Package leaflet: Information for the patient

Tacrolimus Mylan 0.5 mg hard capsules
Tacrolimus Mylan 1 mg hard capsules
Tacrolimus Mylan 5 mg hard capsules

tacrolimus

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 Tacrolimus Mylan is and what it is used for

Tacrolimus Mylan contains the active substance tacrolimus which is an immunosuppressant. Following your organ transplant (e.g. liver, kidney, heart), your body's immune system will try to reject the new organ.

Tacrolimus Mylan is used to control your body's immune response enabling your body to accept the transplanted organ.

Tacrolimus Mylan is often used in combination with other medicines that also suppress the immune system.

You may also be given Tacrolimus Mylan for an ongoing rejection of your transplanted liver, kidney, heart or other organ when any previous treatment you were taking was unable to control this immune response after your transplantation.

2. What you need to know before you take Tacrolimus Mylan

Do not take Tacrolimus Mylan

- If you are allergic to tacrolimus or any of the other ingredients of this medicine (listed in section 6).
- If you are allergic to sirolimus or to any macrolide antibiotic (e.g. erythromycin, clarithromycin, josamycin).

Warnings and precautions

Talk to your doctor or pharmacist before taking Tacrolimus Mylan:
- if you are taking any medicines mentioned below under 'Other medicines and Tacrolimus Mylan'.
- if you have or have had liver problems
- if you need to receive any vaccinations
- if you or a family member have been diagnosed with heart problems (e.g. congestive heart failure, bradyarrhythmias)
- if you have been diagnosed with a heart condition called "Congenital Long QT Syndrome" or "QT prolongation".

Your doctor may need to adjust your dose of Tacrolimus Mylan.

During treatment tell your doctor or pharmacist:
- if you have diarrhoea for more than one day
- if you feel strong abdominal pain accompanied with or without other symptoms, such as chills, fever, feeling sick (nausea) or being sick (vomiting)
- if you have a change of the electrical activity of your heart called "QT prolongation".

You should keep in regular contact with your doctor. From time to time, your doctor may need to do blood, urine, heart, eye and neurological tests, to set the right dose of Tacrolimus Mylan.

Patients treated with tacrolimus have been reported to have an increased risk of developing lymphoproliferative disorders (see section 4). Ask your doctor for specific advice on these disorders.

You should limit your exposure to the sun and UV (ultraviolet) light whilst taking Tacrolimus Mylan. This is because immunosuppressants could increase the risk of skin cancer. Wear appropriate protective clothing and use a sunscreen with a high sun protection factor.

Other medicines and Tacrolimus Mylan

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription and herbal preparations.

Tacrolimus Mylan must not be taken with ciclosporin.

Tacrolimus Mylan blood levels can be affected by other medicines you take, and blood levels of other medicines can be affected by taking Tacrolimus Mylan which may require an increase or

decrease in dose. In particular, you should tell your doctor if you are taking or have recently taken medicines like:

- antifungal medicines and antibiotics, particularly so-called macrolide antibiotics, used to treat infections, such as ketoconazole, fluconazole, itraconazole, telithromycin, voriconazole, clotrimazole, erythromycin, clarithromycin, josamycin, rifabutin and rifampicin
- HIV medicines (e.g. ritonavir, nelfinavir, saquinavir), used to treat HIV infection
- HCV protease inhibitors (e.g. telaprevir, boceprevir), used to treat hepatitis C infection
- medicines for stomach ulcer and acid reflux (e.g. omeprazole, lansoprazol or cimetidine)
- antiemetics, used to treat nausea and vomiting (e.g. metoclopramide)
- cisapride or the antacid magnesium-aluminium-hydroxide, used to treat heartburn
- the contraceptive pill or other hormone treatments with ethinylestradiol, hormone treatments with danazol
- medicines used to treat high blood pressure or heart problems (e.g. nifedipine, nicardipine, diltiazem and verapamil)
- amiodarone, used to control arrhythmia (uneven beating of the heart)
- phenytoin, phenobarbital or carbamazepine, used to treat epilepsy
- the corticosteroids prednisolone and methylprednisolone, belonging to the class of corticosteroids used to treat inflammations or suppress the immune system (e.g. in transplant rejection)
- isoniazid, used to treat tuberculosis
- nefazodone, used to treat depression
- Herbal preparations containing St. John's wort (*Hypericum perforatum*) or extracts of *Schisandra sphenanthera*.

Tell your doctor if you are taking or need to take ibuprofen, amphotericin B or antivirals (e.g. ganciclovir, aciclovir). These may worsen kidney or nervous system problems when taken together with Tacrolimus Mylan.

Your doctor also needs to know if you are taking potassium supplements or certain diuretics used for heart failure, hypertension and kidney disease, (e.g. amiloride, triamterene, or spironolactone), non-steroidal anti-inflammatory drugs (NSAIDs, e.g. ibuprofen) used for fever, inflammation and pain, anticoagulants (blood thinners), or oral medicines for diabetes, while you take Tacrolimus Mylan.

If you need vaccinations, tell your doctor in advance that you are taking this medicine.

Taking Tacrolimus Mylan with food and drink

Avoid grapefruit (also as juice) while on treatment with Tacrolimus Mylan since it can affect its levels.

Pregnancy and breast-feeding

If you plan to become pregnant or think that you may be pregnant, ask your doctor or pharmacist for advice before taking any medicine.

Tacrolimus passes into breast milk. Therefore you should not breast-feed whilst using Tacrolimus Mylan.

Driving and using machines

Do not drive or use any tools or machines if you feel dizzy or sleepy, or have problems seeing clearly after taking this medicine. These effects are more frequently observed if you also drink alcohol.

Tacrolimus Mylan contains lactose.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Tacrolimus Mylan

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

Make sure that you receive the same tacrolimus medicine every time you collect your prescription, unless your transplant specialist has agreed to change to a different tacrolimus medicine.

This medicine should be taken twice a day. If the appearance of this medicine is not the same as usual, or if dosage instructions have changed, speak to your doctor or pharmacist as soon as possible to make sure that you have the right medicine.

The starting dose to prevent the rejection of your transplanted organ will be determined by your doctor calculated according to your body weight. Initial doses just after transplantation will generally be in the range of 0.075 – 0.30 mg per kg body weight per day depending on the transplanted organ.

Your dose depends on your general condition and on which other immunosuppressive medication you are taking. Regular blood tests by your doctor will be required to define the correct dose and to adjust the dose from time to time. Your doctor will usually reduce your Tacrolimus Mylan dose once your condition has stabilised. Your doctor will tell you exactly how many capsules to take and how often.

Tacrolimus Mylan is taken orally twice daily, usually in the morning and evening. You should generally take Tacrolimus Mylan on an empty stomach or at least 1 hour before or 2 to 3 hours after the meal. The capsules should be swallowed whole with a glass of water. Avoid grapefruit and grapefruit juice while taking Tacrolimus Mylan. Do not swallow the desiccant contained in the foil wrapper.

If you take more Tacrolimus Mylan than you should

If you have accidentally taken too much see your doctor or contact your nearest hospital emergency department immediately. Someone who has taken an overdose of Tacrolimus Mylan may have any of these symptoms: shaking, headache, feeling or being sick, itchy rash (hives), feeling tired and increased infections.

If you forget to take Tacrolimus Mylan

Do not take a double dose to make up for forgotten individual doses.
If you have forgotten to take your capsules, wait until it is time for the next dose, and then continue as before.

If you stop taking Tacrolimus Mylan

Stopping your treatment may increase the risk of rejection of your transplanted organ. Do not stop your treatment unless your doctor tells you to do so.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tacrolimus Mylan reduces your body's own defence mechanism to stop you rejecting your transplanted organ. Consequently, your body will not be as good as usual at fighting infections. So if you are taking Tacrolimus Mylan you may therefore catch more infections than usual such as infections of the skin, mouth, stomach and intestines, lungs and urinary tract.

If you think you may have any of the following side effects, contact your doctor or go to your nearest hospital emergency room immediately:

Very common (may affect more than 1 in 10 people):
- diabetes mellitus, you may notice increased thirst, needing to urinate more often than usual and increased hunger
- kidney problems

Common (may affect up to 1 in 10 people):
- yellowing of the skin due to liver problems, liver tissue damage and inflammation of the liver
- insufficient function of the kidneys with reduced production of urine, impaired or painful urination
- gastrointestinal perforation, you may have strong abdominal pain accompanied with other symptoms, such as chills, fever, feeling sick and being sick
- inflammations or ulcers causing abdominal pain or diarrhoea, bleedings in the stomach
- fits

Uncommon side effects (may affect up to 1 in 100 people):
- bleeding in the brain, stroke
- difficulties in breathing
- reduction in the number of all types of blood cells
- inflammation of the pancreas
- partial or complete paralysis
- obstruction of the gut

- haemolytic uraemic syndrome, a condition with the following symptoms: low or no urine output (acute renal failure), extreme tiredness, yellowing of the skin or eyes (jaundice) and abnormal bruising or bleeding and signs of infection.
- inflammation of the membrane lining of the stomach wall
- severe mental disorder that can cause abnormal thinking and perceptions
- heart attack
- insufficient function of your transplanted organ
- coma, shock

Rare (may affect up to 1 in 1,000 people):

- Thrombotic Thrombocytopenic Purpura, a condition with the following symptoms: fever and bruising under the skin that may appear as red pinpoint dots, you may feel unexplained extreme tiredness, confusion, and notice yellowing of the skin or eyes (jaundice), with symptoms of kidney problems (low or no urine output).
- Toxic epidermal necrolysis: erosion and blistering of skin or mucous membranes, red swollen skin that can detach in large parts of the body.
- severe shortness of breath
- blindness
- collection of fluid around the heart
- deafness
- problems with blood flow in the liver

Very rare (may affect up to 1 in 10,000 people):

- liver failure
- Stevens-Johnson syndrome: unexplained widespread skin pain, facial swelling, serious illness with blistering of skin, mouth, eyes and genitals, hives, tongue swelling, red or purple skin rash that spreads, skin shedding
- *Torsades de Pointes*: change in the heart frequency that can be accompanied by symptoms, such as chest pain (angina), fainting, dizziness or feeling sick (nausea), palpitations (feeling the heartbeat) and difficulty breathing.
- painful urination with blood in the urine
- abnormal heart scan
- narrowing of the bile vessel

Not known (frequency cannot be estimated from the available data):

- allergic and anaphylactic reactions with the following symptoms: a sudden itchy rash (hives), swelling of hands, feet, ankle, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing) and you may feel you are going to faint.
- benign and malignant tumours have been reported following treatment as a result of immunosuppression
- Posterior Reversible Encephalopathy Syndrome (PRES): headache, altered mental status, fits, and visual disturbances
- pure red cell aplasia (a very severe reduction in red blood cell counts) and haemolytic anaemia (decreased number of red blood cells due to abnormal breakdown accompanied with tiredness) have been reported. You may have no symptoms or depending on the severity of the condition, you may notice: fatigue, apathy, abnormal paleness of the skin, shortness of breath, dizziness, headache, chest pain and coldness in hands and feet.

- agranulocytosis (a severely lowered number of white blood cells accompanied with ulcers in the mouth, fever and infections). You may have no symptoms or you may feel sudden fever, chills and sore throat.

Other possible side effects

Very common (may affect more than 1 in 10 people):
- increased blood sugar, increased potassium in the blood
- difficulty in sleeping
- trembling, headache
- increased blood pressure
- diarrhoea, nausea

Common (may affect up to 1 in 10 people):
- reduced magnesium, phosphate, potassium, calcium or sodium in the blood, fluid overload, increased uric acid or lipids in the blood, decreased appetite, increased acidity of the blood, other changes in the blood salts (seen in blood tests)
- anxiety symptoms, confusion and disorientation, depression, mood changes, nightmare, hallucination, mental disorders
- disturbances in consciousness, tingling and numbness (sometimes painful) in the hands and feet, dizziness, impaired writing ability, nervous system disorders
- blurred vision, increased sensitivity to light, eye disorders
- ringing sound in your ears
- reduced blood flow in the heart vessels, faster heartbeat
- bleeding, partial or complete blocking of blood vessels, reduced blood pressure
- shortness in breath, changes in the lung tissue, collection of liquid around the lung, inflammation of the throat, cough, flu-like symptoms
- inflammations or ulcers in the mouth, collection of fluid in the belly, vomiting, abdominal pains, indigestion, constipation, passing wind, bloating, loose stools, stomach problems
- changes in liver enzymes and function
- itching, rash, hair loss, acne, increased sweating
- pain in joints, limbs or back, muscle cramps
- general weakness, fever, collection of fluid in your body, pain and discomfort, increase of the enzyme alkaline phosphatase in your blood, weight gain, feeling feverish
- insufficient function of your transplanted organ

Uncommon (may affect up to 1 in 100 people):
- changes in blood clotting
- dehydration, reduced protein or sugar in the blood, increased phosphate in the blood.
- brain disorder, speech and language abnormalities, memory problems
- clouding of the eyes
- impaired hearing
- irregular heartbeat, skipped heartbeat, reduced performance of your heart, disorder of the heart muscle, enlargement of the heart muscle, stronger heartbeat, abnormal ECG, heart rate and pulse abnormal
- blood clot in a vein of a limb
- respiratory tract disorders, asthma

- increased blood level of the enzyme amylase, reflux of stomach content in your throat, delayed emptying of the stomach
- dermatitis, burning sensation in the sunlight
- joint disorders
- painful menstruation and abnormal menstrual bleedings
- influenza like illness, increased sensitivity to heat and cold, feeling of pressure on your chest, jittery or abnormal feeling, increase of the enzyme lactate dehydrogenase in your blood, weight loss

Rare (may affect up to 1 in 1,000 people):
- increased muscle stiffness
- cyst formation in your pancreas
- increased hairiness
- thirst, fall
- feeling of tightness in your chest
- decreased mobility
- ulcer

Very rare (may affect up to 1 in 10,000 people):
- muscular weakness
- increase of fat tissue

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA 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 Tacrolimus Mylan

- Keep this medicine out of the sight and reach of children.
- Store below 30°C
- Store in the original package (within the foil pouch) in order to protect from moisture and light.
- Do not use Tacrolimus Mylan after the expiry date which is stated on the carton and blister after {EXP}.Once the foil pouch is opened, the product should be used within 1 year. The expiry date refers to the last day of that month.
- 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 protect the environment.

6. Contents of the pack and other information

What Tacrolimus Mylan contains
Tacrolimus Mylan 0.5 mg hard capsules
The active substance is tacrolimus.
For 0.5mg: Each capsule contains 0.5mg of tacrolimus
The other ingredients are:

- Capsule content: Povidone K-30, Croscarmellose Sodium (E 468), Lactose anhydrous, Magnesium stearate.
- Capsule shell: Titanium dioxide (E-171), Yellow Iron Opxide (E-172), Gelatin

Tacrolimus Mylan 1 mg hard capsules
The active substance is tacrolimus.
For 1 mg: Each capsule contains 1mg of tacrolimus
The other ingredients are:
- Capsule content: Povidone K-30, Croscarmellose Sodium (E 468), Lactose anhydrous, Magnesium stearate.
- Capsule shell: Titanium dioxide (E-171), Gelatin

Tacrolimus Mylan 5 mg hard capsules
The active substance is tacrolimus.
For 5mg: Each capsule contains 5mg of tacrolimus
The other ingredients are:
- Capsule content: Povidone K-30, Croscarmellose Sodium (E 468), Lactose anhydrous, Magnesium stearate.
- Capsule shell: Titanium dioxide (E-171), Red Iron Oxide (E-172), Gelatin

What Tacrolimus Mylan looks like and contents of the pack

Tacrolimus Mylan 0.5 mg hard capsules
Ivory cap and ivory body hard shell capsules with white powder.
Tacrolimus Mylan 0.5 mg hard capsules are supplied as blister strips containing 10 capsules within a protective foil wrapper, including a desiccant protecting the capsules from moisture. The desiccant should not be swallowed.

Tacrolimus Mylan 1 mg hard capsules
White cap and white body hard shell capsules with white powder.
Tacrolimus Mylan 1 mg hard capsules are supplied as blister strips containing 10 capsules within a protective foil wrapper, including a desiccant protecting the capsules from moisture. The desiccant should not be swallowed.

Tacrolimus Mylan 5 mg hard capsules
Red cap and red body hard shell capsules with white powder.
Tacrolimus Mylan 5 mg hard capsules are supplied as blister strips containing 10 capsules within a protective foil wrapper, including a desiccant protecting the capsules from moisture. The desiccant should not be swallowed.

Tacrolimus Mylan is available in blister packs containing blister strips of 10 capsules each.
0.5 mg: 10, 30, 50, 60, 90 and 100 capsules
1 mg: 10, 30, 50, 60, 90 and 100 capsules
5 mg: 10, 30, 50, 60, 90 and 100 capsules

Not all pack sizes may be marketed

Marketing Authorisation Holder

McDermott Laboratories Ltd. T/A Gerard Laboratories

35-36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.

Manufacturer

Laboratorios Cinfa, S.A.
Olaz-Chipi, 10-Políg Areta 31620 Huarte-Pamplona, Navarra,
Spain

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

BE:	Tacrolimus Mylan 0.5mg, 1mg, 5mg capsules, hard
CZ:	Tacrolimus Mylan 0.5mg, 1mg, 5mg
DE:	Tacrolimus dura 0.5mg, 1mg, 5mg Hartkapseln
EL:	Tacrolimus / Generics 0.5mg, 1mg, 5mg σκληρά καψάκια
ES:	Tacrolimus MYLAN 0,5 mg, 1 mg, 5 mg cápsulas duras EFG
HU:	Tacrolimus Mylan 0.5mg, 1mg, 5mg Kemény kapszula
IE:	Tacrolimus Mylan 0.5mg, 1mg, 5mg hard capsules
IT:	Tacrolimus Mylan Generics, 0.5mg, 1mg, 5mg Capsule rigide
NL:	Tacrolimus Mylan
UK:	Capexion 0.5mg, 1mg, 5mg hard capsules

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