PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

SINTREDIUS

Oral solution

Active substance and quantity in unit dose:
prednisolone (as sodium phosphate) 1mg/ml

Inactive ingredients and allergens in the product: see section 2 "Important information about some of the ingredients of the medicine" and section 6 "additional information"

Read the entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine. If you have further questions, please refer to the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Sintredius is indicated for the treatment of:
- Rheumatological disorders and connective tissue diseases such as: rheumatoid arthritis (for primary chronic disease and maintenance therapy), systemic lupus erythematosus (non-organ threatening disease), mild-moderate juvenile dermatomyositis.
- Severe or debilitating allergic conditions, not treatable in a conventional manner such as: bronchial asthma in children, bronchial asthma in adults (for maintenance therapy).
- Sarcoidosis in children and for maintenance therapy in adults.
- Acquired haemolytic anaemia (autoimmune, for maintenance therapy).

Therapeutic group: glucocorticosteroids
Sintredius contains the active ingredient prednisolone, which belongs to a group of medicines called corticosteroids or "steroids". Steroids work by reducing inflammation and lowering the body's immune response.

Sintredius – benefit information
Corticosteroids occur naturally in the body and help to maintain health and well-being. Boosting your body with extra corticosteroids (such as prednisolone) is an effective way to treat various illnesses involving inflammation in the body. Prednisolone reduces this inflammation, which could otherwise go on making your condition worse.

2. BEFORE USING THE MEDICINE

Do not use Sintredius if:
- you are **sensitive (allergic)** to prednisolone or any of the other ingredients of this medicine (listed in section 6). Allergic reactions include mild symptoms such as itching and/or rash. More severe symptoms include swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing.
- you have recently had a live **vaccine** or have a live vaccine planned.
- you have a tropical worm infections.
- you have systemic infections, including fungal infections.
- You have tuberculosis, peptic ulcer, psychosis, herpes (shingles) of the eye.

Special warnings regarding use of the medicine

Before using Sintredius, inform the doctor, especially if you have, have ever had or if anyone in your family has suffered from:
- **severe depression**, manic-depressive illness (bipolar disorder), psychosis or other mental illness. This includes having had depression before or while taking steroid medicines like Sintredius;
- Tuberculosis (TB);
- diabetes;
- epilepsy;
- Visual disturbances including blurred vision - **talk to your doctor** if your vision is blurred, if you feel difficulty reading or any other change in vision that occurs during or after the treatment.
- an eye disease caused by a rise of pressure within the eye (glaucoma);
- thinning of the bones (osteoporosis);
- muscle problems when steroids were taken before;
- stomach ulcers;
- renal failure, high blood pressure, heart failure or recently suffered a heart attack;
- scleroderma (also known as systemic sclerosis, an autoimmune disorder) because daily doses of 15 mg or more may increase the risk of a serious complication called scleroderma renal crisis. Signs of scleroderma renal crisis include increased blood pressure and decreased urine production. The doctor may advise that you have your blood pressure and urine regularly checked;
- any liver problem; your doctor may refer you to additional testing while you are taking this medicine.
- an under-active thyroid (hypothyroidism).
- Kaposi's sarcoma

If any of the above applies to you, or if you are not sure, talk to your doctor or pharmacist before you use this medicine.

Mental health problems while taking prednisolone
Mental health problems can occur while taking steroids like prednisolone (see also section 4, 'side effects').
- These illnesses can be severe.
- Usually they start within a few days or weeks of starting the medicine.
- They are more likely to happen at high doses.
- Most of these problems go away if the dose is lowered or the medicine is stopped. However, if problems do occur, they might need treatment.

Talk to a doctor if you (or someone taking this medicine) show any signs of mental health problems. This is particularly important if you are depressed or might be thinking about suicide. In a few cases, mental health problems have also happened when the doses have been lowered or the medicine stopped altogether.

Chickenpox, shingles or measles: tell your doctor if you have previously had chickenpox, shingles or measles or if you have been vaccinated in the past against these infections. While taking the medicine, avoid being in the vicinity of anybody who has chickenpox, shingles or measles, especially if you have not had these diseases in the past. If you have been in contact with a person who has these diseases in the last 3 months, or if you have chickenpox, shingles or measles, **see a doctor immediately.** Your doctor will advise you on the required treatment. Your doctor may change the dose of your medicine.

Vaccination: if you have recently been vaccinated or are planning to get a vaccine, tell your doctor before taking this medicine, since live vaccine should not be given to people with weakened immune systems caused by high doses of corticosteroids. The immune response to other vaccines may be reduced.

Discontinuation of the treatment: consult a doctor before stopping treatment with the medicine. Do not stop treatment abruptly. Your doctor will instruct you on how to reduce the dose gradually over several weeks or months.

Your doctor will prescribe you the lowest effective dose for your condition, for the shortest amount of time, to prevent side effects.

Children and Adolescents
Corticosteroids cause a dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible.

Elderly
If you are elderly, your doctor will monitor your condition carefully while taking the medicine as the elderly may experience more side effects.

Tests and follow-up:
During the treatment period you may be referred by your doctor to perform blood and urine tests and blood pressure. Regular checkups with doctors (including vision checkups in three month-intervals) are advised during long term treatment.

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist.
This is especially important if you are taking:
- Medicines for **epilepsy** such as carbamazepine, phenobarbitone, phenytoin or primidone;
- **Antibiotics** such as rifampicin, rifabutin, erythromycin, fluoroquinolones;
- **Mifepristone** (used to terminate pregnancy);
- **Ritonavir** (used in HIV treatment);
- **Oral contraceptives, estrogen;**
- **Somatropin** (used to treat growth problems);
- Medicines for **diabetes** such as insulin, glibenclamide or metformin;
- Medicines used to treat **high blood pressure**, such as diuretics (water tablets) like bendroflumethiazide and furosemide;
- **Warfarin** or other blood thinner;
- **Aspirin** or similar medicines (NSAIDs – non steroidal anti-inflammatory drugs);
- **Theophylline** (used to treat asthma);
- Medicines to treat **fungal infections** such as amphotericin, ketoconazole;
- **Acetazolamide** (used to treat glaucoma);
- **Carbenoxolone** (used to treat stomach ulcers);
- **Methotrexate** (used for rheumatoid arthritis, psoriasis and certain types of cancer);
- Any medicine which belongs to a group of medicines called **sympathomimetics**;
- Formoterol, salbutamol, salmeterol, terbutaline, bambuterol, fenoterol and similar medicines (**bronchodilators**) at high doses;
- Medicines used to treat **myasthenia gravis**;
- Medicines used to make **x-rays clearer**;
- **Ciclosporin** (used to stop the body rejecting bone marrow or organ transplants)
- Ritodrine

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
Some medicines may increase the effects of Sintredius and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat).

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
Pregnancy
During pregnancy treatment should only be initiated after a careful benefit/risk assessment has been performed and at the lowest effective dose. Because growth retardation and damage to the unborn child cannot be excluded upon prolonged treatment with glucocorticoids during pregnancy, please inform your doctor if you want to become pregnant, are already pregnant or if you are assuming that you are pregnant.
Breastfeeding
Glucocorticoids, such as Sintredius pass into breast milk. Damage to the infant is not reported to date. Nevertheless, when high doses of prednisolone are given, you should avoid breastfeeding for 4 hours after a dose. Please consult your doctor if you are breastfeeding or planning to breastfeed.
Fertility
After high prednisolone doses (30 mg/day for at least 4 weeks) reversible disturbances of spermatogenesis has been observed, which lasted for several months after stop taking the medicine.

Driving and using machines
There is no known effect on the ability to drive and use machines.

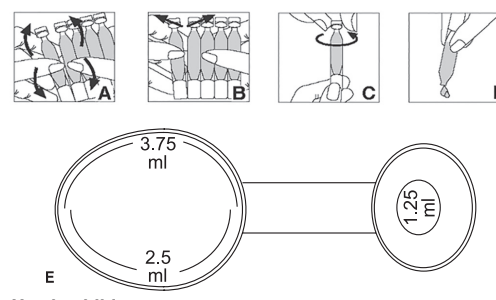
Important information about some of the ingredients of the medicine:
Sintredius contains sucrose and glycerol
This medicine contains 1.5 grams of sucrose per container. This should be taken into account in patients with diabetes mellitus. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
This medicine contains 0.25 grams of glycerol in each container.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the product according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen of the product.
The dosage and treatment regimen will be determined by the doctor only.

Do not exceed the recommended dose.
- It is best to take the oral solution undiluted.
- The solution should be taken by mouth.
- The solution should preferably be taken as a single dose in the morning. However, divided daily dosage may be employed if required.
- In children, the medicine should preferably be taken as a single dose on alternate days.
- Shake well before use.
- If you are on long-term therapy, make sure your supply of the medicine is regular and does not run out.
- Since opening many containers on the same day could lead to dosing errors, this 5 ml presentation is suitable for treatments not exceeding 30 mg daily. The dosage depends on the condition being treated and, for an adult, can vary widely between 10 mg and 30 mg daily in divided doses. Your doctor will give you the smallest dose that works for your condition.
- When you need to take more than two containers all at once, each opened container should be placed on a tray or suitable surface after opening and dispensing the content. This can help you avoiding dosing errors due to loss of count.
- The package contains a measuring spoon dosing 3.75 ml, 2.5 ml and 1.25 ml corresponding to partial doses.
- All opened single-dose containers should be discarded once the required dose is removed.

Instructions for use
1. Flex the single-dose container in the two directions (see figure A).
2. Separate the single-dose container from the strip (see figure B).
3. Turn the cap counter clockwise as indicated in figure C.
4. Apply mild pressure on the container to dispense the medicine as prescribed (see figure D). For the dose of 5 ml, drink the full amount of the single-dose container. In case a partial dose has to be dispensed, the measuring spoon included in the package should be used to dispense 1.25 ml, or 2.5 ml, or 3.75 ml (see figure E).
5. After administering a partial dose, the opened single-dose container must be discarded.



Use in children
To treat acute asthma attacks, your child's doctor may prescribe:
- For children **younger than 2 years old**, up to 10 mg daily, for up to three days;
- For children **2 to 5 years old**, up to 20 mg daily. Treatment for up to three days is usually sufficient, but the length of the course will be decided by your doctor, according to the number of days necessary to recover.
- For children **older than 5 years old**, 30 mg daily or more (up to 40 mg daily). Since opening many containers on the same day could lead to dosing errors, in case more than 30 mg daily have been prescribed, ask your child's doctor, as a different prednisolone presentation (e.g. high dosage tablets) might be more appropriate.

If you accidentally took a higher dose, contact your doctor or nearest hospital emergency room **immediately**. **If you took an overdose or if a child accidentally swallowed the medicine,** contact your doctor or nearest hospital emergency room immediately and bring the package with you.

If you forget to take the medicine, take the next dose as soon as you remember, unless it is almost time for your next dose. **Do not** take a double dose to make up for a forgotten dose.

If you stop taking the medicine talk to your doctor. Your doctor may want to reduce your dose gradually.

Do not stop taking the medicine unless you have been told to do so by your doctor, even if you feel better, as it can make you ill. If you stop taking the medicine suddenly, this can cause withdrawal symptoms such as fever, sickness, pain in the muscles and joints, runny nose, sore, red and sticky eyes (conjunctivitis), itchy skin, weight loss, headache, vomiting, decrease in blood pressure.

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. SIDE-EFFECTS

Like all medicines, this medicine can cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.
Steroids including prednisolone can cause **severe mental health problems,** such as those listed below. These are common in both adults and children. **If you notice any of these problems talk to a doctor immediately:**
- Feeling depressed, including thinking about suicide.
- Feeling high (mania) or having moods that go up and down.
- Feeling anxious, having problems sleeping, having difficulty in thinking or being confused and losing your memory.
- Feeling, seeing or hearing things which do not exist (hallucinations). Having strange and frightening thoughts, changing how you act or having feelings of being alone.

The following side effects may be signs of an allergic reaction. If you notice any of the below, stop taking Sintredius and tell your doctor immediately:
- itching or skin rashes;
- swelling of the face, lips or throat;
- difficulty in breathing or wheeziness;

Some side effects such as mood swings (feeling depressed or happy mood) or stomach problems may occur immediately. If you feel bad in any way, you should continue to take your medicine, **but you should see your doctor immediately.**
Some side effects only occur after weeks or months. These include weakness of the hands and feet or development of a more rounded face.

The following side effects can occur if steroids are given in high doses for a long time:
- generally feeling unwell;
- feeling sick (nausea), vomiting;
- hiccups;
- indigestion or stomach discomfort, dyspepsia, diarrhoea;
- stomach ulcer (which can rupture and bleed) or ulcer in the oesophagus (gullet);
- thrush;
- inflammation of the pancreas causing abdominal pain (pancreatitis) ;
- muscle weakness;
- muscle pain;
- thinning of bones which makes fractures more likely (osteoporosis), osteonecrosis;
- damage to tendons;
- joint stiffness causing limited movement, pain and muscle spasms;
- fluid retention causing swelling;
- feeling dehydrated;
- high blood pressure (hypertension);
- slow healing of wounds, thinning of the skin, bruising, acne, marks which look like stretch marks, excessive sweating, rush, urticaria;
- small red, purple or blue spots found along the surface of the skin (caused by blood vessels under the skin);
- low adrenal gland function;
- irregular or stopped menstrual periods;
- swollen round face (*Cushingoid facies* or moon-face);
- increased hairiness in women;
- increased appetite and weight gain;
- intolerance to carbohydrates, diabetes worsening;
- mood changes, dependence, depression, difficulty sleeping, irritability, anxiety, worsening of schizophrenia;
- worsening of epilepsy;
- raised pressure in the eyes (glaucoma), cataracts, thinning and inflammation of the cornea (part of the eye), worsening of viral or fungal eye diseases, blurred vision and visual impairment, choroid and retinal disorders (chorioretinopathy), bulging eye, papilloedema;
- heart attack (sudden severe chest pains);
- changes in body chemistry, sodium retention, decrease in potassium levels in the body, imbalance of salts, protein total abnormal;
- increase in the number of white blood cells;
- formation of blood clots;
- porphyria
- Steven-Johnson syndrome
- long-term use of high dose steroids, may lead to a weakening of the immune system, which can increase the risk of your condition getting worse (malignancy).
- dizziness, vertigo;
- headache
- not known: slow heart rate
- Scleroderma renal crisis in patients already suffering from scleroderma (an autoimmune disorder). Signs of scleroderma renal crisis include increased blood pressure and decreased urine production.
- Kaposi's sarcoma (a type of cancer) has also been reported to occur in patients receiving corticosteroids. However, once the treatment has been stopped, this may go away.
- This medicine can make it easier for you to pick up infections which may very rarely be fatal. Infections such as chickenpox and measles can be made worse or TB (tuberculosis) may recur.

Additional side effects in children and adolescents:
- Slowing growth in infants, children and adolescents;
- Increase in intracranial pressure after cessation of treatment, which is manifests as severe headaches with blurred vision or temporary vision problems in children.

If one of the side-effects appear or worsen, or if you suffer from side-effects that were not mentioned in the leaflet, consult your doctor or pharmacist.

Reporting of side effects
Side effects can be reported to the Ministry of Health through link "reporting side effects due to drug treatment" located in the home page of the Ministry of Health website (www.health.gov.il) which refers to online form, or by entering the following link: https://sideeffects.health.gov.il
Additionally, you may also report to Kamada LTD by email: pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
Do not use after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
Store the medicine in a safe place below 30°C. Store in the original package.
Container for single use only. Once opened you must discard any unused solution. In case of administration of partial doses, the opened container must be discarded once the required dose is removed.
Once opening the bag containing 5 single-dose containers, it should be used within 14 days.
The medicine should not be disposed via wastewater or household waste. Ask the pharmacist how to dispose medicines no longer in use. These measures will help to protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, this medicine also contains: Sucrose, Glycerol, Disodium phosphate anhydrous, Honey flavour, vanilla/cream flavour, masking flavour, sodium dihydrogen phosphate monohydrate, Disodium edetate (EDTA), Water for injections.

What Sintredius Oral Solution looks like and contents of the pack
Sintredius is a clear, light brown, particles-free solution.
It is available in single-dose polyethylene containers. One single-dose container has 5 ml of oral solution. The single-dose containers are grouped in strips of five. Each strip is packaged in a plastic-aluminum (PET/Al/PE) over-pouch. Each carton package contains two over-pouches (10 single-dose containers) and a measuring spoon (dosing 3.75 ml, 2.5 ml and 1.25 ml, corresponding to partial doses).
The package includes 10 single-dose containers.

Marketing Authorization Holder: Kamada Ltd., Beit Kama.
Manufacturer: GENETIC S.p,A .,Salerno ,Italy
For Dompé farmaceutici S.p.A., Milano, Italy

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Registration number of the medicine in the National Drug Registry of the Ministry of Health: 168-82-35801