**PROFESSIONAL INFORMATION**

**SCHEDULING STATUS:** S3

**1 NAME OF THE MEDICINE**

# Sintrine® Oral Granules

SANDOZ A Novartis Division

**2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each sachet of SINTRINE ORAL GRANULES contains 4,15 mg of montelukast sodium equivalent to 4,00 mg of montelukast.
SINTRINE ORAL GRANULES contains sweetener (mannitol (484,70 mg per sachet)).

For full list of excipients, see section 6.1.

**3 PHARMACEUTICAL FORM**

Oral granules.
White to off white granules.

**4 CLINICAL PARTICULARS**

**4.1. Therapeutic indications**

SINTRINE ORAL GRANULES is indicated in paediatric patients 2 to 5 years of age for the prophylaxis and chronic treatment of atopic asthma.

**4.2. Posology and method of administration**

**Posology**

This medicine is to be given to a child under adult supervision. The recommended dose for paediatric patients 2 to 5 years of age is one sachet of 4 mg oral granules daily to be taken in the evening.

**Administration of SINTRINE ORAL GRANULES**

SINTRINE ORAL GRANULES can be administered either directly in the mouth or mixed with a spoonful of cold or room temperature soft food (e.g., applesauce, ice cream, carrots and rice). The sachet should not be opened until ready to use. After opening the sachet, the full dose of SINTRINE ORAL GRANULES must be administered immediately (within 15 minutes). If mixed with food, SINTRINE ORAL GRANULES must not be stored for future use.
SINTRINE ORAL GRANULES are not intended to be dissolved in liquid for administration. However, liquids may be taken subsequent to administration. SINTRINE ORAL GRANULES can be administered without regard to the timing of food ingestion.

**General recommendations**

The therapeutic effect of SINTRINE ORAL GRANULES on parameters of asthma control occurs within one day. Patients should be advised to continue taking SINTRINE ORAL GRANULES even if their asthma is under control, as well as during periods of worsening asthma.
No dosage adjustment is necessary for patients with renal insufficiency, or mild to moderate hepatic impairment.
There are no data on patients with severe hepatic impairment. The dosage is the same for both male and female patients.

**Therapy with SINTRINE ORAL GRANULES in relation to other treatments for asthma**

SINTRINE ORAL GRANULES can be added to a patient's existing treatment regimen.

**Method of administration**

Oral use as described above.

**4.3 Contraindications**

- Known sensitivity to montelukast or to any of the excipients in SINTRINE ORAL GRANULES (see sections 2 and 6.1).
- Children under the age of 2 years, as safety and efficacy of SINTRINE ORAL GRANULES have not been demonstrated.

**4.4. Special warnings and precautions for use**

Patients should be advised never to use oral montelukast to treat acute asthma attacks, including status asthmaticus and to keep their usual appropriate rescue medication for this purpose readily available. SINTRINE ORAL GRANULES is not indicated for use in the reversal of bronchospasm in acute asthma attacks. If an acute attack occurs, a short-acting inhaled β-agonist should be used. Patients should seek their doctors' advice as soon as possible if they need more inhalations of short-acting β-agonists than usual.

SINTRINE ORAL GRANULES 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 β -agonists as prophylaxis and have available for rescue a short-acting inhaled β agonist.

Montelukast should not be abruptly substituted for inhaled or oral corticosteroids.
There are no data demonstrating that oral corticosteroids can be reduced when SINTRINE ORAL GRANULES is given concomitantly.

**Renal Insufficiency**

Since SINTRINE ORAL GRANULES and its metabolites are not excreted in the urine, the pharmacokinetics of SINTRINE ORAL GRANULES were not evaluated in patients with renal insufficiency. No dosage adjustment is recommended in these patients.
Patients on therapy with anti-asthma medicines including SINTRINE ORAL GRANULES may present with systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition which is often treated with systemic corticosteroid therapy. These cases have been sometimes associated with the reduction or withdrawal of oral corticosteroid therapy. Although a causal relationship with leukotriene receptor antagonism has not been established, medical practitioners 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 medicines.

Neuropsychiatric events have been reported in adults, adolescents, and children taking SINTRINE ORAL GRANULES (see section 4.8). Patients and medical practitioners should be alert for neuropsychiatric events. Patients and/or caregivers should be instructed to notify their medical practitioners if these changes occur. Prescribers should carefully evaluate the risks and benefits of continuing treatment with SINTRINE ORAL GRANULES if such events occur.

**SINTRINE ORAL GRANULES as an alternative treatment option to low-dose inhaled corticosteroids for mild, persistent asthma**

Montelukast is not recommended as monotherapy in patients with moderate persistent asthma. The use of montelukast as an alternative treatment option to low-dose inhaled corticosteroids for children 2 to 5 years old with mild persistent asthma should only be considered for patients who do not have a recent history of serious asthma attacks that required oral corticosteroid use and who have demonstrated that they are not capable of using inhaled corticosteroids (see section 4.1). Mild persistent asthma is defined as asthma symptoms more than once a week but less than once a day, nocturnal symptoms more than twice a month but less than once a week, normal lung function between episodes. If satisfactory control of asthma is not achieved at follow-up (usually within one month), the need for an additional or different anti-inflammatory therapy based on the step system for asthma therapy should be evaluated. Patients should be periodically evaluated for their asthma control.

**Information for Patients:**

- Patients should be advised to take SINTRINE ORAL GRANULES daily as prescribed, even when they are asymptomatic, as well as during periods of worsening asthma, and to contact their physicians if their asthma is not well controlled.
- Patients should be advised that SINTRINE ORAL GRANULES are not for the treatment of acute asthma attacks. They should have appropriate short-acting inhaled β -agonist medication available to treat asthma exacerbations.
- Patients should be advised that, while using SINTRINE ORAL GRANULES, 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 SINTRINE ORAL GRANULES should be instructed not to decrease the dose or stop taking any other anti-asthma medications unless instructed by a physician.
- Patients who have exacerbations of asthma after exercise should be instructed to continue to use their usual regimen of inhaled β -agonists as prophylaxis unless otherwise instructed by their medical practitioner. All patients should have available for rescue a short-acting inhaled β -agonist.
- Patients with known aspirin sensitivity should be advised to continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking SINTRINE ORAL GRANULES.

**4.5. Interaction with other medicinal products and other forms of interaction**

Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma. In medicine-interactions studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following medicinal products: theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/norethindrone 35/1), terfenadine, digoxin and warfarin.
The area under the plasma concentration curve (AUC) for montelukast was decreased approximately 40 % in subjects with co-administration of phenobarbital. Since montelukast is metabolised by CYP 3A4, 2C8, and 2C9, caution should be exercised, particularly in children, when montelukast is co-administered with inducers of CYP 3A4, 2C8, and 2C9, such as phenytoin, phenobarbital and rifampicin.

*In vitro* studies have shown that montelukast is a potent inhibitor of CYP 2C8. However, data from a clinical medicine 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).

*In vitro* studies have shown that montelukast is a substrate of CYP 2C8, and to a less significant extent, of 2C9, and 3A4. In a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) gemfibrozil increased the systemic exposure of montelukast by 4.4-fold. No routine dosage adjustment of montelukast is required upon co-administration with gemfibrozil or other potent inhibitors of CYP 2C8, but the medical practitioner should be aware of the potential for an increase in adverse reactions.
Based on *in vitro* data, clinically important medicine interactions with less potent inhibitors of CYP 2C8 (e.g., trimethoprim) are not anticipated. Co-administration of montelukast with itraconazole, a strong inhibitor of CYP 3A4, resulted in no significant increase in the systemic exposure of montelukast.

**4.6 Fertility, pregnancy and lactation**

**Pregnancy**

The safety of montelukast in pregnant and lactating women has not been established.
SINTRINE ORAL GRANULES should not be used during pregnancy.
During worldwide marketing experience, congenital limb defects have been reported in offspring of women treated with SINTRINE ORAL GRANULES during pregnancy.
A causal relationship between these events and SINTRINE ORAL GRANULES has not been established.

**Lactation**

Studies in rats have shown that montelukast is excreted in milk (see section 5.3). It is unknown whether montelukast/metabolites are excreted in human milk. SINTRINE ORAL GRANULES should not be used in breastfeeding mothers.

**4.7. Effects on ability to drive and use machines**

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

**4.8. Undesirable effects**

**Tabulated list of Adverse Reactions:**

| System organ class | Adverse reactions | Frequency category |
|---|---|---|
| **Infections and infestations** | Upper respiratory infection | Frequent |
| **Blood and lymphatic system Disorders** | Increased bleeding tendency, thrombocytopenia | Less frequent |
| **Immune system disorders** | Hypersensitivity reactions including anaphylaxis, hepatic eosinophilic infiltration | Less frequent |
| **Psychiatric disorders** | Dream abnormalities including nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behaviour or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor), disturbance in attention, memory impairment, tics, hallucinations, disorientation, suicidal thinking and behaviour (suicidality), obsessive-compulsive symptoms, dysphemia | Less frequent |
| **Nervous system disorders** | Headache, hyperkinesia | Frequent |
| | Dizziness, drowsiness, paraesthesia/hypoesthesia, seizure | Less frequent |
| **Cardiac disorders** | Palpitations | Less frequent |
| **Respiratory, thoracic and mediastinal disorders** | Epistaxis, Churg-Strauss Syndrome (CSS) (see section 4.4), pulmonary eosinophilia | Less frequent |
| **Gastro-intestinal disorders** | Diarrhoea, nausea, vomiting, abdominal pain | Frequent |
| | Dry mouth, dyspepsia | Less frequent |
| **Hepatobiliary disorders** | Elevated levels of serum transaminases (ALT, AST) | Frequent |
| | Hepatitis (including cholestatic, hepatocellular, and mixed-pattern liver injury). | Less frequent |
| **Skin and subcutaneous tissue Disorders** | Rash | Frequent |
| | Bruising, urticaria, pruritus, angioedema, erythema nodosum, erythema multiforme, eczematous, dermatitis, rash | Less frequent |
| **Musculoskeletal and connective tissue disorders** | Arthralgia, myalgia including muscle cramps | Less frequent |
| **Renal and urinary disorders** | Enuresis in children | Less frequent |
| **General disorders and administration site conditions** | Pyrexia, thirst | Frequent |
| | Asthenia/fatigue, malaise, oedema | Less frequent |

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.
Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

**4.9 Overdose**

No specific information is available on the treatment of overdosage with SINTRINE ORAL GRANULES.
In chronic asthma studies, montelukast has been administered at doses up to 200 mg/day to adult patients for 22 weeks and in short-term studies, up to 900 mg/day to patients for approximately one week without clinically important adverse experiences.
There have been reports of acute overdose in post-marketing experience and clinical studies with montelukast. These include reports in adults and children with a dose as high as 1000 mg. 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.

**Symptoms of overdose**

The most frequently occurring adverse experiences were consistent with the safety profile of montelukast and included abdominal pain, somnolence, thirst, headache, vomiting, and psychomotor hyperactivity.

**Management of overdose**

No specific information is available on the treatment of overdose with montelukast. It is not known whether montelukast is dialysable by peritoneal- or haemo-dialysis.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1. Pharmacodynamic properties**

Pharmacological classification: A.10.3 Others (Medicines acting on respiratory systems)
ATC-code: R03D C03

**Mechanism of action**

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 receptors (CysLT) found in the human airway and cause airway actions, including bronchoconstriction, mucous secretion, vascular permeability, and eosinophil recruitment.

**Pharmacodynamic properties**

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). In adult and paediatric patients 2 to 14 years of age, montelukast, compared with placebo, decreased peripheral blood eosinophils while improving clinical asthma control.

**5.2. 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.
After administration of the 4 mg chewable tablet to paediatric patients 2 to 5 years of age in the fasted state, $C_{max}$ is achieved 2 hours after administration. The mean $C_{max}$ is 66 % higher while mean $C_{min}$ is lower than in adults receiving a 10 mg tablet.
The 4 mg granule formulation is bioequivalent to the 4 mg chewable tablet when administered to adults in the fasted state. In paediatric patients 6 months to 2 years of age, $C_{max}$ is achieved 2 hours after administration of the 4 mg granules formulation. $C_{max}$ is nearly 2-fold greater than in adults receiving a 10 mg tablet. The co-administration of applesauce or a high-fat standard meal with the granule formulation did not have a clinically meaningful effect on the pharmacokinetics of montelukast as determined by AUC.

**Distribution**

Montelukast is more than 99 % bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8 to11 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. Cytochrome P450 2C8 is the major enzyme in the metabolism of montelukast. Additionally, CYP 3A4 and 2C9 may have a minor contribution, although itraconazole, an inhibitor of CYP 3A4, was shown not to change pharmacokinetic variables of montelukast in healthy-subjects that received 10 mg montelukast daily. Based on *in vitro* results in human liver microsomes, therapeutic plasma concentrations of montelukast do not inhibit cytochromes P450 3A4, 2C9, 1A2, 2A6, 2C19, or 2D6. The contribution of metabolites to the therapeutic effect of montelukast is minimal.

**Elimination**

The plasma clearance of montelukast averages 45 ml/min in healthy adults. Following an oral dose of 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.

**Special populations**

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), a decrease in plasma theophylline concentration was observed. This effect was not seen at the recommended dose of 10 mg once daily.

**6. PHARMACEUTICAL PARTICULARS**

**6.1. List of excipients**

Hydroxypropyl cellulose (klucel LF), mannitol (Pearlitol DC300) and magnesium stearate.

**6.2. Incompatibilities**

Not applicable

**6.3. Shelf life**

24 months

**6.4. Special precautions for storage**

Store at or below 25 °C.
Store in the original package in order to protect from light and moisture.
Do not use after the expiry date stated on the sachet / carton.

**6.5. Nature and contents of container**

Pouch laminate sachet (PET/Aluminium foil/PE).
The sachets are packed in an outer cardboard carton.
Packs sizes of 7, 10, 14, 20, 28, 30 and 100 sachets.
Not all pack sizes may be marketed.

**6.6. Special precautions for disposal and other handling**

No special requirements.

**7. HOLDER OF CERTIFICATE OF REGISTRATION**

Sandoz SA (Pty) Ltd[1]
Waterfall 5-Ir,
Magwa Crescent West
Waterfall City
Jukskei View
2090
Marketed by sanofi aventis south africa (pty) ltd.

**8. REGISTRATION NUMBER**

47/10.3/0743

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 08 March 2022

**10. DATE OF REVISION OF THE TEXT**

Not applicable.

[1]Company Reg. No.: 1990/001979/07

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**PATIENT INFORMATION LEAFLET**

**SCHEDULING STATUS:** S3

# Sintrine® Oral Granules

**Active ingredient: montelukast sodium equivalent to 4,00 mg of montelukast.**
**SINTRINE ORAL GRANULES contains sweetener (484,70 mg mannitol per sachet).**

SANDOZ A Novartis Division

**Read all of this leaflet carefully before you start taking SINTRINE ORAL GRANULES**

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- SINTRINE ORAL GRANULES has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

**What is in this leaflet**



**1. What SINTRINE ORAL GRANULES is and what it is used for**

SINTRINE ORAL GRANULES contains the active substance montelukast and is used in children (2 to 5 years) for the chronic treatment of atopic (allergic) asthma and to prevent asthma symptoms.

**How it works**

Montelukast, the active ingredient in SINTRINE ORAL GRANULES is a leukotriene receptor antagonist that blocks substances called leukotrienes.
Leukotrienes cause narrowing and swelling of airways in the lungs. By blocking leukotrienes, SINTRINE ORAL GRANULES improves asthma symptoms and helps control asthma.

**2. What you need to know before you give SINTRINE ORAL GRANULES to your child**

**Do not give SINTRINE ORAL GRANULES to your child:**

- If your child is hypersensitive (allergic) to montelukast or any of the other ingredients of SINTRINE ORAL GRANULES (listed in section 6).
- If your child is younger than 2 years old.

**Warnings and precautions**

Talk to your doctor or pharmacist before giving SINTRINE ORAL GRANULES to your child:

- If your child's asthma or breathing gets worse, tell your doctor immediately.
- SINTRINE ORAL GRANULES is not meant to treat acute asthma attacks. If an attack occurs, follow the instructions your doctor has given you for your child. Always have your child's emergency asthma pump or emergency medicine for asthma attacks with you.
- If your child's gets asthma attacks during exercise and your child's doctor has prescribed an emergency asthma pump medicine for your child to use before or during exercise, your child should keep using that medicine.
- It is important that your child take all asthma medications prescribed by his/her doctor. SINTRINE ORAL GRANULES should not be used instead of other asthma medications your doctor has prescribed for your child.
- If your child is on anti-asthma medicines, be aware that if he/she develops a combination of symptoms such as flu-like illness, pins and needles or numbness of arms or legs, worsening of pulmonary symptoms and/or rash, you should consult your doctor.
- Your child should not take acetyl-salicylic acid (aspirin) or anti-inflammatory medicines (also known as non-steroidal anti-inflammatory drugs or NSAIDs) if they make his/her asthma worse.

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- If your child develops symptoms such as behaviour changes or mood changes while taking SINTRINE ORAL GRANULES, you should consult your child's doctor.

**Other medicines and SINTRINE ORAL GRANULES**
Always tell your healthcare provider if your child is taking any other medicine. This includes all complementary or traditional medicines.

Some medicines may affect how SINTRINE ORAL GRANULES works, or SINTRINE ORAL GRANULES may affect how your child's other medicines work.
Tell your doctor if your child is taking the following medicines before starting SINTRINE ORAL GRANULES:
- phenobarbital (used for treatment of epilepsy).
- phenytoin (used for treatment of epilepsy).
- rifampicin (used to treat tuberculosis and some other infections).
- gemfibrozil (used to treat high fat levels in your blood).

**SINTRINE ORAL GRANULES with food and drink**
You can give SINTRINE ORAL GRANULES to your child with or without food. For more information see section 3 on "How to take SINTRINE ORAL GRANULES" below.

**Pregnancy and breastfeeding**
This subsection is not applicable for SINTRINE ORAL GRANULES since they are intended for use in children 2 to 5 years of age.

**Driving and using machines**
This subsection is not applicable for the SINTRINE ORAL GRANULES 4 mg granules since they are intended for use in children 2 years to 5 years of age, however the following information is relevant to the active ingredient, montelukast.
SINTRINE ORAL GRANULES is not expected to affect your ability to drive a car or operate machinery. However, individual responses to medication may vary. Certain side effects (such as dizziness and drowsiness) that have been reported with SINTRINE ORAL GRANULES may affect some patients' ability to drive or operate machinery.

## 3. How to take SINTRINE ORAL GRANULES

Do not share medicines prescribed for your child with any other person.
Always have your child take SINTRINE ORAL GRANULES exactly as your doctor or pharmacist has told you. Check with your child's doctor or pharmacist if you are not sure.
- You should give SINTRINE ORAL GRANULES to your child under supervision every evening.
- Keep giving SINTRINE ORAL GRANULES to your child even when your child has no symptoms.

**For children 2 to 5 years of age**
The recommended dose is one sachet of SINTRINE ORAL GRANULES to be taken by mouth each evening.
If you are giving SINTRINE ORAL GRANULES to your child, be sure that your child does not take any other products that contain the same active ingredient, montelukast. Check with your doctor, pharmacist or other healthcare provider if you are not sure.

**How should I give SINTRINE ORAL GRANULES to my child?**
This medicine is for oral use.
- Do not open the sachet until ready to use.
- SINTRINE ORAL GRANULES can be given either:
  - directly in the mouth;
  - OR mixed with a spoonful of cold or room temperature soft food (for example, applesauce, ice cream, carrots and rice).
- Mix all of the contents of the SINTRINE ORAL GRANULES into a spoonful of cold or room temperature soft food, taking care to see that the entire dose is mixed with the food. Be sure the child is given the entire spoonful of the granule/food mixture immediately (within 15 minutes).
  IMPORTANT: Never store any granule/food mixture for use at a later time.
- SINTRINE ORAL GRANULES is not intended to be dissolved in liquid. However, your child may take liquids after swallowing SINTRINE ORAL GRANULES.
- SINTRINE ORAL GRANULES can be taken without regard to the timing of food intake.

Your doctor will tell you how long your child's treatment with SINTRINE ORAL GRANULES will last.
If you have the impression that the effect of SINTRINE ORAL GRANULES is too strong or too weak, tell your doctor or pharmacist.

**If your child takes more SINTRINE ORAL GRANULES than he/she should**
In the event of overdosage, consult your doctor, pharmacist or other healthcare provider. If neither is available, contact the nearest hospital or poison control centre and take your child's box of SINTRINE ORAL GRANULES with you.

The most frequently occurring symptoms reported with overdose in adults and children included abdominal pain, sleepiness, thirst, headache, vomiting, and hyperactivity.

**If you forget to give SINTRINE ORAL GRANULES to your child**
Give SINTRINE ORAL GRANULES to your child exactly as your doctor has told you. However, if you forget to give SINTRINE ORAL GRANULES to your child, just give the usual amount of one sachet once daily.
Do not give your child a double dose to make up for a forgotten dose.

**If your child stops taking SINTRINE ORAL GRANULES**
SINTRINE ORAL GRANULES can treat your child's asthma only if he/she continues taking it. It is important for your child to continue taking SINTRINE ORAL GRANULES for as long as your doctor has told you. It will help control your child's asthma.
If you have any further questions on the use of this medicine, ask your child's doctor or pharmacist.

## 4. Possible side effects

SINTRINE ORAL GRANULES can have side effects.

Not all side effects reported for SINTRINE ORAL GRANULES are included in this leaflet. Should your child's general health worsen or if your child experiences any untoward effects while taking SINTRINE ORAL GRANULES, please consult your healthcare provider for advice.

**If any of the following happens, your child should stop taking SINTRINE ORAL GRANULES and you should tell your doctor immediately or go to the casualty department at your nearest hospital:**
- Swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing.

These are all very serious side effects. If your child has them, he/she may have had a serious allergic reaction to SINTRINE ORAL GRANULES and may need urgent medical attention.

**Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:**
- behaviour and mood related changes: agitation including aggressive behaviour or hostility, depression, hallucinations, disorientation, suicidal thoughts and actions
- seizure
- increased bleeding tendency
- tremor
- rapid or fast heart beating (palpitations)
- combination of symptoms such as flu-like illness, pins and needles or numbness of arms and legs, worsening of lung symptoms and/or rash (Churg-Strauss syndrome) (see section 2)
- low blood platelet count (that your doctor will see from a blood test)
- severe skin reactions (erythema multiforme) that may occur without warning
- inflammation of the liver (hepatitis)

These are all serious side effects. If your child has them, he/she may need urgent medical attention.

**Other side effects while the medicine has been on the market**
***Frequent:***
- upper respiratory infection
- diarrhoea, nausea, vomiting
- rash
- fever
- elevated liver enzymes (that your doctor will see from a blood test)

***Less frequent:***
- behaviour and mood related changes: dream abnormalities, including nightmares, trouble sleeping, sleepwalking, irritability, feeling anxious, restlessness, disturbance in attention, memory impairment, uncontrolled muscle movements, obsessive-compulsive symptoms, stuttering
- dizziness, drowsiness, pins and needles/numbness
- nosebleed
- dry mouth, indigestion
- bruising, itching, hives
- joint or muscle pain, muscle cramps
- bedwetting in children
- weakness/tiredness, feeling unwell, swelling
- tender red lumps under the skin, most commonly on your shins (erythema nodosum)

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

**Reporting of side effects**
If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of SINTRINE ORAL GRANULES. Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

## 5. How to store SINTRINE ORAL GRANULES

**STORE ALL MEDICINES OUT OF REACH OF CHILDREN.**
- Store at or below 25 °C.
- Store in the original package in order to protect from light and moisture.
- The sachets should not be opened until required for use.
- Do not use after the expiry date stated on the sachet / carton.
- Return all unused medicines to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

## 6. Contents of the pack and other information

**What SINTRINE ORAL GRANULES contains**
Each sachet of SINTRINE ORAL GRANULES contains 4,15 mg of montelukast sodium equivalent to 4,00 mg of montelukast.
SINTRINE ORAL GRANULES contains sweetener (mannitol 484,70 mg per sachet).
Excipients: Hydroxypropyl cellulose (klucel LF), mannitol (Pearlitol DC300) and magnesium stearate.

**What SINTRINE ORAL GRANULES looks like and contents of the pack**
Oral granules.
White to off white granules.
Pouch laminate sachet (PET/Aluminium foil/PE).
The sachets are packed in an outer cardboard carton.
Packs sizes of 7, 10, 14, 20, 28, 30 and 100 sachets.
Not all pack sizes may be marketed.

**Holder of Certificate of Registration**
Sandoz SA (Pty) Ltd[1]
Waterfall 5-Ir
Magwa Crescent West
Waterfall City
Jukskei View
2090
Marketed by sanofi aventis south africa (pty) ltd.

**This leaflet was last revised in**
Not applicable

**Registration number**
47/10.3/0743

[1]Company Reg. No.: 1990/001979/07

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**PASIËNTINLIGTINGSPAMFLET**

**SKEDULERINGSTATUS:** S3

# Sintrine® Oral Granules (mondelikse korrels)

**Aktiewe bestanddeel: natriummontelukast gelykstaande aan 4,00 mg montelukast.**
**SINTRINE ORAL GRANULES bevat mannitol.**

SANDOZ A Novartis Division

**Lees hierdie hele pamflet noukeurig deur voordat u SINTRINE ORAL GRANULES begin neem.**
- Hou hierdie pamflet. U sal dit dalk weer moet lees.
- Vra asseblief vir u dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer as u nog vrae het.
- SINTRINE ORAL GRANULES is vir u persoonlik voorgeskryf en u moet u medisyne nie met ander mense deel nie. Dit kan skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u s'n.

**Wat in hierdie pamflet is**


## 1. Wat SINTRINE ORAL GRANULES is en waarvoor dit gebruik word

SINTRINE ORAL GRANULES bevat die aktiewe stof montelukast en word in kinders (2 tot 5 jaar) gebruik vir die chroniese behandeling van atopiese (allergiese) asma en om asmasimptome te voorkom.

**Hoe dit werk:**
Montelukast, die aktiewe bestanddeel in SINTRINE ORAL GRANULES is 'n leukotrien-reseptorantagonis wat stowwe genaamd leukotriene blok.
Leukotriene veroorsaak vernouing en swelling van lugweë in die longe. Deur leukotriene te blok, verbeter SINTRINE ORAL GRANULES asmasimptome en help dit om asma te beheer.

## 2. Wat u moet weet voordat u SINTRINE ORAL GRANULES vir u kind gee

**Moenie SINTRINE ORAL GRANULES vir u kind gee nie:**
- As u kind hipersensitief (allergies) is vir montelukast of vir enige van die ander bestanddele van SINTRINE ORAL GRANULES (gelys in afdeling 6).
- As u kind jonger as 2 jaar oud is.

**Waarskuwings en voorsorgmaatreëls**
Praat met u dokter of apteker voordat u SINTRINE ORAL GRANULES vir u kind gee:
- As u kind se asma of asemhaling vererger, moet u dadelik vir u dokter sê.
- SINTRINE ORAL GRANULES is nie bedoel om akute asma-aanvalle te behandel nie. Sou 'n aanval plaasvind, moet u die instruksies volg wat u dokter u vir u kind gegee het. Hou altyd u kind se noodasmapomp of noodmedisyne vir asma-aanvalle byderhand.
- As u kind asma-aanvalle tydens oefening kry en u kind se dokter vir hom/haar 'n noodasmapompmedisyne voorgeskryf het om voor of tydens oefening te gebruik, moet u kind aanhou om daardie medisyne te gebruik.
- Dit is belangrik dat u kind alle asmamedikasies neem wat sy/haar dokter voorgeskryf het. SINTRINE ORAL GRANULES moet nie in plaas van ander asmamedikasies, wat u dokter vir u kind voorgeskryf het, gebruik word nie.
- As u kind op teen-asmamedisynes is, moet u weet dat as hy/sy 'n kombinasie van simptome, soos griepagtige siekte, naalde-en-spelde of gevoelloosheid in die arms of bene, verergering van longsimptome en/of 'n velsuitslag ontwikkel, u u dokter moet raadpleeg.
- U kind moet nie asetielsalisielsuur (aspirien) of anti-inflammatoriese medisyne (ook nie-steroïdale anti-inflammatoriese middels of NSAIM's genoem) neem as dit sy/haar asma vererger nie.
- As u kind simptome soos gedrags- of gemoedsveranderinge ontwikkel terwyl hy/sy SINTRINE ORAL GRANULES neem, moet u u kind se dokter raadpleeg.

**Ander medisyne en SINTRINE ORAL GRANULES**
Sê altyd vir u gesondheidsorgverskaffer as u kind enige ander medisyne neem. (Dit sluit alle komplementêre of tradisionele medisynes in.)

Sommige medisyne kan beïnvloed hoe SINTRINE ORAL GRANULES werk, of SINTRINE ORAL GRANULES kan beïnvloed hoe u kind se ander medisyne werk.
Sê vir u dokter as u kind die volgende medisyne neem voordat hy/sy begin om SINTRINE ORAL GRANULES te neem:
- fenobarbitaal (word gebruik vir die behandeling van epilepsie)
- fenitoïen (word gebruik vir die behandeling van epilepsie)
- rifampisien (word gebruik vir die behandeling van tuberkulose en sommige ander infeksies)
- gemfibrosiel (word gebruik vir die behandeling van hoë vetvlakke in die bloed).

**SINTRINE ORAL GRANULES met kos en drinkgoed**
U kan SINTRINE ORAL GRANULES met of sonder kos vir u kind gee. Sien afdeling 3 hieronder oor "Hoe om SINTRINE ORAL GRANULES te neem" vir meer inligting.

**Swangerskap en borsvoeding**
Hierdie onderafdeling is nie van toepassing op SINTRINE ORAL GRANULES nie, aangesien dit bedoel is vir gebruik in kinders wat 2 tot 5 jaar oud is.

**Bestuur en gebruik van masjiene**
Hierdie onderafdeling is nie van toepassing op die SINTRINE ORAL GRANULES 4 mg korrels nie, aangesien dit bedoel is vir gebruik in kinders wat 2 tot 5 jaar oud is, maar die inligting hieronder hou verband met die aktiewe bestanddeel, montelukast.
Na verwagting sal SINTRINE ORAL GRANULES nie u vermoë om 'n motor te bestuur of masjinerie te bedryf, beïnvloed nie. Individuele reaksie op medikasie kan egter verskil. Sekere newe-effekte (soos duiseligheid en lomerigheid) wat met SINTRINE ORAL GRANULES aangemeld is, kan sommige pasiënte se vermoë om te bestuur of masjinerie te bedryf, beïnvloed.

## 3. Hoe om SINTRINE ORAL GRANULES te neem

Moenie medisyne wat vir u kind voorgeskryf is met enigiemand anders deel nie.
Laat u kind SINTRINE ORAL GRANULES altyd neem presies soos u dokter of apteker vir u gesê het. Raadpleeg u kind se dokter of apteker as u nie seker is nie.
- U moet SINTRINE ORAL GRANULES elke aand onder toesig vir u kind gee.
- Hou aan om SINTRINE ORAL GRANULES vir u kind te gee, selfs al het hy/sy geen simptome nie.

**Vir kinders 2 tot 5 jaar oud:**
Die aanbevole dosis is een sakkie SINTRINE ORAL GRANULES wat elke aand per mond geneem moet word.
As u SINTRINE ORAL GRANULES vir u kind gee, moet u sorg dat u kind nie enige ander produkte neem wat dieselfde aktiewe bestanddeel, montelukast, bevat nie. Raadpleeg u dokter, apteker of ander gesondheidsorgverskaffer as u nie seker is nie.

**Hoe moet ek SINTRINE ORAL GRANULES vir my kind gee?**
Hierdie medisyne is vir mondelikse gebruik.
- Moenie die sakkie oopmaak totdat dit gebruik gaan word nie.
- SINTRINE ORAL GRANULES kan hetsy:
  - direk in die mond gegee word;
  - OF met 'n lepelvol koue of kamertemperatuur sagte kos (byvoorbeeld appelmoes, roomys, wortels en rys) gemeng word.
- Meng al die inhoud van die SINTRINE ORAL GRANULES in 'n lepelvol koue of kamertemperatuur sagte kos, en maak seker dat die hele dosis met die kos gemeng is. Sorg dat die kind die hele lepelvol korrel-/kosmengsel dadelik (binne 15 minute) kry. BELANGRIK: Moet nooit enige korrel-/kosmengsel vir gebruik op 'n latere stadium bêre nie.
- SINTRINE ORAL GRANULES is nie bedoel om in vloeistof opgelos te word nie. U kind kan egter vloeistowwe neem nadat hy/sy die SINTRINE ORAL GRANULES ingesluk het.
- SINTRINE ORAL GRANULES kan geneem word sonder om die tydsberekening van voedselinname in ag te neem.

U dokter sal vir u sê hoe lank u kind se behandeling met SINTRINE ORAL GRANULES sal duur.
As u die indruk kry dat die uitwerking van SINTRINE ORAL GRANULES te sterk of te swak is, moet u vir u dokter of apteker sê.

**As u kind meer SINTRINE ORAL GRANULES neem as wat hy/sy moes**
In die geval van oordosering, moet u u dokter, apteker of ander gesondheidsorgverskaffer raadpleeg. As beide nie beskikbaar is nie, moet u die naaste hospitaal of gifbeheersentrum kontak en u kind se boksie SINTRINE ORAL GRANULES saam met u neem.

Die simptome wat die gereeldste voorkom wat met oordosering in volwassenes en kinders aangemeld is, het abdominale pyn, slaperigheid, dors, hoofpyn, braking en hiperaktiwiteit ingesluit.

**As u vergeet om SINTRINE ORAL GRANULES vir u kind te gee**
Gee u kind se SINTRINE ORAL GRANULES altyd presies soos u dokter vir u gesê het. As u egter vergeet om SINTRINE ORAL GRANULES vir u kind te gee, moet u net die gewone hoeveelheid van een sakkie een keer per dag gee.
Moenie vir u kind 'n dubbeldosis gee om op te maak vir 'n vergete dosis nie.

**As u kind ophou om SINTRINE ORAL GRANULES te neem**
SINTRINE ORAL GRANULES kan u kind se asma slegs behandel as hy/sy dit aanhou neem. Dit is belangrik dat u kind aanhou om SINTRINE ORAL GRANULES te neem vir so lank as wat u dokter vir u gesê het. Dit sal help om u kind se asma te beheer.
Vra u kind se dokter of apteker as u enige verdere vrae oor die gebruik van hierdie medisyne het.

## 4. Moontlike newe-effekte

SINTRINE ORAL GRANULES kan newe-effekte hê.

Nie alle newe-effekte wat vir SINTRINE ORAL GRANULES aangemeld is, is in hierdie pamflet vervat nie. As u kind se algemene gesondheid agteruitgaan of as u kind enige ongunstige uitwerkings ervaar terwyl hy/sy SINTRINE ORAL GRANULES neem, moet u u verskaffer van gesondheidsorg asseblief om advies raadpleeg.

**As enige van die volgende goed gebeur, moet u kind ophou om SINTRINE ORAL GRANULES te neem en moet u dadelik vir u dokter sê of u naaste hospitaal se ongevalle-afdeling besoek:**
- Swelling van die hande, voete, enkels, gesig, lippe en mond of keel, wat dit moeilik kan maak om te sluk of asem te haal.

Hierdie is alles baie ernstige newe-effekte. As u kind dit ervaar, het hy/sy dalk 'n ernstige allergiese reaksie op SINTRINE ORAL GRANULES gehad en verg dalk dringende mediese aandag.

**Sê dadelik vir u dokter of besoek u naaste hospitaal se ongevalle-afdeling as u enige van die volgende opmerk:**
- gedrags- en gemoedsverwante veranderinge: agitasie, wat aggressiewe gedrag of vyandiggesindheid insluit, depressie, hallusinasies, disoriëntasie, selfmoordgedagtes en -aksies
- toevalle
- geneig om makliker te bloei
- bewing
- snelle of vinnige hartklop (palpitasies)
- 'n kombinasie van simptome, soos griepagtige siekte, naalde-en-spelde of gevoelloosheid van die arms en bene, verergering van longsimptome en/of veluitslag (Churg-Strauss-sindroom) (sien afdeling 2)
- lae bloedplaatjietelling (wat u dokter met 'n bloedtoets sal sien)
- erge velreaksies (erythema multiforme) wat sonder waarskuwing kan voorkom
- inflammasie van die lewer (hepatitis)

Hierdie is alles ernstige newe-effekte. As u kind dit het, verg hy/sy dalk dringende mediese aandag.

**Ander newe-effekte sedert die medisyne op die mark gekom het**
***Dikwels:***
- boonste lugweginfeksie
- diarree, naarheid, braking
- veluitslag
- koors
- verhoogde lewerensieme (wat u dokter met 'n bloedtoets sal sien)

***Minder dikwels:***
- gedrags- en gemoedsverwante veranderinge: abnormale drome, wat nagmerries insluit, sukkel om te slaap, loop in die slaap, prikkelbaarheid, voel angstig, rustelooosheid, aandag-afleibaarheid, swak geheue, onbeheerde spierbewegings, obssessief-kompulsiewe-simptome en 'n gehakkel
- duiseligheid, lomerigheid, naalde-en-spelde/gevoelloosheid
- neusbloeding
- droë mond, slegte spysvertering
- kneusing, gejeuk, galbulte
- gewrigs- of spierpyn, spierkrampe
- kinders wat bed natmaak
- swakheid/moegheid, voel onwel, swelling
- gevoelige rooi knoppe onder die vel, meestal op die maermerries (erythema nodosum)

As u enige newe-effekte opmerk wat nie in hierdie pamflet genoem word nie, moet u asseblief vir u dokter of apteker sê.

**Aanmelding van newe-effekte**
As u newe-effekte kry, moet u met u dokter of apteker praat. U kan newe-effekte ook by SAHPRA aanmeld aan die hand van die **"6.04 Adverse Drug Reaction Reporting Form"** wat aanlyn onder SAHPRA se publikasies verskyn: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van SINTRINE ORAL GRANULES te voorsien.
Vermoedelike nadelige reaksies kan ook direk by die Houer van die Sertifikaat van Registrasie (HCR) aangemeld word by Patientsafety.sacg@novartis.com.

## 5. Hoe om SINTRINE ORAL GRANULES te bewaar

**BEWAAR ALLE MEDISYNES BUITE DIE BEREIK VAN KINDERS.**
- Bewaar teen of onder 25 °C.
- Bewaar in die oorspronklike pakkie om teen lig en vog te beskerm.
- Die sakkies moet nie oopgemaak word totdat dit gebruik moet word nie.
- Moenie gebruik na die vervaldatum wat op die sakkie/boksie aangedui is nie.
- Neem alle ongebruikte medisyne terug na u apteker toe.
- Moenie ongebruikte medisyne in dreine of rioolstelsels (bv. toilette) weggooi nie.

## 6. Inhoud van die pakkie en ander inligting

**Wat SINTRINE ORAL GRANULES bevat**
Elke sakkie SINTRINE ORAL GRANULES (mondelikse korrels) bevat 4,15 mg natriummontelukast gelykstaande aan 4,00 mg montelukast.
SINTRINE ORAL GRANULES bevat versoeter (mannitol 484,70 mg per sakkie).
Eksipiënte: hidroksipropielsellulose (klucel LF) , mannitol (Pearlitol DC300) en magnesiumstearaat.

**Hoe SINTRINE ORAL GRANULES lyk en inhoud van die pakkie**
Mondelikse korrels.
Wit tot naaswit korrels.
Gelamineerde sakkie (PET/Aluminiumfoelie/PE).
Die sakkies is in 'n buitenste kartonhouer verpak.
Pakkiegroottes van 7, 10, 14, 20, 28, 30 en 100 sakkies.
Nie alle pakgroottes word noodwendig bemark nie.

**Houer van Sertifikaat van Registrasie**
Sandoz SA (Edms) Bpk[1]
Waterfall 5-Ir
Magwasingel Wes
Waterfall City
Jukskei View
2090
Bemark deur sanofi aventis suid-afrika (edms) bpk.

**Hierdie pamflet is laas hersien op**
Nie van toepassing nie

**Registrasienommer**
47/10.3/0743

[1]Maatskappyregistrasieno.: 1990/001979/07

V1.0 (24/01/2022)
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| B-612 Graphic Studio<br>ul. Wólczańska 143<br>90-525 Łódź, Poland<br>+48 42 633 612 7<br>email: biuro@b612.pl | Artwork creator:<br>Sara Szewczyk | Creation date:<br>09-May-2022 | Proof No.:<br>1 |
| Artwork Order No.:<br>300022056 | AW identifier No. New:<br>46300782-ZA | AW identifier No. Old:<br>0 | |

Artwork Order description:
**LEAFLET_SINTRINE_OGR_4MG_ZA**

Packaging site: CM, TR, KOCAELI, GENVEON (ESO SZ HUB)

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|---|---|
| Dimension: | **150 x 500 mm** |
| Tech. Drawing No.: | Montelukast_4_mg_OGR_NAFS |
| Production code: | 12487 |
| Live text: | ☒ Yes ☐ No ☐ Both |
| Condensed font: | ☐ Yes ☒ No ☐ Both |
| Font type: | FuturaEF, Myriad Pro |
| Minimum font size body text: | 5 pt |
| Variable data prefixes font size: | N/A |

Printing colours: ■ Black
Technical colours: ■ Cutting
Print enhancements: N/A

Braille: N/A

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