# Tacrograf®

## FORMS AND PRESENTATION

dioxide, sodium lauryl sulphate.
PHARMACOLOGICAL PROPERTIE

marnacodynamic properties
Therapeutic class: Immunosuppressants.
ATC code: L04AD02.
At the molecular level, the effects of Tacrolin
The FKBP12-Tacrolimus computers. ATC code LOADID.
At the molecular level, the effects of Tacrolimus appear to be mediated by binding to a cytosolic protein (FKBP12) which is responsible for the intracellular accumulation of the comprehence of the molecular level, the molecular level, the molecular level, the molecular level of the comprehence inhibition of T-cell signal transduction pathways, the proceeding teaching that of advances are of the single protest immunosuppressive agent and has proven activity in both in vitro and in vitro experiments.

Incolfirms is a highly potent immunosuppressive agent and has proven activity in both in vitro and in vitro experiments.

In particular, Tacrolimus an high set formation of cytothocic lymphocytes, which are mainly responsible for grad received. Tacrolimus suppresses T-cell activation and T-helpe dependent T-cell profilements in well as the formation of symphosius could an interdedinary and the expression of the interdation? exceptor.

Plemancolimitie preparties
Absorption
In man Tacceliman has been shown to be able to be absorbed fluoroghout the gustionistedimal tract. Following onal administration of Taccelimans expands peak concentrations (C.
Taccelimans inflood are achieved in approximately 1-3 hour. In some patients, Taccelimans appears to be continuously absorbed over a prolonged period yielding a relatively that also
Tacceliman in Bood and achieved in the proximately 1-3 hour. In some patients, Taccelimans appears to be continuously absorbed over a prolonged period yielding a relatively that also
After call deministration (II 3) rung [sky] to low term spin parts. Analy-date concentrations of Taccelimans were achieved within 1 days in the majority of patients.
In hardary also/pct. Tacceliman 5.05 rag, Tacceliman In great Taccelimans "and propositions" and proposition of Taccelimans were achieved within 1 days in the majority of patients.
In hardary also/pct. Tacceliman 5.05 rag, Tacceliman In great Taccelimans "are greated believe to shown to be brocardens; when administrated as equivalent does
The rate and center of absorption of Taccelimans is general under finded conditions. The processes of find decises the rate and center of absorption of Taccelimans, the effect being procuouscult after allight and The effect on allign-2-arbelyolythem runs is superconcentration and the absorption of Taccelimans, the effect being procuouscult after allight and The effect on allign-2-arbelyolythem runs is superconcentration and the absorption of Taccelimans, the effect being procuouscultural and the effect of a subject and the effect of the procure of the absorption of Taccelimans, the effect being procuouscultural and the effect of absorption of Taccelimans, the effect being procuouscultural and the effect of absorption of Taccelimans, the effect being procuouscultural and the effect of absorption of Taccelimans are advantaged to the effect of absorption of Taccelimans and the effect of the eff

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can tested on which though a considerable 470 inters. Geogrammon mixed.

Tacordisms is widely metabolized in the liver, primarily by the cytechrone P459-3A4. Tacordisms is also considerably metabolized in the intestinal wall. There are several metabolities widely metabolized in the intestinal wall. There are several metabolities is widely metabolized in the intestinal wall. There are several metabolities is destribed to be pleasured to the original properties and the properties of the contribute to pleasured by the pleasured to the contribute to pleasured original activity of Tacordisms activity. In systemic circulation only one of the intestive metabolities is special at low concentrations. Therefore, metabolities do not contribute to pleasured original activity of Tacordisms.

activity. In systemic circulation only one of the inactive metabolites is present at low concentrations. Therefore, metabolites do not contribute to pharmacological activity of Tacrolinus. Elimination

Tacrolinus is a low-clearance subdiance. In healthy subject, the new gets and body clearance (TBC) estimated from whole blood concentrations was 2.51 lb. In shall liver, kinded to transplant projects have a TBC approximately view that of dash liver transplant princise. Factors such as low heartscort and protein levels, which result in an increase in the unbound function of Tacrolinus, or corticoloroid-induced increased metabolism, are considered to be expossible for the higher cleance ratio observed following transplantation.

The hill-file of Tacrolinus is long and variable. In healthy subjects, the mean half-file in whole blood is approximately 43 tone. In shall and podintic liver transplant projects. The companies of the project of the projects of the projec

recipions.

Following introverous and onal administration of VC-labeled Tacrolimus, most of the radioactivity was eliminated in the foces. Approximately 2 % of the radioactivity was eliminated in the foces. Approximately 2 % of the radioactivity was eliminated in the series. Less than 1 % of unchanged Tacrolimus was detected in the urine and foces, indicating that Tacrolimus is almost completely metabolized prior to elimination: Bille being the

erophylaxis of transplant rejection in liver, kidney or heart allograft recipients, ment of allograft rejection resistant to treatment with other immunosuppressive medicinal products

- Hypersensitivity to any of the excipients

PRECAUTIONS
- Particular at 1 - 1 - 1

does supervision of a transplant speciality. Enforcing our resistants with the cost optioning bady trouting significant, inflations or instantiative in significant standards or significant to include a supervision of the performance of the p

blood glucose levels, electrolyses (particularly petassium), live and read flunction telss, hematology parameters, coagulation values, and plasma proton determinations. If climicary necessary and plasma proton determinations of the immunopersposive regimens based be considered.

- When substances with a potential for interaction-particularly shong inhibitors of CVTPA4 (such as lactocontass)ed, vericontass)e, lettlemorgies or existente regimens of the confirmation of confirmation of the confirmation of confirmation of confirmation of the confirmation of the confirmation of confirmatio

concentrations and the theraponic effect of Tacolumus.

The combined administration of cyclosporine and Tacolumus should be avoided and care should be taken when administrating Tacolumus to patients with survey pre-assays and cyclosporine.

High potentiam intrake or potassium-apuring distracts should be avoided.

Certain combinations of Tacolumus with dugs between to have rephrescoice or neuroscic effects may increase the risk of those effects.

The immunosuppressions may affect the response to vaccination and vaccination during mentance with Tacolumus may be less effective. The use of five attenuated vaccines should be avoided.

Certain combinations of Tacolumus with dugs between to have rephrescoice or neuroscic effects may increase the risk of those effective. The use of five attenuated vaccines should be avoided.

Certain conditions with the company of the properties of the special contractions of the properties of the special confidence in the contraction of the properties of th

to necessary in patients with severe liver impairment. lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficie

## PREGNANCY AND LACTATION

PRECNANCY AND LACTATION

Human data show the Theoritims crosses the placents. Limited data from organ transplant recipients show no cvidence of an incressed risk of adverse effects on the course and outcome of preguency under Tacroliums teamment compared with other immunosuppressive medicatel products. To date, no other relevant epidemiological data are available. Tacroliums teamment can be considered any request stream with the resist in some fail analyses and when the precise dending littliffs the potential in the off facts in case of instruct outpour, mentioning of the newborn for the potential adverse effects of Tacroliums is recommended (in particular the effects on the kidneys). There is a risk for persuate effects (v) (<3 week) (incidence of 66 of 125 of

DRIGHTENATIONS

The Committee of the Com

restorables.

In vito the following auditations have been shown to be potential sitabilities of Tacrofismus metabolism: Bermocriptine, cortisone, duptone, ergotarnine, geshodene, linkcaine, mephenyotin, nicoranode, miduodame, andweighen, noredisferiore, quinisfice, turnoriden, trobenskempcin.

Cappellin jaine have new reported to increase the blood level of Tacrofismus and should therefore be avoided. Larsequend and cyclosporine may potentially inhibit CYPIAH-mediated metabolism of Tacrofismus and through increase Tacrofismus whole blood concentrations.

Tacrofismus is not been reported to increase Tacrofismus whole blood therefore be avoided. Larsequend and cyclosporine may potentially inhibit CYPIAH-mediated metabolism of Tacrofismus and theory in Economical Tacrofismus and the Color interactions perfectly located to plasma proteins through the contribution of the active substances known to have high affinity for plasma proteins should be considered (e.g., NSAID), color proteins in increasions that may increase systemic exposure of Tacrofismus include prokinetic agents (such as metoclopamnide and cisoprate), cinetifine and compensate administration between the control location and controlled levels (CYPAH administers neutrally location to decreased Tacrofismus include prokinetic agents (such as metoclopamnide and cisoprate), cinetifine and CYPAH administer neutrillus location to decreased Tacrofismus local levels

magescians alturiame hydroxide.

CPA44 althors repairably leading to decreased Tacoliums blood levels

CPA44 althors repairably leading to decreased Tacoliums blood levels

- Storeg interactions have been observed with inflampicia, photypisis or St. John's Wort (Hypericam perforatum) which may require increased Tacoliums doses in almost all patients.

- High dose producedose or methy hydroxinoidene administered for the teatment of actas rejection have the potential to horse administered for the teatment of actas rejection have the potential to horse.

- Carlamanagem, remainted and somital there the potential to decount Environment Constrainteniss.

- Tacoliums is a known CYP3A4 inhibitor, thus concomitant use of Tacoliums with medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medicinal products known to be metabolized by CYP3A4 may affect the metabolism of such medi

- medicial products.

  On displaying displaying a product of the production of the prod
- Tracolimus has been shown to increase the blood level of phenytoin.

  As Tacrolimus may reduce the clearance of steroid-based contraceptives leading to increased hormone exposure, particular care should be exercised when deciding upon or
- owledge of interactions between Tacrolimus and statins is available. Available data suggests that the pharmacokinetics of statins are largely unaltered by the co-ac
- ave shown that Tacrolimus could notentially decrease the clearance and increase the half-life of nentobarbital and phenazone

Unter attackons isolates to consocial volumental effects.

Concurrent use of Hardinan with mischail and products insocial enter Concurrent use of Hardinan with mischail and products insocial enter the Concurrent use of Hardinan with mischail products insocial enter the Concurrent way of the Concurrent to the Concurre

AUVENCE LEFECTS

The abress drug reaction profile associated with immunosuppressive agent is often difficult to eshabits owing to the underlying disease and the concurrent use of multiple medications. Many of the adverse drug reactions is fasted as follows: Very common (£-1100, v-1100) and (£-1100, v-1100) are (£-11000); vary part (£-110000); vary to abverse reactions is defined as follows: Very common (£-1100, v-1100), v-1100, v-11000); vary part (£-110000); vary to abverse reactions is defined as follows: Very common (£-1100, v-1100); vary part (£-110000); vary to an extra be estimated from the outside shealth with the contribution of t

b) In Dymphatic system disorders: Ameriia, loxogeniir, thromboytopenia, abnormal kukocytosis red blood cell analyses (common); congulopathies, abnormal congulation and analyses, puraysponia, nontropenia (uncommon); throrebotic florenbocytopenic purpusa, lyopprofitorobinomia (ran); system disorders: Bendache, tremer (very common); scirums, distinutes in oneconsense, permishenism and upostelluciosa, peripheral neuropathies, dizzinosa, impaired writing, yalem disorders (common); coma, central nervous system homorthages and cerebovascular accidents, paralysis and puresis, encephadopathy, speech and language shnormalities.

mensate (incomment), hypothesis (next), trapillurals (very rest)

- Pop (denders, Blanches) (see indeets (comment), classed (incomment), blanches (rate),

- Ear and hyprith disorders. Turnian (comment), broadcass (incomment), darlines neurosurosy (race); imprint fluering (very race),

- Ear and hyprith disorders. Turnian (comment), broadcass (incomment), darlines neurosurosy (race); imprint fluering (very race),

- Respetatory, floraci, of an effective floracions (incomment), darlines neurosurosy (race); imprint floracing (very race),

- Edisporticul floracions. Eliment, natessed, very comment, gashoristerel floral lung (incolens, planting) (excl., male conception), and influent floracions (incomment), darlines neurosurosy (incomment), darlines neurosurosy (incomment), darlines neurosurosi, proprieta (incomment), proprieta (i

emic conditions, diabetes mellitus, hyperkalemia (very common); hypomagnesemia, hypophosphatemia, hypokalemia, hyporaesed appetite, anorexia, metabolic acidosis, hyperlipidemia, hypercholeskerolemia, hypertriplyceridemia, other electrolyte abno

- Endocrine disorders Hirstainn (mex)

- Mediodine and antimic disorders: Hypophycimic conditions, diabetes mellitus, hypochalemia (very common); hypomagnesemia, hypophychalemia, hypochalemia, hypoc

DOSAGE AND ADMINISTRATION

crograff\* therapy requires careful monitoring by adequately qualified and equipped personnel.

se medicinal product should only be prescribed, and changes in immunosuppressive therapy initiated by physicians experienced in immunosuppressive therapy and the product of the product parties.

Locusidations

commended initial desages presented below are intended to act solely as a guideline. Tacrogntfll dosing should primarily be based on clinical assessments of rejection and tolerability patient individually aided by blood level monitoring. If clinical signs of rejection are queuers, alteration of the immunosuppressive regions should be considered, and, dosing may commence could, if necessary, by administering the capsale contents supported in vaster, via susceptible to thing. Tacrolimus is rotately administered in conjunction ter immunosuppressive agents in the initial post-operative period. The Tacrognill' dose may vary depending upon the immunosuppressive gittens chosen.

with other immunosupressive agains in the initial pool-operative period. The Tarongar' does may vary apapuring upon the immunosupressive grittens.

Bit is recommended furt the cral daily does be adminished in two divided dooss (e.g. morning and evening). Capules should be taken immediately following removal from the bitisher. The capulas should be seadouted with fluid referribely water).

Capulas should a sensorally be adminished on an empty shound or at least 1 hour before or 2 to 3 hours after a meal, to achieve maximal absorption.

Danation of doing:
To appress graft rejection, immunosuppression must be maintained, consequently, no limit to the datastion of our thecapy can be given.

Danation of doing the control of the completion of surgery.

Prophysics of transplant rejection – adults: Oral Tacongar'' the completion of surgery.

Prophysics of frameplant rejection – adults: Oral Tacongar'' the completion of surgery.

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Prophysics of frameplant rejection – adults: Oral Tacongar'' the control oral prophysics of transplant properties.

Prophysics of frameplant rejection – adults: Oral Tacongar'' does are usually reduced in the post-transplant propin It is possible in some cases to withdraw concentration immunosuppressive therepy, leading to Tacongar'' does are usually reduced in the post-transplant propin It is possible in some cases to withdraw concentration immunosuppressive theorem, leading to Tacongar'' monotherapy. Post-transplant improvement in the condition of the patient may after the pharmacokinctics of Tacongar'' and on vessestiate thems does adultament.

- Does againstend turning post-suspanes post-on-concentrate immunospersionel density, leading to Theregard' monotherapy. Pol-densiplant improvement in the condition of the patient may alter the plantmucoknetics or lacengard arms and processing for the does alignificant.

In the condition of the condition of the patient may alter the plantmucoknetics or lacengard arms and processing for the condition of does or Consequent may alter the patients of the condition of the condition

- Regulation theory— Same and contactor intersect intersignal videos, supported in consociation interply, an interaction of some contactor in states (or some contactor) and a contact of the contactor in the con

r corncesserones.

of transplant rejection — children: Following antibody induction, if Tacrograf\*\* therapy is initiated orally, the recommended starting dose is 0.10 - 0.30 mg/kg/day administered

-Prophysics of Transplant rejection - diabher: Following anathoby induction, if Transpurth "bearpy is initiated only, the recommended sharing dose is 0.10 - 0.30 mg kg/day adminisheed as two disided doses; or, menting and evening).

-Dose adjustment during problemapping proid in adults and children. Transpurth "beas are usually reduced in the problemapping report. Post-transplant report. Post-transplant reprovement in the condition of the printent may after be phasemachasises of the reports and may necessary and the problemant and the printent problemant and the problemant and

range.

Frend impairment: As the pharmacolines of Cherquiff are unaffected by read function, no done adjustment is required. However, owing to the nephrotoxic potential of Tacogniff-cuerful monitoring of read function is recommended (including serial secure constitutes, calculation of creatings of continue cleanmen and monitoring of urine couput).

Face: Incomprison to Cheacasins, like, he destress may require legislar Through "South to adjustment with a serial read of the continue of continue and monitoring of urine couput).

Face: Incomprison to Cheacasins, like, he printed in require disposition of the Tacogniff when the continue of the contin

Thereports drug monitoring. Doing should primarily be based on clinical assessments of rejection and boterbility in each individual patient aduct by whole blood incorgan\* trongureses monitoring.

As an aid to optimize doing, several immunossousy and as available for determining Eurograph\* concentrations in whole blood including a semi-automated microparticle enzyme immunossousy (MRLA). Comparisons of concentrations from the published literature to includinal values in clinical practice should be sensored wine are all knowledge of the assay methods employed. In current clinical practice, whole blood levels are monitored using minuscosay methods. Blood rough levels do frazegar should be remointed using each product of the product of the foreign and the production, and design and the production, and design in the food and the production, the foreign and the production, and the production, and the production, and the members are producted in the contract of the comparison production and the production, and time immensure flavors the production of the comparison production and the production, and time immensure flavors production are producted and the production, and time immensure flavors production are producted and the production, and time immensure flavors production are producted and the production, and time immensure flavors production are producted and the production, and time immensure flavors production are producted and the production, and time immensure flavors production are producted as the production of the

ERIONAGE
services with over design is limited. Several cases of accidental overdosage have been reported, symptoms have included treme, bandache, museca and vermiting, infections, urticaria, any and increases in Bood uses integrate, seame constaine and increase in alternate antistantedness levels, supportantly treatment should be conducted.

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STORAGE CONDITIONS

## This is a medicament - A medicament is a product which affects your health, and its or

A medicament is a product which affects your health, and its consumption contrary to instructions is diagnose for you Follow which; the doctor's prescription, the method of use, and the instructions of the plannacist the soul different medicament - The doctor and the plannacist nee coparts in medicine, its benefits and risks - Do not by yoused filtering the period of treatment prescribed for you - Do not tryou affect instruction without consulting your doctor - Medicaments keep out of reach of children.