

## Package leaflet: Information for the patient

### Sandimmun® 50 mg/ml concentrate for solution for infusion

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 on to 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. See Section 4.

#### **What is in this leaflet**

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

#### **1. What Sandimmun is and what it is used for**

##### **What Sandimmun is**

The name of your medicine is Sandimmun. It contains the active substance ciclosporin. The concentrate is used to prepare a solution which is administered by intravenous infusion. This belongs to a group of medicines known as immunosuppressive agents. These medicines are used to lower the body's immune reactions.

##### **What Sandimmun is used for and how it works**

Sandimmun is used to control the body's immune system following an organ transplant, including bone marrow and stem cell transplantation. It prevents rejection of transplanted organs by blocking the development of certain cells which would normally attack the transplanted tissue.

#### **2. What you need to know before Sandimmun is used**

Sandimmun will only be prescribed for you by a doctor with experience in transplants.

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

##### **Do not use Sandimmun:**

- if you are allergic to ciclosporin or any of the other ingredients of this medicine (listed in section 6; also see section "Sandimmun contains castor oil and ethanol").
- 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 use Sandimmun and **tell your doctor** if the above applies to you. If you are not sure, talk to your doctor or pharmacist before taking Sandimmun.

## **Warnings and precautions**

### **Before and during treatment with Sandimmun, tell your doctor straight away:**

- if you have any signs of infection, such as fever or a sore throat. Sandimmun 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 transplant operation.
- 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 Sandimmun, tell your doctor straight away.

### **Sunlight and sun protection**

Sandimmun 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 Sandimmun:**

- 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 applies to you (or you are not sure), tell your doctor before taking Sandimmun. This is because this medicine contains alcohol (see section below "Sandimmun contains castor oil and ethanol").

### **Monitoring during your treatment with Sandimmun**

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 Sandimmun works or why this medicine has been prescribed for you, ask your doctor.

### **Children and adolescents**

There is limited experience with Sandimmun in children.

### **Elderly population (65 years of age and older)**

There is limited experience with Sandimmun in elderly patients. Your doctor should monitor how well your kidneys work.

### **Other medicines and Sandimmun**

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 Sandimmun 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 Sandimmun) 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), cannabidiol (uses amongst others include treatment of seizures).
  - 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 H<sub>2</sub>-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 (an anti-diabetic medicine), immunosuppressives (everolimus, sirolimus), ambrisentan and specific anti-cancer medicines called anthracyclines (such as doxorubicin).
- Mycophenolate sodium or mycophenolate mofetil (an immunosuppressant) and eltrombopag (used to treat bleeding disorders).

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

### **Sandimmun with food and drink**

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

### **Pregnancy and breast-feeding**

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

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

## **Hepatitis C**

Tell your doctor if you have hepatitis C. Your liver function may change with treatment of hepatitis C and this may affect the levels of ciclosporin in your blood. Your doctor may need to closely monitor ciclosporin blood levels and make adjustments to the dose after you start treatment for hepatitis C.

## **Driving and using machines**

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

## **Sandimmun contains castor oil and ethanol**

Sandimmun concentrate for solution for infusion contains castor oil which may cause severe allergic reactions.

Sandimmun concentrate for solution for infusion contains 278 mg of alcohol (ethanol) in each ml which is equivalent to 34.4 % v/v. A 100 mg dose of Sandimmun contains 556 mg ethanol. This is equivalent to nearly 14 ml beer or 6 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

## **3. How Sandimmun is used**

Carefully follow all the instructions given to you by your doctor. Check with your doctor if you are not sure.

### **How much Sandimmun you will be given**

Your doctor will work out the correct dose of Sandimmun for you. This depends on your body weight and what you are being given the medicine for.

- The total dose each day is usually between 3 to 5 mg per kilogram of your weight. This is divided into 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.

### **How Sandimmun will be used**

The medicine will be diluted before use 1:20 to 1:100 with saline or 5% glucose and then given to you by slow infusion over approximately 2 to 6 hours. Diluted medicine must be thrown away after 24 hours.

### **How long Sandimmun will be used**

You will be switched to ciclosporin in the form of capsules or oral solution (both of which are taken by mouth) as soon as possible.

### **If you have been given more Sandimmun than you should**

Too much of the medicine can affect your kidneys. You will have regular blood tests and visits to the hospital. This will give you the chance to talk to your doctor about your treatment and talk about any problems you may be having.

If you think you have been given too much Sandimmun, tell your doctor immediately.

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:

- Signs of anaphylactoid reactions appeared following intravenous administration of Sandimmun. These reactions can consist of flushing of the face and upper chest, fluid in the lungs, shortness of breath, wheezing, blood pressure changes (you may feel you are going to faint) and accelerated heartbeat (tachycardia).
- 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:** 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:** may affect up to 1 in 10 people.

- Fits (seizures).
- Liver problems.
- High level of sugar in your blood.
- Tiredness,
- Loss of appetite.
- Nausea (feeling sick), vomiting, abdominal discomfort/ pain, 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:** may affect up to 1 in 100 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:** may affect up to 1 in 1,000 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:** may affect up to 1 in 10,000 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**.

**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.
- Hearing impairment.

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 or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, website: [www.hpra.ie](http://www.hpra.ie). By reporting side effects, you can help provide more information on the safety of this medicine.

### **5. How to store Sandimmun**

- 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.
- This medicine does not require any special temperature storage conditions.

- Once an ampoule has been opened, the contents should be used immediately.
- Following dilution, the solution should be used immediately or stored in a refrigerator (2°C – 8°C) and discarded after 24 hours
- Do not throw away any medicines via wastewater or household waste. These measures will help to protect the environment.

## **6. Contents of the pack and other information**

### **What Sandimmun contains**

- The active substance is ciclosporin. One ml of the concentrate for solution for infusion contains 50 mg ciclosporin.
- The other ingredients are: ethanol anhydrous, castor oil polyoxyl.

### **What Sandimmun looks like and contents of the pack**

Sandimmun concentrate for solution for infusion is supplied in ampoules containing 1 ml or 5 ml concentrate. The concentrate is a clear brown/yellow oily liquid. It is used by your doctor or nurse to prepare a solution which will be given to you by slow intravenous infusion.

Pack with 10 ampoules of 1 ml.

Pack with 10 ampoules of 5 ml.

Not all pack sizes may be available.

### **Marketing Authorisation Holder**

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### **Manufacturer**

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**This medicinal product is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:**

Netherlands	Sandimmune
Austria, Belgium, Croatia, Czech Republic, Denmark, Finland,	Sandimmun
France, Germany, Greece, Hungary, Iceland, Ireland, Italy,	
Luxemburg, Norway, Poland, Portugal, Slovakia, Slovenia, Spain,	
Sweden, United Kingdom (Northern Ireland)	

**This leaflet was last revised in {MM/YYYY}**

### **Other sources of information**

Detailed information on this medicine is available on the website of the Health Products Regulatory Authority: [www.hpra.ie](http://www.hpra.ie).