

SANDIMMUN NEORAL[®] ORAL SOLUTION

Ciclosporin (100 mg/mL)

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What Sandimmun Neoral is used for

The name of your medicine is Sandimmun Neoral and it contains the active substance ciclosporin. It is one of a group of medicines known as immunosuppressive agents. These medicines are used to diminish the body's immune reactions.

How Sandimmun Neoral works

If you have received a graft transplant the function of Sandimmun Neoral is to control your body's immune system. Sandimmun Neoral prevents rejection of transplanted organs by blocking the development of special cells which would normally attack the transplanted tissue.

If you suffer from a non-transplant disease where your body's own immune response attacks the cells in your body (autoimmune diseases), Sandimmun Neoral suppresses immunoreactions in those diseases. Such autoimmune diseases are vision-threatening eye disease (intermediary or posterior uveitis and Behçet's uveitis), severe cases of certain skin diseases (psoriasis), severe rheumatoid arthritis and a kidney disease, called nephrotic syndrome.

Before you use Sandimmun Neoral

If you are receiving Sandimmun Neoral for transplantation, it will only be prescribed for you by a doctor with experience in transplantation medicine.

You will notice that the advice contained in this leaflet may vary depending on whether you are receiving this medicine for transplantation or taking it for your autoimmune disease.

Follow all the doctor's instructions carefully. They may differ from the general information contained in this leaflet.

When you must not use it

If you are allergic (hypersensitive) to ciclosporin or any of the other ingredients of Sandimmun Neoral listed at the end of this leaflet.

If this apply to you, tell your doctor without taking Sandimmun Neoral.

If you think you may be allergic, ask your doctor for advice.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Tell your doctor if you are pregnant or intend to become pregnant. Experience with Sandimmun Neoral in pregnancy is limited. In general, Sandimmun Neoral should not be taken during pregnancy. If it is necessary for you to take this medicine, your doctor will discuss with you the benefits and potential risks of taking it during pregnancy. Tell your doctor if you are breast-feeding. Breast-feeding is not recommended during the treatment with Sandimmun Neoral since ciclosporin, the active ingredient in Sandimmun Neoral, passes into breast milk and may affect your baby.

Before you start to use it

Due to the alcohol (ethanol) contained in Sandimmun Neoral (see also Important information about one of the ingredients):

- If you have or had alcohol related problems
- If you have epilepsy or have any liver problems
- If you are pregnant
- If you breast-feed your child
- If the drug is given to a child

If any of these applies to you, tell your doctor before taking Sandimmun Neoral

- Sandimmun Neoral suppresses the immune system, causing an increased risk of developing cancers, particularly of the skin and lymphoid system. Therefore you should limit your exposure to sunlight and UV light by wearing appropriate protective clothing and frequently applying a sunscreen with a high protection factor.
- Sandimmun Neoral by suppressing the immune system also may influence your body's ability to fight against infection. If you experience any symptoms of infection (e.g fever, sore throat). In such cases you should inform your doctor immediately.
- If you experience liver problems

- If you have kidney problems. Your doctor will carry out regular blood tests and may adjust your dose if necessary
 - If high blood pressure develops. Your doctor will check your blood pressure regularly and may give you blood pressure reducing agent if necessary.
 - Sandimmun Neoral may reduce the amount of magnesium in your body. Your doctor may, therefore, give you magnesium supplements to take, especially just after your operation if you have had a transplant.
 - If you have high levels of potassium in your blood
 - If you suffer from gout,
 - If you need to receive a vaccine. Seek your doctor's advice first
 - Of any other medicines you receive (see also "Taking other medicines").
- If you get any of these symptoms, tell your doctor straight away

If you receive Sandimmun Neoral for a non-transplant disease (intermediary or posterior uveitis and Behçet's uveitis, severe rheumatoid arthritis and nephrotic syndrome), you should not take Sandimmun Neoral in case of

- kidney problems (except for nephrotic syndrome)
- uncontrolled infections
- any type of cancer
- uncontrolled high blood pressure (hypertension). If hypertension develops during therapy and cannot be controlled, Sandimmun Neoral should be stopped.

Sandimmun Neoral should not be given to children for a non-transplant disease except for the treatment of nephrotic syndrome. When given for Behçet's uveitis, Sandimmun Neoral should be used with caution in patients having neurological symptoms of the disease.

Your doctor will closely supervise your therapy with Sandimmun Neoral if you are treated for psoriasis or you are an elderly. If you are treated with Sandimmun Neoral due to psoriasis, you should not concurrently receive UVB-rays or phototherapy.

Taking Sandimmun Neoral with food and drink

Do not take Sandimmun Neoral with grapefruit or grapefruit juice since this can influence Sandimmun Neoral's effects.

Older people

There is limited experience with the administration of Sandimmun Neoral in elderly. Your renal function should be monitored with particular care. If you are over the age of 65 years with psoriasis, you should only be treated in case of disabling disease.

Children and adolescents

Except for the treatment of nephrotic syndrome, the experience with Sandimmun Neoral in children is still limited.

Important information about one of the ingredients of Sandimmun Neoral

For Sandimmun Neoral oral solution: This medicinal product contains ethanol (alcohol).

Alcohol may be harmful for those suffering from alcoholism, epilepsy, brain injury or liver disease as well as for pregnant or breast-feeding women and children.

Taking other medicines

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines. Remember also those not prescribed by a doctor.

Ask your doctor for advice if you need concurrent treatment:

- with medicines that may impact your potassium levels such as medicines containing potassium or potassium supplements, diuretics or water tablets called “potassium sparing diuretics”, certain blood pressure reducing agents
- with methotrexate, a medicine to treat tumors, severe psoriasis and severe rheumatoid arthritis
- with medicines which may increase or reduce the blood levels of Sandimmun Neoral. The doctor might check the ciclosporin concentration in your blood when initiating or discontinuing other medical treatment.
- Medicines which may decrease the Sandimmun Neoral concentrations: barbiturates (medicines used to help to sleep) certain anticonvulsives (e.g. carbamazepine, phenytoine), octreotide (known as Sandostatin[®]), antibacterial medicines used to treat tuberculosis, orlistat (used to help weight loss), herbal medicines containing St. John’s Wort, ticlopidine (used after stroke), certain blood pressure reducing agents (bosentan), and an antifungal medicine used to treat infections of the toes and nails (terbinafine).
- Medicines which may increase the Sandimmun Neoral concentrations:

antibiotics (e.g. erythromycin, azithromycin), antifungals (voriconazole, itraconazole), medicines used for heart problems or high blood pressure (diltiazem, nicardipine, verapamil, amiodarone), metoclopramide (used to stop sickness), oral contraceptives, danazol (used to treat menstrual disorders), medicines used to treat gout (allopurinol), cholic acid and derivatives (used to treat gallstones), protease inhibitors used to treat HIV, imatinib (used to treat leukaemia or tumors), colchicine

- with other medicines which may affect the kidneys, such as antibacterial agents (gentamycin, tobramycin, ciprofloxacin), antifungal agents containing amphotericin B, agents against urinary tract infection containing trimetoprim, anti-cancer agents containing melphalan, medicines used to reduce the amount of acid in your stomach (acid secretion inhibitors of the H₂-receptor antagonist type), tacrolimus, pain killers (non-steroid anti-inflammatory drugs such as diclofenac), fibric acid derivatives (used to lower fat in the blood).
- with nifedipine (used to treat high blood pressure and heart pain), you might get swollen gums.
- with digoxin (used to treat heart problems), cholesterol lowering agents (HMG-CoA reductase inhibitors also called statins), prednisolone, etoposide (used to treat cancer), repaglinide (oral antidiabetic agent), immunosuppressives (everolimus, sirolimus), ambrisentan and specific anticancer drugs called anthracyclines (e.g. doxorubicin)

How to use Sandimmun Neoral

Follow your doctor’s instructions carefully. Do not exceed the recommended dosage.

How much to use

- Your doctor will work out the correct dose of Sandimmun Neoral for you depending on your body weight and whether you are taking Sandimmun Neoral following a transplant or as a treatment for severe psoriasis, rheumatoid arthritis, nephrotic syndrome or uveitis. Your doctor will also tell you how often to take your medicine.
- Generally, the higher doses are used before and just after transplantation and the lower doses are used once your

transplanted organ or bone marrow has stabilised. Your doctor will adjust your dose to one that is ideal for you. To do this he may need to do some blood tests.

- For the treatment of endogenous uveitis, the total daily dose is usually 5 - 7 mg/kg body weight per day initially. For maintenance treatment, the daily dose should not exceed 5 mg/kg per day.
- For the treatment of nephrotic syndrome, the total daily dose is depending on your kidney function and age. Your doctor will decide a suitable dose for you.
- For the treatment of severe rheumatoid arthritis, the total daily dose is usually within the range of 3-5 mg/kg body weight per day divided in two doses
- For the treatment of severe psoriasis, the total dose is usually within the range of 2.5-5.0 mg/kg body weight per day divided in two doses.
- Follow your doctor's instructions exactly and never change the dose yourself, however well you feel.

If you were previously taking Sandimmun (ciclosporin) Soft Gelatin Capsules or Oral Solution:

Sandimmun Neoral and Sandimmun both contain ciclosporin as the active ingredient. However, Sandimmun Neoral is an improved formulation of ciclosporin and is, therefore, different to Sandimmun. Because of this difference, the absorption of ciclosporin into your blood should be much more reliable with Sandimmun Neoral.

Absorption of ciclosporin with Sandimmun Neoral is much less likely to be affected by taking it with food, again resulting in more consistent levels of ciclosporin in your blood. This is thought to be of particular importance in the prevention of rejection following transplantation, especially in the longer term.

Because of the difference in absorption of ciclosporin, your doctor will probably want to monitor you more closely for a short period following transfer from Sandimmun to Sandimmun Neoral, to make sure that you get the ideal dose for you. If your doctor transfers you from Sandimmun to Sandimmun Neoral, you should **not** go back to taking Sandimmun unless your doctor tells you to.

When you change from Sandimmun to Sandimmun Neoral, you may have some side-effects. If this happens, please tell your doctor or pharmacist as it may mean that your dose needs to be reduced. NEVER

reduce the dose yourself, unless a doctor has told you to.

If you were previously taking a different oral formulation of ciclosporin:

Your doctor will monitor you more closely for a short period following transfer from one oral formulation to another one.

When you change from one oral formulation of ciclosporin to another one, you may experience some side-effects. If this happens, please tell your doctor or pharmacist as it may mean that your dose needs to be adjusted. NEVER adjust the dose yourself, unless a doctor has told you to.

When and how to take Sandimmun Neoral

It is important to take your doses of Sandimmun Neoral at the same time every day, particularly if you are a transplant patient. Your daily doses should always be given in 2 divided doses.

Sandimmun Neoral oral solution should be diluted with, preferably orange or apple juice; however, other drinks such as soft drinks can be used according to individual taste. Immediately before taking the oral solution, it should be stirred well.

Initial use of Sandimmun Neoral oral solution

1. Raise flap in center of the metal sealing ring.



2. Tear off the sealing ring completely.



3. Remove the black stopper and throw it away.



4. Push the tube unit with the white stopper firmly into the neck of the bottle.



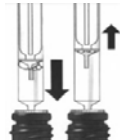
5. Choose the syringe depending on the prescribed volume. For volume less than 1 mL or equal to 1 mL, use the 1-mL syringe. For volume greater than 1 mL, use the 4-mL syringe. Insert the nozzle of the syringe into the white stopper.



6. Draw up prescribed volume of solution (position the lower part of the plunger ring in front of the graduation corresponding to the prescribed volume).



7. Expel any large bubbles by depressing and withdrawing plunger a few times before removing syringe containing prescribed dose from bottle. The presence of a few tiny bubbles is of no importance and will not affect the dose in any way.



8. Push the medicine out of the syringe into a small glass with some liquid. Avoid any contact between the syringe and the liquid in the glass. The medicine can be mixed just before you take it. Stir and drink the entire mixture right away. Please take the medicine immediately after preparation.



9. After use, wipe syringe on outside only with a dry tissue and replace in its cover. White stopper and tube should remain in bottle. Close bottle with cap provided.



Subsequent use

Commence at point 5.

If you have any questions about this medicinal product, please contact your doctor or pharmacist.

How long to use Sandimmun Neoral

Your doctor will tell you how long you will need to take Sandimmun Neoral for, depending on whether you are taking it following transplantation or for the treatment of a severe skin condition, rheumatoid arthritis, uveitis or nephrotic syndrome.

Continue taking Sandimmun Neoral as your doctor tells you.

If you have questions about how long to take Sandimmun Neoral, talk to your doctor or your pharmacist.

If you forget to use Sandimmun Neoral

If you forget to take a dose, take another one as soon as you remember, unless it is almost time for your next dose. Then go on as before. Do not take a double dose to replace the missed one.

If you use too much (overdose)

If you accidentally take too much of your medicine, tell your doctor immediately, or go to your nearest hospital emergency unit. You may require medical attention.

While you are using Sandimmun Neoral

Things you must do

Monitoring during your treatment with Sandimmun Neoral

Your doctor will check

- the levels of ciclosporin in your blood, especially for transplant patients,
- your blood pressure regularly before initiation of therapy and during treatment,
- your liver and kidney function,
- your blood lipids/fat.

If you have any questions about how Sandimmun Neoral works or why this medicine has been prescribed for you, ask your doctor.

Things you must not do

Stopping your treatment with Sandimmun Neoral may increase the risk of rejection of your transplanted organ. Do not stop taking Sandimmun Neoral even if you feel well, unless your doctor tells you to.

Things to be careful of

Driving and using machines

This medicine may affect your ability to drive or use machines. If the tablets make you feel sick, dizzy or tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

Side effects

Like all medicines Sandimmun Neoral can cause side-effects, although not everybody gets them.

The dose of this medicine needs to be carefully adjusted by your doctor. Too much can affect the kidneys. You will, therefore, have regular blood tests and visits to the hospital, particularly after transplantation. This will give you the chance to talk to your doctor about your treatment and mention any problems you are having.

Some side effects could be serious

- Like other drugs that diminish the immune system, ciclosporin may influence your body's ability to fight against infection and may cause tumours or other cancers, particularly of the skin. If you experience vision changes, loss of coordination, clumsiness, memory loss, difficulty speaking or understanding what others say, and muscle weakness, these can be the signs and symptoms of an infection of the brain called progressive multifocal leukoencephalopathy.
- Brain disorders with signs such as seizures, confusion, disorientation, decreased responsiveness, personality changes, agitation, sleeplessness, sight disturbances, blindness, coma, paralysis of part or all of the body, stiff neck, loss of co-ordination with or without abnormal speech or eyes movements.
- Swelling at the back of the eye which may be associated with blurred vision and possible visual impairment due to an increase in pressure inside the head (benign intracranial hypertension).
- Liver problems and damage with or without yellow skin and eyes, nausea, loss of appetite and dark urine.
- Kidney disorder with or without severely decreased urine output.
- Low level of red blood cells or platelets which may be associated with pale, skin, tiredness, breathlessness, dark urine (sign of breakdown of red blood cells), bruising or bleed with no obvious reasons, confusion, disorientation and decreased alertness.

If you experience any of these, tell your doctor straight away.

Some side effects are very common

Very common side-effects - may affect more than 1 in 10 patients - are: loss of appetite, high level of sugar in the blood, involuntary shaking of the body, headache, high blood pressure, nausea, vomiting,

abdominal pain, diarrhea, overgrowth of the gums, excessive body and facial hair growth and kidney disorders.

Some side effects are common

Common side-effects - may affect between 1 and 10 in every 100 patients - are: low level of white blood cells, seizures, numbness or tingling, hot flushes, stomach ulcer, liver disorder, acne, rash, fever and general swelling .

Some side effects are rare. Rare side-effect

- may affect between 1 and 10 in every 10,000 patients - is: abnormal menstrual cycle

If any of these affects you severely, tell your doctor.

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

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website portal.bpfk.gov.my (Consumers →Reporting).

Storage and disposal of Sandimmun Neoral

- Storage

The oral solution should be stored at room temperature between 15°C and 30°C and not in the refrigerator, or below 20C as it contains oily components which tend to solidify at low temperatures.

Below 20°C (e.g., in the refrigerator) the oral solution may become gelatinous but this effect will disappear if the solution is put again at room temperature. Small flakes or small amounts of sediment may however still be observed. If the oral solution by mistake is placed in the refrigerator, it should reach room temperature before it can be used again. Flakes or sediment are of no importance to the medicine's effect or safety, and measuring with the dosing pipette will still be accurate.

The content of the bottle is stable for 2 months after opening.

Store your medicine in a safe place where children cannot reach it. Your medicine could harm them.

- Disposal

Do not use this medicine after the expiry date shown on the package.

Any unused product or waste material should be disposed of in accordance with local requirements.

Product Description

What it looks like

Sandimmun 100 mg per mL oral solution

Your medicine is called Sandimmun Neoral and comes in the form of an oral solution. One mL oral solution contains 100 mg of the active substance ciclosporin. Sandimmun Neoral oral solution is a clear, faintly yellow-brownish liquid in a 50 mL glass bottle, with two syringes for measuring the dose. The 1-mL syringe is used to measure doses less than or equal to 1 mL (each graduation of 0.05 mL corresponds to 5 mg of ciclosporin). The 4-mL syringe is used to measure doses greater than 1 mL and up to 4 mL (each graduation of 0.1 mL corresponds to 10 mg of ciclosporin).

Ingredients

Sandimmun 100 mg per mL oral solution

- The active substance is ciclosporin.
- The other ingredients of the oral solution are: DL-alpha-tocopherol, ethanol anhydrous, propylene glycol, corn oil-mono-di-triglyceride, macrogolglycerol hydroxystearate (Ph.Eur./polyoxyl 40 hydrogenated castor oil (USP)

MAL Number

Sandimmun Neoral Oral Solution
100mg/mL: MAL19962143ACRZ

Manufacturer

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Product Registration Holder

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Date of revision

(Information issued on 09/02/2012)
15/10/2015

Serial Number

BPFK(R4/1)131015/00360