

SANDIMMUN NEORAL[®]

Ciclosporin (25 mg, 100 mg Soft Gelatin Capsule & 100mg/mL Oral Solution)

What is in this leaflet

1. What Sandimmun Neoral is used for
2. How Sandimmun Neoral works
3. Before you use Sandimmun Neoral
4. How to use Sandimmun Neoral
5. While you are using Sandimmun Neoral
6. Side effects
7. Storage and Disposal of Sandimmun Neoral
8. Product Description
9. Manufacturer and Product Registration Holder
10. Date of Revision

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 applies 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 section 'Important information about one of the ingredients of Sandimmun Neoral'):

- 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 medicine 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), 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 section "Taking other medicines").

If any of the above apply, 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 elderly and being treated for psoriasis. If you are treated with Sandimmun Neoral due to your 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. Children from 1 year of age have received Sandimmun Neoral in standard dosage with no particular problems. In several studies, children required and tolerated higher doses of Sandimmun Neoral per kg body weight than those used in adult.

Important information about one of the ingredients of Sandimmun Neoral

For Sandimmun Neoral soft gelatin capsules: This medicinal product contains ethanol (alcohol), i.e., up to 500 mg per dose in the transplantation indications equivalent to 12.6 mL beer, 5 mL wine per dose.

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. It may be necessary to change the dose, to take other precautions, or in some cases to stop taking one of the medicines.

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 (gentamycine, tobramycine, 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 medicines 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 that spread over your teeth.
- with drugs whose concentrations may increase when used together with Sandimmun Neoral including aliskiren (to treat high blood pressure), digoxin (used to treat heart problems), cholesterol lowering agents (HMG-CoA reductase inhibitors also called statins), prednisolone, etoposide (used to treat cancer), bosentan (used to reduce blood pressure), dabigatran (oral anticoagulant used to prevent stroke), repaglinide (oral antidiabetic agent), immunosuppressives (everolimus, sirolimus), ambrisentan and specific anticancer medicines called anthracyclines (e.g. doxorubicine)

- with drugs whose concentrations may decrease when used together with Sandimmun Neoral including mycophenolate sodium or mofetil (an immunosuppressant) and eltrombopag (used to treat bleeding disorders).

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.
- If you have had an **organ or bone marrow transplant** the total dose is usually within the range of 2 mg/kg body weight per day and 15 mg/kg body weight per day divided in two doses. 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 mg/kg body weight per day and 7 mg/kg body weight per day divided in two doses.
- For the treatment of **nephrotic syndrome**, the total daily dose is usually within the range of 2.5 mg/kg body weight per day and 5 mg/kg body weight per day in adults and 2.5 mg/kg body weight per day and 6 mg/kg body weight per day in children divided in two doses.
- 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 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.

Swallow the capsules whole with a glass of water.

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.

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

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 grey stopper and throw it away.



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



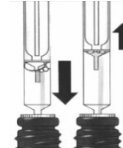
5. Choose the syringe depending on the prescribed volume. For volume less than 1 mL or equal to 1 mL, use the 1-mL syringe. For volume greater than 1 mL, use the 4-mL syringe. Insert the nozzle of the syringe into the white stopper.



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 the 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, but no grapefruit juice. 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.

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

You may feel sleepy, disoriented, or have blurred vision after taking Sandimmun Neoral. Be careful when driving or operating machinery while you are taking Sandimmun Neoral until you know how it affects you.

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 medicine 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 bleeding with no obvious reasons, confusion, disorientation, decreased alertness and kidney problems.

If you experience any of these, tell your doctor straight away. If you experience any serious side effects, stop taking this medicine and tell your doctor immediately.

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, constipation, diarrhoea, overgrowth of the gums, excessive body and facial hair growth and kidney disorders.

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

Rare side-effect - may affect up to 1 in every 1,000 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 visiting the website npra.gov.my [Consumers→ Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)].

Storage and disposal of Sandimmun Neoral

- Storage

Sandimmun Neoral gelatin capsules

Sandimmun Neoral capsules may be stored below 30°C. Sandimmun Neoral capsules should be left in the blister pack until required for use. When a blister is opened, a characteristic smell is noticeable. This is normal and does not mean that there is anything wrong with the capsule.

Sandimmun Neoral oral solution

Sandimmun Neoral oral solution should be stored below 30°C, but not below 20°C for more than 1 month, as it contains oily components of natural origin which tend to solidify at low temperatures. A jelly-like formation may occur below 20°C, which is however reversible at temperatures up to 30°C. Minor flakes or slight sediment may still be observed. These phenomena do not affect the efficacy and safety of the product and the dosing by means of the pipette remains accurate. After opening, Sandimmun Neoral oral solution should be used within 2 months.

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 Neoral 25 mg, 100 mg soft gelatin capsules

Your medicine is called Sandimmun Neoral and comes in the form of soft gelatin capsule. Each soft gelatin capsules contains the active substance ciclosporin (25 mg, 100 mg respectively).

Sandimmun Neoral 25 mg soft gelatin capsules are blue to grey, oval and marked with 'NVR 25 mg' in red..

Sandimmun Neoral 100 mg soft gelatin capsules are blue to grey, oblong and marked with 'NVR 100 mg' in red.

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 Neoral 25 mg, 100 mg soft gelatin capsules

- The active substance is ciclosporin (25 mg, 100 mg respectively).
- The other ingredients of Sandimmun Neoral are: alpha-tocopherol, ethanol anhydrous, propylene glycol, corn oil-mono-di-triglycerides, macroglycerol hydroxystearate (Ph.Eur.)/polyoxyl 40 hydrogenated castor oil (USP), gelatin, glycerol 85%. Colorants: iron oxide black (for 25mg and 100mg capsule), carminic acid, and titanium dioxide (E 171).

Sandimmun Neoral 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, macroglycerol hydroxystearate (Ph.Eur.)/polyoxyl 40 hydrogenated castor oil (USP)

MAL Number

Sandimmun Neoral Capsule 25 mg:

MAL19962142ACRZ

Sandimmun Neoral Capsule 100 mg:

MAL19962140ACRZ

Sandimmun Neoral Oral Solution

100mg/mL: MAL19962143ACRZ

Manufacturer

Sandimmun Neoral soft gelatin capsules

Catalent Germany Eberbach GmbH,

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Sandimmun Neoral oral solution

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Product Registration Holder

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