese toestande).

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Geen spesifieke inligting is beskikbaar omtrent die behandeling van oordosering van **MONTEFLO** nie. Navorsingstudies oor kroniese asma in volwasse pasiënte het bewys dat doserings van tot 200 mg/dag oor `n periode van 22 dae geen ernstige newe-effekte toon nie. Dieselfde is in korttermyn navorsingstudies met doserings tot en met 900 mg/dag bevind. Meeste oordoseringsverslae toon aan dat geen ernstige newe-effekte tydens oordoserings aangemeld is nie. Die volgende newe-effekte kan meer dikwels tydens die gebruik van **MONTEFLO** ervaar word: lomerigheid, midriase, hiperkinesie en buikpyn. Dis is onbekend of montelukast deur middel van peritoneale dialise of hemodialise verwyder kan word.

IDENTIFIKASIE:
MONTEFLO 4: Ligte rooskleurige, ovaal bikonvekse, onbedekte koutablet met 'n breeklyn aan albei kante. Die breeklyn is slegs vir voorkoms en nie om die dosis te halveer nie.
MONTEFLO 5: Ligte rooskleurige, ronde bikonvekse, onbedekte koutablet met 'n breeklyn aan albei kante. Die breeklyn is slegs vir voorkoms en nie om die dosis te halveer nie.
MONTEFLO 10: Bruin gekleurde, ronde bikonvekse, onbedekte tablet met 'n breeklyn aan albei kante. Die breeklyn is slegs vir voorkoms en nie om die dosis te halveer nie.

AANBIEDING:
MONTEFLO 4, **5** en **10** is beskikbaar in silwer gekleurde CFBAlu/Alu stulpverpakkings van 10 tablette, 30 tablette per pak.

BERGINGSINSTRUKSIES:
Berg by of onder 25 °C. Beskerm teen lig en vog. Hou die stulpverpakkings in die buitenste karton totdat dit vir gebruik benodig word. HOU BUITE DIE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:
MONTEFLO 4: 44/10.2.2/0257
MONTEFLO 5: 44/10.2.2/0262
MONTEFLO 10: 44/10.2.2/0286

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