

Package leaflet: Information for the patient

NEORAL® 25mg soft capsules

NEORAL® 50mg soft capsules

NEORAL® 100mg soft capsules

ciclosporin

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it onto others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Neoral is and what it is used for
2. What you need to know before you take Neoral
3. How to take Neoral
4. Possible side effects
5. How to store Neoral
6. Contents of the pack and other information

1. What Neoral is and what it is used for

What Neoral is

The name of your medicine is Neoral. It contains the active substance ciclosporin.

This belongs to a group of medicines known as immunosuppressive agents. These medicines are used to lower the body's immune reactions.

What Neoral is used for and how Neoral works

- If you have had an organ transplant, bone marrow and stem cell transplantation, the function of Neoral is to control your body's immune system. Neoral prevents rejection of transplanted organs by blocking the development of certain cells which would normally attack the transplanted tissue.
- If you have an autoimmune disease, in which your body's immune response attacks your body's own cells, Neoral stops this immune reaction. Such diseases include eye problems which threaten your vision (endogenous uveitis, including Behcet's uveitis), severe cases of certain skin diseases (atopic dermatitis, or eczema and psoriasis), severe rheumatoid arthritis and a kidney disease called nephrotic syndrome.

2. What you need to know before you take Neoral

If you are taking Neoral following a transplant it will only be prescribed for you by a doctor with experience in transplants and/or autoimmune diseases.

The advice in this leaflet may vary depending on whether you are taking the medicine for a transplant or for an autoimmune disease.

Follow all your doctor's instructions carefully.

They may differ from the general information contained in this leaflet.

Do not take Neoral:

- If you are allergic to ciclosporin or any of the other ingredients of this medicine (listed in section 6)
- With products containing *Hypericum perforatum* (St John's Wort).
- With products containing *dabigatran etexilate* (used to avoid blood clots after surgery) or *bosentan and aliskiren* (used to reduce high blood pressure)

Do not take Neoral and tell your doctor if the above applies to you. If you are not sure, talk to your doctor before taking Neoral.

Warnings and precautions

Before and during treatment with Neoral, tell your doctor straight away:

- If you have any signs of infection, such as fever or a sore throat. Neoral suppresses the immune system and may also affect your body's ability to fight against infection.
- If you have liver problems
- If you have kidney problems. Your doctor will carry out regular blood tests and may change your dose if necessary.
- If you develop high blood pressure. Your doctor will check your blood pressure regularly and may give you a medicine to lower blood pressure if necessary.
- If you have low levels of magnesium in your body. Your doctor may 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 have gout

- If you need to have a vaccination

If any of the above applies to you before or during treatment with Neoral, tell your doctor straight away.

Sunlight and sun protection

Neoral suppresses your immune system.

This increases your risk of developing cancers, particularly of the skin and lymphoid system. You should limit your exposure to sunlight and UV light by:

- Wearing appropriate protective clothing
- Often applying a sunscreen with a high protection factor

Talk to your doctor before taking Neoral:

- If you have or have had alcohol-related problems
- If you have epilepsy
- If you have any liver problems
- If you are pregnant
- If you are breast-feeding
- If this medicine is being prescribed for a child

If any of the above apply to you (or you are not sure), tell your doctor before taking Neoral. This is because this medicine contains alcohol (see section below "Neoral contains ethanol").

Monitoring during your treatment with Neoral

Your doctor will check:

- the levels of ciclosporin in your blood, especially if you have had a transplant
- your blood pressure before the start of your treatment and regularly during treatment
- how well your liver and kidneys are working
- your blood lipids (fats)

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

In addition if you are taking Neoral for a non-transplant disease (intermediary or posterior uveitis and Behcet's uveitis, atopic dermatitis, severe rheumatoid arthritis or nephrotic syndrome), do not take Neoral:

- if you have kidney problems (except for nephrotic syndrome)
- if you have an infection which is not under control with medication
- if you have any type of cancer
- if you have high blood pressure (hypertension) which is not under control with medication. If you get high blood pressure during treatment and it cannot be controlled, Neoral should be stopped by your doctor.

Do not take Neoral if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before taking Neoral.

If you are being treated for Behcet's uveitis, your doctor will monitor you particularly carefully if you have neurological symptoms (for example: increased forgetfulness, personality changes noticed over time, psychiatric or mood disorders, burning sensation in limbs, decreased sensation in limbs, tingling sensation in limbs, weakness of limbs, walking disturbances, headache with or without nausea and vomiting, vision disturbances including restricted movement of eyeball).

Your doctor will closely monitor you if you are elderly and are being treated for psoriasis or atopic dermatitis. If you have been prescribed Neoral to treat your psoriasis or atopic dermatitis, you must not be exposed to any UVB-rays or phototherapy during treatment.

Children and adolescents

Neoral should not be given to children for a non-transplant disease, except for treatment of nephrotic syndrome.

Elderly population (65 years of age and older)

There is limited experience with Neoral in elderly patients. Your doctor should monitor how well your kidneys work. If you are over 65 and have psoriasis or atopic dermatitis, you should only be treated with Neoral if your condition is particularly severe.

Other medicines and Neoral

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular tell your doctor or pharmacist if you are taking any of the following medicines before or during Neoral treatment:

- Medicines that may affect your potassium levels. These include medicines which contain potassium, potassium supplements, water tablets (diuretics) called potassium-sparing diuretics and some medicines which lower your blood pressure.
- Methotrexate. This is used to treat tumours, severe psoriasis and severe rheumatoid arthritis.
- Medicines which may increase or decrease the level of ciclosporin (the active substance of Neoral) in your blood.

Your doctor might check the level of ciclosporin in your blood when starting or stopping treatment with other medicines.

– Medicines which may increase the level of ciclosporin in your blood include: antibiotics (such as erythromycin or azithromycin), anti-fungals (voriconazole, itraconazole), medicines used for heart problems or high blood pressure (diltiazem, nifedipine, verapamil, amiodarone), metoclopramide (used to stop sickness), oral contraceptives, danazol (used to treat menstrual problems), 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 tumours), colchicine, telaprevir (used to treat hepatitis C).

– Medicines which may decrease the level of ciclosporin in your blood include: barbiturates (used to help you to sleep), some anti-convulsant medicines (such as carbamazepine or phenytoine), octreotide (used to treat acromegaly or neuroendocrine tumours in the gut), anti-bacterial medicines used to treat tuberculosis, orlistat (used to help weight loss), herbal medicines containing St. John's wort, ticlopidine (used after a stroke), certain medicines which lower blood pressure (bosentan), and terbinafine (an anti-fungal medicine used to treat infections of the toes and nails).

• Medicines which may affect your kidneys. These include: anti-bacterial medicines (gentamycin, tobramycin, ciprofloxacin), anti-fungal medicines which contain amphotericin B, medicines used for urinary tract infections which contain trimethoprim, medicines for cancer which contain melphalan, medicines used to lower 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 medicines (used to lower the amount of fat in the blood).

• Nifedipine. This is used to treat high blood pressure and heart pain. You might get swollen gums that might grow over your teeth if you are taking nifedipine during your treatment with ciclosporin.

• Digoxin (used to treat heart problems), medicines which lower cholesterol (HMG-CoA reductase inhibitors also called statins), prednisolone, etoposide (used to treat cancer), repaglinide (oral anti-diabetic medicine), immunosuppressives (everolimus, sirolimus), ambrisentan and specific anti-cancer medicines called anthracyclines (such as doxorubicin).

If any of the above applies to you (or you are not sure), talk to your doctor or pharmacist before taking Neoral.

Neoral with food and drink

Do not take Neoral with grapefruit or grapefruit juice. This is because these can affect how Neoral works.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking this medicine. Your doctor will discuss with you the potential risks of taking Neoral during pregnancy.

• Tell your doctor if you are pregnant or intend to become pregnant. Experience with Neoral in pregnancy is limited. In general, 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 treatment with Neoral. This is because ciclosporin, the active substance, passes into breast milk. This may affect your baby.

Driving and using machines

Neoral contains alcohol. This may affect your ability to drive and use machines.

Neoral contains ethanol

Neoral contains approximately 12.0 vol. % ethanol (alcohol), which corresponds to up to 500 mg per dose used in transplant patients. This is equivalent to nearly 15 ml beer or 5 ml wine per dose. Alcohol may be harmful if you have alcohol related problems, epilepsy, brain injury, liver problems or if you are pregnant or breastfeeding. It may also be harmful if this medicine is given to children.

Neoral contains castor oil

Neoral contains castor oil, which may cause stomach discomfort and diarrhoea.

3. How to take Neoral

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Do not take more than the recommended dose.

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

How much Neoral to take

Your doctor will work out the correct dose of Neoral for you. This depends on your body weight and what you are taking the medicine for. Your doctor will also tell you how often to take your medicine.

In adults:

Organ, bone marrow and stem cell transplantation

– The total dose each day is usually between 2 mg and 15 mg per kilogram body weight. This is divided in two doses.

– Usually, higher doses are used before and just after your transplant. 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, your doctor may need to do some blood tests.

Endogenous uveitis

– The total dose each day is usually between 5 mg and 7 mg per kilogram body weight. This is divided in two doses.

Nephrotic syndrome

– The total dose each day for adults is usually 5 mg per kilogram body weight. This is divided in two doses. In patients with kidney problems, the first dose taken each day should not be more than 2.5 mg per kilogram body weight.

Severe rheumatoid arthritis

– The total dose each day is usually between 3 mg per kilogram of your body weight and 5 mg per kilogram body weight. This is divided in two doses.

Psoriasis and atopic dermatitis

– The total dose each day is usually between 2.5 mg per kilogram of your body weight and 5 mg per kilogram body weight. This is divided in two doses.

• In children:

Nephrotic syndrome

– The total dose each day for children is usually 6 mg per kilogram body weight. This is divided in two doses. In patients with kidney problems, the first dose taken each day should not be more than 2.5 mg per kilogram body weight.

Follow your doctor's instructions exactly and never change the dose yourself, even if you feel well.

Switch from Sandimmun to Neoral

You may have already been taking another medicine called Sandimmun soft gelatin capsules or Sandimmun oral solution. Your doctor may decide to change to this medicine, Neoral soft gelatin capsules.

• These medicines all contain ciclosporin as the active ingredient.

• Neoral is a different, improved formulation of ciclosporin compared to Sandimmun. Ciclosporin is absorbed into your blood better with Neoral and absorption is less likely to be affected by taking the medicine with food. This means that the levels of ciclosporin in your blood stay more constant with Neoral than with Sandimmun.

If your doctor changes you from Sandimmun to Neoral:

• Do not go back to taking Sandimmun unless your doctor tells you to.

• Following your transfer from Sandimmun to Neoral, your doctor will monitor you more closely for a short time. This is because of the change in how ciclosporin is absorbed into your blood. Your doctor will make sure that you get the right dose for your individual needs.

• You may have some side effects. If this happens, tell your doctor or pharmacist.

Your dose may need to be lowered.

Never lower your dose yourself, unless a doctor has told you to.

If your doctor switches you from one oral formulation of ciclosporin to another

After you change from one oral formulation of ciclosporin to another:

• Your doctor will monitor you more closely for a short time.

• You may have some side effects. If this happens, tell your doctor or pharmacist.

Your dose may need to be changed.

Never change your dose yourself, unless a doctor has told you to.

When to take Neoral

Take Neoral at the same time every day.

This is very important if you have had a transplant.

How to take Neoral

Your daily doses should always be taken in 2 divided doses.

Remove the capsules from the blister.

Swallow the capsules whole with water.

How long to take Neoral

Your doctor will tell you how long you need to take Neoral for. This depends on whether you are taking it after a transplant or for the treatment of a severe skin condition, rheumatoid arthritis, uveitis or nephrotic syndrome. For severe rash, the treatment usually lasts for 8 weeks.

Keep taking Neoral for as long as your doctor tells you.

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

If you take more Neoral than you should

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

If you forget to take Neoral

- If you forget to take a dose, take it as soon as you remember it. However, if it is almost time for your next dose, skip the missed dose. Then go on as before.
- Do not take a double dose to make up for a forgotten dose.

If you stop taking Neoral

Do not stop taking Neoral unless your doctor tells you to. Keep taking Neoral even if you feel well. Stopping your treatment with Neoral may increase the risk of your transplanted organ being rejected. If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Some side effects could be serious. Tell your doctor straight away if you notice any of the following serious side effects:

- Like other medicines that act on 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. Signs of infection might be fever or sore throat.
- Changes in your sight, loss of coordination, being clumsy, memory loss, difficulty speaking or understanding what others say, and muscle weakness. These might be signs of an infection of the brain called progressive multifocal leukoencephalopathy.
- Brain problems with signs such as seizures, confusion, feeling disorientated, being less responsive, personality changes, feeling agitated, sleeplessness, changes to your sight, blindness, coma, paralysis of part or all of the body, stiff neck, loss of coordination with or without unusual speech or eye movements.
- Swelling at the back of the eye. This may be associated with blurred vision. It may also affect your sight because of the higher pressure inside your head (benign intracranial hypertension).
- Liver problems and damage with or without yellow skin and eyes, nausea, loss of appetite and dark urine.
- Kidney problems which may greatly reduce the amount of urine you produce.
- Low level of red blood cells or platelets. The signs include pale skin, feeling tired, being breathless, having dark urine (this is a sign of the breakdown of red blood cells), bruising or bleeding with no obvious reasons, feeling confused, feeling disorientated, being less alert and having kidney problems.

Other side effects include:

Very common side effects: *These side effects may affect more than 1 in 10 people.*

- Kidney problems.
 - High blood pressure.
 - Headache.
 - Shaking of your body which you cannot control.
 - Excessive growth of body and facial hair.
 - High level of lipids in your blood.
- If any of these affects you severely, tell your doctor.

Common side effects: *These side effects may affect between 1 and 10 in every 100 people.*

- Fits (seizures).
 - Liver problems.
 - High level of sugar in your blood.
 - Tiredness.
 - Loss of appetite.
 - Nausea (feeling sick), vomiting, abdominal pain, constipation, diarrhoea.
 - Excessive hair growth.
 - Acne, hot flushes.
 - Fever.
 - Low level of white blood cells.
 - Feeling numb or tingling.
 - Pain in your muscles, muscle spasm.
 - Stomach ulcer.
 - Gum tissue overgrowing and covering your teeth.
 - High level of uric acid or potassium in your blood, low levels of magnesium in your blood.
- If any of these affects you severely, **tell your doctor.**

Uncommon side effects: *These side effects may affect between 1 and 10 in every 1,000 people.*

- Symptoms of brain disorders including sudden fits, mental confusion, sleeplessness, disorientation, disturbance of vision, unconsciousness, sense of weakness in the limbs, impaired movements.
 - Rash.
 - General swelling.
 - Weight gain.
 - Low level of red blood cells, low level of platelets in your blood which could increase the risk of bleeding.
- If any of these affects you severely, tell your doctor.

Rare side effects: *These side effects may affect between 1 and 10 in every 10,000 people.*

- Nerve problems with numbness or tingling in fingers and toes.
 - Inflammation of the pancreas with severe upper stomach pain.
 - Muscle weakness, loss of muscle strength, pain in muscles of the legs or hands or anywhere in the body.
 - Destruction of red blood cells, involving kidney problems with symptoms such as swelling of the face, stomach, hands and/ or feet, decreased urination, breathing difficulty, chest pain, fits, unconsciousness.
 - Changes in menstrual cycle, breast enlargement in men.
- If any of these affects you severely, tell your doctor.

Very rare side effects: *These side effects may affect between 1 and 10 in every 100,000 people.*

- Swelling at the back of the eye which may be associated with an increase in pressure inside the head and eyesight disturbances.
- If this affects you severely, tell your doctor.

Other side effects with frequency not known: Frequency cannot be estimated from the available data.

- Serious liver problems both with and without yellowing of the eyes or skin, nausea (feeling sick), loss of appetite, dark coloured urine, swelling of the face, feet, hands and/or the whole body.
 - Bleeding underneath the skin or purple skin patches, sudden bleeding with no apparent cause.
 - Migraine or severe headache often with feeling and being sick (nausea, vomiting) and being sensitive to light.
 - Pain in legs and feet
- If any of these affects you severely, tell your doctor. If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

Additional side effects in children and adolescents

There are no additional side effects to be expected in children and adolescents compared to adults.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPR A Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Neoral

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the package.
- Do not store your capsules in a hot place (maximum temperature 25°C).
- Leave your capsules in the foil. Only remove them when it is time to take your medicine.
- When a blister is opened, a characteristic smell is noticeable. This is normal and does not mean that there is anything wrong with the capsules.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What NEORAL contains

NEORAL 25mg soft capsules contain 25mg ciclosporin
NEORAL 50mg soft capsules contain 50mg ciclosporin
NEORAL 100mg soft capsules contain 100mg ciclosporin

They also contain the following other ingredients: DL- α -tocopherol, absolute ethanol, propylene glycol, corn-oil-mono-di-triglycerides, polyoxyl 40 hydrogenated castor oil, iron oxide black (E172)(25mg and 100mg only), titanium dioxide (E171), glycerol 85%, gelatin, carminic acid. The products imported from Greece and Romania also contain in

the red printing ink; aluminium chloride, sodium hydroxide and hypromellose.

NEORAL 25mg soft capsules are oval-shaped, blue-grey, capsules marked with 'NVR' and '25mg' in red ink.

NEORAL 50mg soft capsules are oblong-shaped, yellow-white, capsules marked with 'NVR' and '50mg' in red ink.

NEORAL 100mg soft capsules are oblong-shaped, blue-grey, capsules marked with 'NVR' and '100mg' in red ink.

Pack size: NEORAL soft capsules are available in blister packs of 30 or 50 capsules, contained in an outer cardboard carton.

Product procured from within the EU, repackaged and distributed by the parallel product authorisation holder: PCO Manufacturing, Unit 10, Ashbourne Business Park, Rath, Ashbourne, Co. Meath.

MANUFACTURER

NEORAL capsules are manufactured by RP Scherer GmbH, Eberbach/Baden, Germany or Novartis Pharmaceuticals UK Ltd, Wimbleshurst Road, Horsham, West Sussex, RH12 5AB, UK or Novartis Pharma GmbH, Roonstrasse 25, D-90429 Nürnberg, Germany or Novartis (Hellas) AEBE, 12th Km Athens-Lamia, No 1, 14451 Metamorphosis, Greece.

Product Authorisation number: PPA 465/136/1-3

NEORAL is a registered trademark of Novartis AG.

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria Sandimmun - Neoral 25 mg Kapseln; Sandimmun - Neoral 50 mg Kapseln; Sandimmun - Neoral 100 mg Kapseln

Belgium Neoral - Sandimmun 25 mg; Neoral - Sandimmun 50 mg; Neoral-Sandimmun 100 mg

Bulgaria Sandimmun Neoral 25 mg capsule; Sandimmun Neoral 50 mg capsule; Sandimmun Neoral 100 mg capsule

Cyprus Sandimmun Neoral 25 mg ; Sandimmun Neoral 50 mg; Sandimmun Neoral 100 mg

Czech Republic Sandimmun Neoral 25 mg; Sandimmun Neoral 50 mg; Sandimmun Neoral 100 mg

Denmark Sandimmun Neoral

Estonia Sandimmun Neoral

Finland Sandimmun Neoral

France NEORAL

Germany Sandimmun Optoral 25 mg Weichkapseln; Sandimmun Optoral 50 mg Weichkapseln; Sandimmun Optoral 100 mg Weichkapseln

Greece SANDIMMUN NEORAL

Hungary Sandimmun Neoral 25 mg lágy kapszula; Sandimmun Neoral 50 mg lágy kapszula; Sandimmun Neoral 100 mg lágy kapszula

Iceland Sandimmun Neoral

Ireland Neoral

Italy Sandimmun Neoral

Latvia Sandimmun Neoral 25 mg mīkstās kapsulas; Sandimmun Neoral 50 mg mīkstās kapsulas; Sandimmun Neoral 100 mg mīkstās kapsulas

Lithuania Sandimmun Neoral

Luxembourg Sandimmun Optoral 25 mg Weichkapseln ; Sandimmun Optoral 50 mg Weichkapseln; Sandimmun Optoral 100 mg Weichkapseln

Malta Sandimmun Neoral

Netherlands Neoral 25 mg, capsules; Neoral 100 mg, capsules

Norway Sandimmun Neoral

Poland Sandimmun Neoral

Portugal Sandimmun Neoral

Romania SANDIMMUN NEORAL capsule moi, 25 mg; SANDIMMUN NEORAL,capsule moi, 50 mg ;

Slovak Republic Sandimmun Neoral 25 mg ; Sandimmun Neoral 50 mg ; Sandimmun Neoral 100 mg

Slovenia Sandimmun Neoral 25 mg mehke kapsule; Sandimmun Neoral 50 mg mehke kapsule; Sandimmun Neoral 100 mg mehke kapsule

Spain Sandimmun Neoral 25 mg cápsulas blandas; Sandimmun Neoral 50 mg cápsulas blandas; Sandimmun Neoral 100 mg cápsulas blandas

Sweden Sandimmun Neoral

United Kingdom Neoral Soft Gelatin Capsules 25mg; Neoral Soft Gelatin Capsules 50mg; Neoral Soft Gelatin Capsules 100mg

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