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	Description	Tacrolimus 0,5 / 1 / 5 mg	
	Market	IE-MT	
	Language	English	
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	Date	23.11.12 (Tacrolimus (ACC-IE-MT)NEW-PIL)	
Prepared By Regulatory Affairs		Checked By Regulatory Affairs	Approved By Quality Assurance



Package Leaflet: Information for the user

**Tacrolimus 0.5 mg
Hard capsules
Tacrolimus 1 mg
Hard capsules
Tacrolimus 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.

What is in this leaflet

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

1. What Tacrolimus capsule is and what it is used for

Tacrolimus belongs to a group of medicines called immunosuppressant. After your organ transplant (e.g. liver, kidney or heart), your body's defence system will try to reject the new organ. Tacrolimus is used to prevent rejection of newly transplanted organs Tacrolimus can also be prescribed to treat rejection of transplanted organ. If you have been taking medicines to prevent rejection and they are not sufficiently effective then your doctor will have changed your treatment by starting you on Tacrolimus.

Tacrolimus is often used in combination with other medicinal products which also suppress the immune system

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

Do not take Tacrolimus Capsules:

- if you are allergic to Tacrolimus or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to macrolide types of antibiotics e.g. erythromycin, clarithromycin, josamycin.

Warnings and precautions:

Talk to your doctor or pharmacist before taking Tacrolimus Capsules

- You will need to take tacrolimus every day as long as you need immunosuppression to prevent rejection of your transplanted organ. You should keep in regular contact with your doctor.
- During your treatment period of tacrolimus capsules, your doctor may want to carry out a number of tests (including blood, urine, heart function, visual and neurological tests) from time to time. These investigations are normal and will help your doctor to decide on the most appropriate dose of Tacrolimus for you.
- Do not take any herbal remedies, e.g. St. John's wort (*Hypericum perforatum*) or other herbal medicines, as these can influence the action of tacrolimus and hence the dose you need to take. If in doubt, contact your doctor before taking any herbal medicine.
- If you have liver problems or have had a disease which may have affected your liver, please tell your doctor as this may affect the dose of tacrolimus capsules that you receive.
- If you have had diarrhoea for more than one day, please tell your doctor, because it might be necessary to adjust the dose of Tacrolimus capsules that you receive.
- Limit your exposure to sunlight and UV light while you are using tacrolimus capsules by wearing protective clothing that gives full coverage and using sunscreen with a high protection factor. This is because of the possible risk of cancerous changes of the skin in immunosuppressive therapy.
- If you need to have any vaccinations, please inform your doctor in advance. Your doctor will advise you on the best course of action.

Other medicines and Tacrolimus capsules:

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

Tacrolimus must not be taken with ciclosporin. Tacrolimus blood levels can be affected by other medicines you take, and blood levels of other medicines can be affected by taking Tacrolimus. Consequently it may be necessary to increase or reduce the dose of tacrolimus. In particular, you should tell your doctor if you are taking or have recently taken medicines with active substances like:

- antifungal medicines and antibiotics (in particular those known as macrolide antibiotics) for the treatment of infections, such as ketoconazole, fluconazole, itraconazole, voriconazole, clotrimazole, erythromycin, clarithromycin, josamycin and rifampicin
- HIV protease inhibitors, for example ritonavir
- omeprazole or lansoprazole, to treat stomach ulcers
- hormone treatments with ethinylestradiol (such as the contraceptive pill) or danazol
- medicines used to treat high blood pressure such as nifedipine, nicardipine, diltiazem and verapamil
- medicines known as 'statins' to treat high cholesterol and triglyceride levels
- the anti-epilepsy medicines phenobarbital and phenytoin
- the corticosteroids prednisolone and methylprednisolone
- the John's wort (Hypericum perforatum) or other herbal medicines (see Warnings and Precautions)
- antiemetics, used to treat nausea and vomiting (e.g. metoclopramide)
- cisapride or the antacid magnesium-aluminium-hydroxide, used to treat heartburn

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

Tell your doctor if you have to use (or are currently using) ibuprofen, amphotericin B or anti-viral drugs (such as aciclovir). These medicines can exacerbate kidney and nervous system disorders if they are taken with tacrolimus capsule.

While you are using tacrolimus capsules, your doctor must also be informed if you are taking potassium supplements or potassium-sparing diuretics (certain water pill such as amiloride, triamterene or spironolactone), certain painkillers (known as NSAIDs, such as ibuprofen), anticoagulants or oral medicines to treat diabetes.

Taking Tacrolimus Capsules with food and drink:

You should generally take Tacrolimus capsules on an empty stomach or at least 1 hour before or 2 to 3 hours after a meal. Grapefruit and grapefruit juice must not be consumed while taking Tacrolimus capsules.

Pregnancy, breast-feeding and fertility:

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Tacrolimus is excreted into breast milk. Therefore you should not breast-feed whilst receiving Tacrolimus.

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 Tacrolimus capsules. These effects are observed more frequently when Tacrolimus capsules is used together with alcohol.

Tacrolimus Capsules contains Lactose

Tacrolimus capsules 0.5/1/5 mg contains 0.050/0.048/0.098 g of lactose respectively. When taken according to the dosage recommendations each dose supplies 0.050/0.048/0.098 g of lactose respectively. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicinal product. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

3. How to take Tacrolimus capsule

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

The starting dose of tacrolimus capsules to prevent rejection of your transplanted organ will be decided by your doctor and will be related to your body weight. The first dose directly after the transplant operation will usually be between 0.075 and 0.30 mg per kg body weight per day depending on the transplanted organ.

Your dose will depend on your general condition and any other immunosuppressive drugs you are using. Your doctor should carry out regular blood tests in order to find the correct dose and occasionally in order to adjust it. Your doctor will normally reduce the dose of tacrolimus capsules when your condition has stabilised. Your doctor will tell you exactly how many tacrolimus capsules you must take and how often.

Tacrolimus capsules is taken orally twice daily, usually in the morning and evening. You should generally take tacrolimus 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. Take the capsule immediately following removal from the blister. Avoid grapefruit juice while taking tacrolimus.

If you take more Tacrolimus Capsules then you should

If you take too many capsules by accident, see your doctor immediately or contact the accident and emergency department of the nearest hospital.

If you forget to take Tacrolimus Capsules

Do not take a double dose to make up for a forgotten dose.

If you have forgotten to take your tacrolimus capsules, wait until it is time to take the next dose, and then continue as usual.

If you stop taking Tacrolimus Capsules

Stopping treatment with tacrolimus capsules can increase the risk of rejection of your transplanted organ. Do not stop the treatment unless your doctor tells you to.

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.

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

Severe effects have been reported, including allergic and anaphylactic reactions. Benign and malignant tumours have been reported following tacrolimus treatment as a result of immunosuppression.


Possible side effects are listed under headings of frequency, using the following categories:

- very common: may affect more than 1 in 10 people
- common: may affect up to 1 in 10 people
- uncommon: may affect up to 1 in 100 people
- rare: may affect up to 1 in 1,000 people
- very rare: may affect up to 1 in 10,000 people
- not known: frequency cannot be estimated from the available data

Very common

- increased blood sugar
- diabetes mellitus
- increased potassium in the blood



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- difficulty in sleeping
- trembling
- Headache
- increased blood pressure
- diarrhoea
- Nausea
- kidney problems

Common

- reduction in blood cell counts (platelets, red or white blood cells), increase in white blood cell counts, changes in red blood cell counts
- 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
- anxiety symptoms, confusion and disorientation, depression, mood changes, nightmare, hallucinations, mental disorders
- fits, 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 pharynx, cough, flu-like symptoms
- inflammations or ulcers causing abdominal pain or diarrhoea, bleedings in the stomach, inflammations or ulcers in the mouth, collection of fluid in the belly, vomiting, abdominal pains, indigestion, constipation, flatulence, bloating, loose stools, stomach problems
- changes in liver enzymes and function, yellowing of the skin due to liver problems, liver tissue damage and inflammation of the liver
- itching, rash, hair loss, acne, increased sweating
- pain in joints, limbs or back, muscle cramps
- insufficient function of the kidneys, reduced production of urine, impaired or painful urination
- general weakness, fever, collection of fluid in your body, pain and discomfort, increase of the enzyme alkaline phosphatase in your blood, weight gain, feeling of temperature disturbed.
- insufficient function of your transplanted organ

Uncommon

- changes in blood clotting, reduction in all blood cell counts
- dehydration, reduced protein or sugar in the blood, increased phosphate in the blood
- coma, bleeding in the brain, stroke, paralysis, brain disorder, speech and language abnormalities, memory problems
- opacity of the lens
- impaired hearing
- irregular heartbeat, stop of heartbeat, reduced performance of your heart, disorder of the heart muscle, enlargement of the heart ventricles (lower chambers), stronger heartbeat, abnormal ECG, heart rate and pulse abnormal
- blood clot in a vein of a limb, shock
- difficulties in breathing, respiratory tract disorders, asthma
- paralysis of intestine, 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
- inability to urinate, painful menstruation and abnormal menstrual bleeding
- failure of some organs, 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
- haemolytic-uraemic syndrome which is characterised by acute renal failure (low urine output /or no urine output), microangiopathic haemolytic anaemia (decreased number of red blood cells with extreme tiredness) and a low platelet count with abnormal bruising or bleeding and signs of infection. It may be fatal.

Rare

- small bleedings in your skin due to blood clots
- increased muscle stiffness
- collection of fluid around the heart
- blindness
- deafness (hearing impaired)
- acute breathlessness
- cyst formation in your pancreas
- problems with blood flow in the liver
- increased hairiness
- serious illness with blistering of skin, mouth, eyes and genitals
- thirst
- feeling of tightness in your chest
- decreased mobility
- ulcer
- thrombotic thrombocytopenic purpura which is characterised by fever and bruising under the skin that may appear as red pinpoint dots, with or without unexplained extreme tiredness, confusion, yellowing of the skin or eyes (jaundice), with symptoms of low urine output (or no urine output). It may be fatal.

Very rare

- muscular weakness
- echocardiogram abnormal
- liver failure
- narrowing of the bile vessel
- painful urination with blood in the urine
- increase of fat tissue
- Stevens-Johnson syndrome appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. The rash may progress to widespread blistering or peeling of the skin. Additional signs to look for include ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). Skin rashes are often accompanied by flu-like symptoms. It may be fatal

Not known

- pure red cell aplasia which causes a very severe reduction in red blood cell counts accompanied by tiredness
- agranulocytosis which causes a severely lowered number of white blood cells accompanied with ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). Skin rashes are often accompanied by flu-like symptoms. It may be fatal

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

5. How to store Tacrolimus capsule

- 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 carton and blister after "EXP". The expiry date refers to the last day of that month.
- Store below 25°C. Store in the original package in order to protect from moisture.
- 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 Capsules contains:

The active substance is Tacrolimus.
For 0.5 mg: Each hard capsule contains 0.5 mg tacrolimus (as tacrolimus monohydrate).
For 1 mg: Each hard capsule contains 1 mg tacrolimus (as tacrolimus monohydrate).
For 5 mg: Each hard capsule contains 5 mg tacrolimus (as tacrolimus monohydrate).

The other ingredients are: lactose monohydrate, croscarmellose sodium (E468), hypromellose (E464), magnesium stearate (E 470b)

Capsule Shell composition for Tacrolimus 0.5 mg: Gelatin, titanium dioxide (E 171) iron oxide yellow (E 172), sodium laurilsulfate

Capsule Shell composition for Tacrolimus 1 mg: Gelatin, titanium dioxide (E 171), sodium laurilsulfate

Capsule Shell composition for Tacrolimus 5 mg: Gelatin, titanium dioxide (E 171), iron oxide red (E 172), sodium laurilsulfate

Printing ink of capsule shell: Shellac, propylene glycol, potassium hydroxide, black iron oxide (E172)

What Tacrolimus Capsules looks like and contents of the pack:

Tacrolimus Capsules 0.5mg:
Light yellow / Light yellow hard gelatin capsules, approximately 11.40mm, size "5" imprinted with "TCR" on cap & "0.5" on body containing white to off white granular powder.

Tacrolimus Capsules 1mg:
White / White hard gelatin capsules, approximately 11.40mm, size "5" imprinted with "TCR" on cap & "1" on body containing white to off white granular powder

Tacrolimus Capsules 5 mg:
Pink/Pink hard gelatin capsules, approximately 14.30mm, size "4" imprinted with "TCR" on cap & "5" on body containing white to off white granular powder.

Tacrolimus Capsules are available in blisters packs of
Tacrolimus 0.5 mg capsules
Packs of 20, 30, 50, 60 and 100 hard capsules.

Tacrolimus 1 mg capsules
Packs of 20, 30, 50, 60, 90 and 100 hard capsules.

Tacrolimus 5 mg capsules
Packs of 30, 50, 60 and 100 hard capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer:

Accord Healthcare Limited
Sage House, 319, Pinner Road,
North Harrow, Middlesex, HA1 4HF,
United Kingdom

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

Name of the member state	Name of the medicinal product
The Netherlands	Tacrolimus Accord 0,5/1/5 mg capsule hard
Austria	Tacrolimus Accord 0,5/1/5 mg Hartkapseln
Bulgaria	Tacrolimus Accord 0,5/1/5 mg capsules hard
Czech Republic	Tacrolimus Accord 0,5/1/5 mg tvrdé tobolky
Denmark	Tacrolimus Accord
Finland	Tacrolimus Accord 0,5/1/5 mg kapseli kova
Germany	Tacrolimus Accord 0,5/1/5 mg Hartkapseln
Greece	Tacrolimus Accord 0,5/1/5 mg Καπάκιο, σκληρό
Hungary	Tacrolimus Accord 0,5/1/5 mg kemény kapszula
Ireland	Tacrolimus 0.5/1/5 mg hard capsules
Italy	Tacrolimus Accord Healthcare 0,5/1/5 mg capsule rigide
Latvia	Tacrolimus Accord 0,5/1/5 mg cietās kapsulas
Lithuania	Tacrolimus Accord 0,5/1/5 mg kietos kapsules
Malta	Tacrolimus 0,5/1/5 mg capsule hard
Norway	Tacrolimus Accord 0,5/1/5mg kapsler harde
Poland	Tacrolimus Accord
Portugal	Tacrolimus Accord
Romania	Tacrolimusum Accord 0,5/1/5 mg capsule
Slovak Republic	Tacrolimusum Accord 1/5 mg tvrdé kapsule
Slovenia	Takrolimus Accord 1/5 mg trde kapsule
Spain	Tacrolimus Accord 0,5/1/5 mg cápsulas duras EFG
Sweden	Tacrolimus Accord 0,5/1/5 mg kapsel hård

The leaflet was last approved in 11/2012.