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tablet

EVEROLIMUS

Sobhan Oncology

(5mg & 10mg)

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have further question, ask your doctor or your pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.

In this leaflet:

1- What Everolimus is and what it is used for

Everolimus, an inhibitor of mechanistic target of rapamycin (mTOR), is an antineoplastic agent and a macrolide immunosuppressant. Everolimus is used to treat: (fact 3859)
Advanced hormone receptor-positive, human epidermal growth receptor 2-negative breast cancer:
Treatment of postmenopausal women with advanced hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole.
Advanced neuroendocrine tumors of pancreatic origin:
Treatment of progressive neuroendocrine tumors of pancreatic origin in adult patients with unresectable, locally advanced, or metastatic disease.
Limitations of use – Not indicated for the treatment of patients with functional carcinoid tumors.
Advanced renal cell carcinoma:
Treatment of adult patients with advanced renal cell carcinoma after failure of treatment with Sunitinib or Sorafenib.
Renal angiomyolipoma with tuberous sclerosis complex:
Treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex not requiring immediate surgery.
Subependymal giant cell astrocytoma:
Treatment of adult and pediatric patients with subependymal giant cell astrocytoma associated with tuberous sclerosis complex who require therapeutic intervention but are not candidates for curative surgical resection.
Off-label uses:
Carcinoid tumors, progressive, advanced –
Data from a randomized, double-blind, placebo-controlled phase III trial in patients with low grade or intermediate-grade neuroendocrine tumors associated with carcinoid syndrome support the use of everolimus (in combination with octreotide long-acting repeatable) for this condition.
Waldenstrommacroglobulinemia, relapsed or refractory –
Data from phase II trial in patients with relapsed/refractory Waldenstrommacroglobulinemia support the use of everolimus for this condition. Additional trials may be necessary to further define the role of everolimus in this condition.(Fact 3857)

2- Before you take Everolimus

Do not take Everolimus:
If you are allergic (hypersensitive) to the active ingredient and any other ingredient in Everolimus, sirolimus,other rapamycin derivatives products. (Fact 3860)
If you are pregnant or think that you might be pregnant.
If you are breast feeding. (Fact 3860)
Pediatric: The safety and effectiveness of everolimus in kidney or liver transplant, advanced renal cell carcinoma, advanced pancreatic neuroendocrine tumors, or renal angiomyolipoma with tuberous sclerosis complex in the absence of subependymal giant cell astrocytoma in patients younger than 18 years have not been established. Everolimus has not been studied in patients younger than 1 year with subependymal giant cell astrocytoma. (Fact 3861)
Elderly: No overall differences in safety or effectiveness were observed between these elderly patients and younger patients. (FDA leaflet)
Take special care with Everolimus:
Pulmonary toxicity:
Noninfectious pneumonitis was reported in up to 19% of patients treated with Everolimus. The incidence of grade 3 and 4 noninfectious pneumonitis was up to 4% and up to 0.2%, respectively. Interstitial lung disease and/or noninfectious fibrosis have been observed with Everolimus. Fatal outcomes have been observed. Noninfectious pneumonitis may respond to drug interruption with or without glucocorticoid therapy. However, fatal cases have also occurred. Pneumonia should be considered in the differential diagnosis .advise patients to promptly report any new or worsening respiratory symptoms.
Infections:
Everolimus has immunosuppressive properties and may predispose patients to bacterial, fungal, viral, or protozoal infections, including infections with opportunistic pathogens. Localized and systemic infections,including pneumonia, mycobacterial infections, other bacterial infections, viral infections (including reactivation of hepatitis B virus), and invasive fungal infections, such as aspergillosis, candidiasis, or P.jiroveci pneumonia,have occurred in patients taking everolimus. Some of these infections have been severe (eg, leading to sepsis or respiratory or hepatic failure) or fatal. Complete treatment of preexisting invasive fungal infections prior to starting treatment with everolimus. Be aware, and ensure that patients are aware, of the increased risk of infection with everolimus; be vigilant for signs and symptoms of infection. If a diagnosis of an infection is made, institute appropriate treatment promptly and consider interruption or discontinuation of everolimus. If a diagnosis of invasive systemic fungal infection is made, discontinue everolimus and treat with appropriate antifungal therapy. Because of the danger of over-immunosuppression of the immune system, this can cause increased susceptibility to infection, use combination immunosuppressant therapy with caution.
Oral ulceration:
Mouth ulcers, stomatitis, and oral mucositis have occurred in patients treated with everolimus at an incidence from 44% for 86%. Grade 3 or 4 stomatitis was reported in 4% to 9% of patients. In such cases, topical treatments are recommended, but avoid alcohol, hydrogen peroxide, iodine-, or thyme-containing mouthwashes because they may exacerbate the condition. Do not use antifungal agents unless fungal infection has been diagnosed.
Renal effects:
Elevations of serum creatinine have been reported. Cases of renal failure (including acute renal failure), some with a fatal outcome have been observed.
In kidney transplant patients, everolimus with standard-dose cyclosporine increases the risk of nephrotoxicity, resulting in a lower glomerular filtration rate. Reduced doses of cyclosporine are required for use in combination with everolimus in order to reduce renal dysfunction. Monitor renal function during the administration of everolimus in combination with cyclosporine. Consider switching to other immunosuppressive therapies if renal function does not improve after dose adjustments or if the dysfunction is thought to be drug related. Exercise caution when using other drugs that are known to impair renal function.
In liver transplant recipients, everolimus has not been studied with standard-dose Tacrolimus. Use reduced doses of Tacrolimus in combination with everolimus in order to minimize the potential risk of nephrotoxicity. Proteinuria has been reported. The use of everolimus with cyclosporine in transplant patients has been associated with increased proteinuria.The risk of Proteinuria increased with higher everolimus whole blood trough concentrations.
Monitor renal function (serum urea nitrogen [BUN]; serum creatinine,urinary protein) at baseline and periodically, especially if risk factors for further impairment exist.
Eliminating calcineurin inhibitors from the immunosuppressive regimen may result in acute rejection.
Vaccines (inactivated): Immunosuppressants may diminish the therapeutic effect of vaccines.
Management: vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after the immunosuppressant is discontinued. Consider therapy modification.
Vaccines (live): Immunosuppressants may enhance the adverse/toxic effect of vaccines. Vaccinal infections may develop. Immunosuppressants may diminish the therapeutic effect of vaccines (Live).
Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. Avoid combination.
Lymphomas and other malignancies:
Patients receiving everolimus are at an increased risk of developing lymphomas and other malignancies, particularly of the skin. The risk appears to be related to the intensity and duration of immunosuppression rather than to the use of any specific agent.
As usual for patients with increased risk of skin cancer, advice patients to limit exposure to sunlight and ultraviolet light by wearing protective clothing and using a sunscreen with a high protection factor.
Kidney graft thrombosis:
An increased risk of kidney arterial and venous thrombosis, resulting in graft loss, was reported, mostly within the first 30 days post transplantation.
Hepatic artery thrombosis:
mTOR inhibitors are associated with an increase in hepatic artery thrombosis. Reported cases mostly have occurred within the first 30 days post-transplant and most also lead to graft loss or death. Therefore,do not administer everolimus earlier 30 days after liver transplant.
Heart transplantation:
Increased mortality, often associated with serious infection, within the first 3 months of post transplantation was observed in a clinical trial of de novo heart transplant patients receiving immunosuppressive regiments with or without induction therapy. Use in heart transplantation is not recommended.
Angioedema:
Everolimus has been associated with the development of angioedema. Concomitant use with other agents known to cause angioedema (eg, ACE inhibitors) may increase the risk for angioedema.
Wound healing and fluid accumulation:
Everolimus delays wound healing and increases the occurrence of wound-related complications, such as wound dehiscence, wound infection, incisional hernia, lymphocele, and seroma. These wound-related complications may require more surgical intervention. Use everolimus with caution in the perisurgical period. Generalized fluid accumulation, including peripheral edema (eg, lymphedema) and other types of localized fluid collection, such as pericardial and pleural effusions and ascites, have also been reported.
Hyperlipidemia:
Increased serum cholesterol and triglycerides requiring the need for antilipid therapy have been reported to occur following initiation of everolimus; the risk of hyperlipidemia is increased with higher everolimus whole blood trough concentrations. Use of antilipid therapy may not normalize lipid levels in patients receiving everolimus.
Monitor for hyperlipidemia and treat appropriately. If possible, achieve optimal lipid control prior to initiating everolimustherapy. Consider the risks and benefits in patients with established hyperlipidemia before initiating an immunosuppressive regimen containing everolimus. Similarly,reevaluate the risks and benefits of continued everolimus therapy in patients with severe refractory hyperlipidemia. Everolimus has not been studied in patients with baseline cholesterol levels greater than 350 mg/dL.
Because of an interaction with cyclosporine, clinical trials of everolimus and cyclosporine in kidney transplant patients strongly discouraged patients from receiving the HMG-CoA reducuctase inhibitors simvastatin and lovastatin.
Diabetes:
Increases in serum glucose are common; may alter insulin and/or oral hypoglycemic therapy requirements in patients with diabetes. Everolimus has been shown to increase the risk of new-onset diabetes mellitus after transplant. Monitor blood glucose concentrations in patients using everolimus, especially when coadministered with other medications known to induce hyperglycemia. If possible, achieve optimal glycemic control prior to initiating everolimus therapy.
Hematologic effects:
Decreasedhemoglobin, lymphocytes,neutrophils, and platelets have been reported in clinical trials. Monitor complete blood cell counts prior to the start of everolimus therapy and periodically thereafter.
The concomitant use of everolimus with cyclosporine may increase the risk of thrombotic microangiopathy/thrombotic thrombocytopenic purpura/hemolytic uremic syndrome.
Infertility:
Everolimus may cause infertility. In females, menstrual irregularities, secondary amenorrhea, and increases in luteinizing hormone and follicle-stimulating hormone have occurred. Azoospermia or oligospermia may be observed. Everolimus is an antiproliferative drug and affects rapidly dividing cells, such as the germ cells.
Galactose intolerance:
Do not administer everolimus to patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency, or glucose-galactosemalabsorption because this may result in diarrhea and malabsorption.
Hazardous agent:
Use appropriate precautions for handling and disposal (NIOSH 2014 [group 1]).
Use in pregnancy: Category D.
Adverse events were observed in animal reproduction studies with exposures lower than expected with human doses. Based on the mechanism of action, may cause fetal harm if administered during pregnancy. Advise women of reproductive potential to avoid pregnancy and use highly effective birth control during treatment and for up to 8 weeks after everolimus discontinuation.
Use in lactation:
It is not known if everolimus is excreted in breast milk.Because of the potential for serious adverse reactions in the breast feeding infant, avoid breast feeding. (Fact 3861)
Laboratory test during the medication therapy:
Monitor renal function, including measurement of serum urea nitrogen, serum creatinine, and urinary protein; fasting serum glucose; complete blood cell count: and lipids, prior to the start of therapy and periodically thereafter. Monitor renal function, particularly when patients have additional risk factors that may further impair renal function. Monitoring of fasting serum glucose and lipid profile is recommended prior to the start of therapy and periodically thereafter, as well as management with appropriate medical therapy. More frequent monitoring is recommended when everolimus is coadministered with other drugs that may induce hyperglycemia. Monitor patients for proteinuria and signs and symptoms of infection. Monitor everolimus and cyclosporine whole blood trough concentrations.
Drug interactions
If you received other drugs; even such as OTC drugs, please tell your physician or pharmacist. The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance.
ACE inhibitors
Increasedrisk of angioedema when everolimusgiven with ACE inhibitors.
Antibacterials
Plasma concentration of everolimus possibly increased by CLARITHROMYCIN, TELITHROMYCIN,manufacturer of everolimus advises avoid concomitant use; plasma concentration of everolimusincreased by ERYTHROMYCIN (consider reducing the dose of everolimus): plasmaconcentration of everolimus reduced byRIFAMPICIN (avoid concomitant use or consider increasing the dose of everolimus)
Antidepressants
Plasma concentration of everolimus possibly reduced by ST JOHN'S WORT-manufacturer of everolimus advises avoid concomitant use.
Antifungals
Plasma concentration of everolimus increased byKETOCONAZOLE-manufacturer of ketoconazole advises avoid concomitant use; plasma concentration of everolimus possibly increased by ITRACONAZOLE, POSACONAZOLE and VORICONAZOLE-manufacturer of everolimus advises avoid concomitant use.
Antipsychotics
Avoid concomitant use of cytotoxics withCLOZAPINE (increased risk of agranulocytosis)
Antivirals
Plasma concentration of everolimus possiblyincreased by ATAZANAVIR, DARUNAVIR, INDINAVIR,and RITONAVIR and.SAQUINAVIR-manufacturer of everolimus advises avoid concomitant use.
Calcium-channel Blockers
Plasma concentration of both drugs may increase when everolimusgiven with• VERAPAMIL (consider reducing the dose of everolimus)
Cyclosporine
Plasmaconcentration of everolimus increased by cyclosporine (consider reducing the dose of everolimus)
Cytotoxics
Plasma concentration of everolimus increased by IMATINIB (consider reducing the dose of everolimus)
Grapefruit Juice
Manufacturer of everolimus advises avoid concomitant use with grapefruit juice. (BNF 1223)

3- How to take Everolimus

Patient receiving Everolimus should be under the supervision of a physician experienced in cancer chemotherapy. Your doctor will decide about the dose, which will depend upon your height and body weight.
General dosing considerations:
Usual adult dose:
Advanced pancreatic neuroendocrine tumors/breast cancer/ renal angiomyolipoma/renal cell carcinoma–
Usual dosage: 10 mg once daily.
Dosageadjustment: severeand/orintolerable adverse reactions may require temporary dose interruption (with or without a dose reduction) or discontinuation. If dose reduction is required, the suggested dosage is approximately 50% lower than the daily dose previously administered.

Everolimus Dosage Adjustment and Management Recommendations for Adverse Reactions for Advanced Pancreatic Neuroendocrine Tumors/ Breast Cancer/Renal Angiomyolipoma/Renal Cell Carcinoma

Adverse reactions	Severity[a]	Dose adjustment[b] and Management recommendations
Noninfectious pneumonitis	Grade 1: asymptomatic, radiographic, findings only	No dose adjustment required. Initiate appropriate monitoring.
	Grade 2: symptomatic, not interfering with ADL[c]	Consider interruption of therapy, rule out infection, and consider treatment with corticosteroids until symptoms improve to ≤ grade 1. Reinitiated everolimus at a lower dose. Discontinue treatment if failure to recover within 4wk.
	Grade 3: symptomatic,interfering with ADL,O2 indicated	Interrupt everolimus until symptoms resolve to ≤ grade 1. Rule out infection, and consider treatment with corticosteroids. Consider reinitiating everolimus at a lower dose. If toxicity recurs at grade 3, consider discontinuation.
	Grade 4: life-threatening, ventilatory support indicated	Discontinue everolimus rule out infection, and consider treatment with corticosteroids
Stomatitis	Grade 1: minimal symptoms, normal diet	No dose adjustment required. Manage with nonalcoholic or salt water (0.9%) mouthwash Several times a day.
	Grade 2: symptomatic but can eat and swallow modified diet	Temporary dose interruptionuntil recovery to grade ≤ 1. Reinitiate everolimus at thesame dose. If stomatitis recursat grade 2, interrupt dose until recovery to grade ≤ 1. Reinitiate everolimus at a lower dose. Manage with topical analgesic mouth treatments(eg, benzocaine, butyl aminobenzoate, tetracaine hydrochloride, menthol, phenol) with or without topical corticosteroids (ie, triamcinolone oral paste).[d]
	Grade 3:symptomatic and unable to adequately aliment or hydrate orally	Temporary dose interruptionuntil recovery to grade ≤ 1. Reinitiate everolimus at a lower dose. Manage with topical analgesic mouth treatments (ie, benzocaine, butyl aminobenzoate, tetracaine hydrochloride, menthol, phenol) with or without topical corticosteroids (ie, triamcinolone oral paste).[d]
	Grade 4:symptoms associated with life-threatening consequences	Discontinue everolimus and treat with appropriate medical associated.
Other nonhematologic toxicities (excluding: metabolic events)	Grade 1:	If toxicity is tolerable, no dose adjustment required. Initiate appropriate medical therapy and monitor.
	Grade 2:	If toxicity is tolerable, no dose adjustment required. Initiate appropriate medical therapy and monitor. If toxicity becomes intolerable, temporary doseInterruption until recovery to grade ≤ 1. Reinitiate everolimus at the same dose. If toxicity recurs at grade 2, interrupt everolimus until recovery to grade ≤ 1. Reinitiate everolimus at a lower dose.
	Grade 3:	Temporary dose interruption until recovery to grade ≤ 1. Initiate appropriate medical therapy and monitor. Consider reinitiating everolimus at a lower dose. If toxicity recurs at grade 3, consider discontinuation.
	Grade 4:	Discontinue everolimus and treat with appropriate medical therapy.
Metabolic events(eg,hyperglycemia,dyslipidemia)	Grade 1:	No dose adjustment required. Initiate appropriate medical therapy and monitor.
	Grade 2:	No dose adjustment required. Manage with appropriate medical therapy and monitor.
	Grade 3:	Temporary dose interruption. Reinitiate everolimus at a lower dose. Manage with appropriate medical therapy and monitor.
	Grade 4:	Discontinue everolimus and treat with appropriate medical therapy.

a Severity grade description:1 = mild symptoms, 2 = moderate symptoms, 3 = severe symptoms, 4 = life-threatening symptoms.
bIf dose reduction is required, the suggested dose is approximately 50% lower than the dose previously administered.
c ADL = activities of daily living.
dAvoid using agents containing alcohol, hydrogen peroxide, iodine, and thyme derivatives in management of stomatitis because they may worsen mouth ulcers.

Subependymal giant cell astrocytoma Initial dosage: 4.5 mg/m2 once daily. Round dose to the nearest strength.
Do not combine tablets and tablets for oral suspension to achieve the desired total dose.
Dosage adjustment: Use therapeutic drug monitoring to guide subsequent dosing.
Adjust dose at 2-week intervals as needed to achieve and maintain trough concentrations of 5 to 15 ng/mL. For trough concentrations less than 5ng/mL, increase the daily dose by 2.5 mg. For trough concentrations greater than 15 ng/mL, reduce the daily dose by 2.5 mg. If dose reduction is required for patients receiving the lowest available strength, administer every other day.
Temporarily interrupt or permanently discontinue treatment for severeor intolerable adverse reactions. If dose reduction is required upon reinitiation reduce the dose of everolimus by approximately 50%. If dose reduction is required for patients receiving the lowest available strength, administer every other day.
Off-label dosing - Carcinoid tumors, advanced:
10 mg once daily (in combination with octreotide long-acting repeatable) until disease progression or toxicity.
Waldenstrommacroglobinemia,relapsed or refractory:10mg once daily until disease progression or toxicity.
Pediatric:
Subependymal giant cell astrocytoma -
1 year and older: See Adults for dosing.
Hepatic function impairment: Advanced neuroendocrine tumors of pancreatic origin/ advanced renal cell carcinoma/breast cancer/renal angiomyolipoma-
Mild hepatic, impairment (Child-Pugh class A): 7.5 mg daily; may be decreased to 5 mg if not well tolerated.
Moderate hepatic impairment (Child-Pugh class B): 5 mg daily; may be decreased to 2.5 mg if not well tolerated.
Severe hepatic impairment (Child-Pugh class C): If the desired benefit outweighs the risk, a dosage of 2.5 mg daily may be used but must not be exceeded.
Liver transplantation/renal transplantation-mild hepatic impairment (Child-Pugh class A): Reduce the initial daily dose by approximately one-third of the normally recommended daily dose; monitor blood concentrations to make further adjustments as necessary.
Moderate or severe hepatic impairment (Child-Pugh class B or C): Reduce the daily dose by one-half the recommended initial daily dose; monitor bloodconcentrations to make further adjustments as necessary.
Sub ependymal giant cell astrocytoma –
Mild or moderate hepatic impairment (Child-Pugh class A or B): Adjustment to the starting dose may not be needed. Subsequent dosing should be individualized based on therapeutic drug monitoring.
Several hepatic impairment (Child-Pugh class C): reduce the starting dose of everolimus by approximately 50% to 2.5 mg/m2 once daily.
Therapeutic drug monitoring:
Everolimus-routine everolimus whole blood therapeutic drug concentration monitoring is recommended for all patients. The recommended everolimus therapeutic range is 3 to 8 ng/mL (liver and renal transplantation) and 5 to 15 ng/mL (subependymal giant cell astrocytoma). Pay close attention to clinical signs and symptoms, tissue biopsies, and laboratory parameters.
It is important to monitor everolimus blood concentrations in patients with hepatic impairment during coadministration of CYP3A4/P-gp inducers or inhibitors, when switching cyclosporine formulations, and/or when cyclosporine dosing is reduced according to recommended target concentrations.
Dosage adjustments of everolimus should be based on trough concentrations obtained 4 or 5 days after a previous dosing change. There is an interaction of cyclosporine on everolimus and, consequently, everolimus concentrations may decrease if cyclosporine exposure is reduced. There is little to no pharmacokinetic interaction of Tacrolimus on everolimus, and, thus, everolimus concentrations do not decrease if the Tacrolimus exposure is reduced.
The everolimus recommended therapeutic range of 3 to 8 ng/mL for liver and renal transplantation is based on a liquid chromatograph coupled to tandem mass spectrometry (LC-MS/MS) assay method. Currently, everolimus whole blood concentrations may be measured by chromatographic or immunoassay methodologies. Because the measured everolimus whole blood concentrations depend on the assay used, individual patient sample concentration values from different assays may not be interchangeable. Consideration of assay results must be made with knowledge of the specific assay used. Therefore, communication should be maintained with the laboratory performing the assay.
Liver transplantation -
Tacrolimus: Both Tacrolimus doses and the target range for whole blood trough concentrations should be reduced when given in a regimen with everolimus in order to minimize the potential risk of nephrotoxicity. Therecommended Tacrolimus therapeutic range when administered with everolimus is whole blood trough (C-oh) concentrations of 3 to 5 ng/mL by 3 weeks after the first dose of everolimus (approximately month 2) and through month 12 posttransplant.
Renal transplantation -
Cyclosporine:
The recommended cyclosporine therapeutic ranges when administered with everolimus are 100 to 200 ng/mL through month 1 posttransplant, 75 to 150 ng/mL at months 2 and 3 posttransplant, 50 to 100 ng/mL at month 4 posttransplant, and 25 to 50 ng/mL from months 6 through 12 posttransplant.
Subependymal giant cell astrocytoma - Monitor everolimus whole blood trough levels routinely in all patients. When possible, use the same assay and laboratory for therapeutic drug monitoring throughout treatment.
Administration:
Hazardous agent; use appropriate precautions for handling and disposal (NIOSH 2014, (group 1]).
Everolimus- Administer once daily: at the same time every day, either consistently with or without food. Tablets should be swallowed whole with a glass of water. The tablets should not be broken, chewed, or crushed (do not administer tablets that are crushed or broken). Avoid contact with or exposure to crushed or broken tablets. Everolimus missed doses may be taken up to 6 hours after regularly scheduled time; if more than 6 hours, resume at next regularly scheduled time.(Fact 3859)
Usual pediatric dose:
Everolimus is recommended for use only in patients with SEGA (subependymal giant cell astrocytoma) who is aged ≥3 years. A prospective, open-label, single-arm trial was conducted to evaluate the safety and efficacy of Everolimus in patients with SEGA associated with TSC. In total, 28 patients received treatment with Everolimus; median age was 11years (range 3-34). Everolimus has not been studied in patients with SEGA <3 years of age. (FDA leaflet)
Usual elderly dose:
In the randomized advanced RCC study, 41%of Everolimus-treated patients were ≥65 years in age, while 7% were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
No dosage adjustment is required in elderly patients (FDA leaflet)
Overdose:
In animal studies, everolimus showed a low acute toxic potential. No lethality or severe toxicity was observed in either mice or rats given single oral doses of 2000 mg/kg. Reported experience with overdose in humans is very limited.
Single doses of up to 70 mg have been administered. The acute toxicity profile observed with the 70 mg dose was consistent with that for the 10 mg dose.(FDA leaflet)

4- Possible side effects

Every medicine has some side effects or risks associated with its use. Although most people take medicines without experiencing any side effects, some may be affected. In these cases, pleaseconsult your physician or pharmacist. Many side effects of antineoplastic therapy are unavoidable and represent the medication's pharmacologic action. Some of these are actually used as parameters to aid in individual dosage titration. The following side/adverse effects have been selected on the basis of their potential clinical significance:
Common or very common
Abdominal pain, anorexia, arthralgia, asthenia, chest pain, convulsions, dehydration, diarrhea, dry mouth, dysphagia, electrolyte disturbance, epistaxis, Eyelid oedema, fatigue, hand-foot syndrome, headache, hypercholesterolaemia, hyperglycaemia, hyperlipidaemia, hypertension, hypoglycaemia, increased susceptibility to aspergillosis, increased susceptibility to candidiasis ,increased susceptibility to infections ,increased susceptibility to pneumonia ,insomnia ,interstitial lung disease ,irritability, nail disorders, peripheral oedema, pneumonitis - renal failure, skin disorders, taste disturbance
Uncommon
Aggression, agitation, Congestive heart failure, flushing, impaired wound healing, rhabdomyolysis.
Frequency not known
Alopecia,bone-marrow suppression, haemorrhage, hepatitis B reactivation, Hyperuricaemia, nausea, oralmucositis, Thromboembolism, tumourlysis syndrome, vomiting .
Side-effects further information
Reduce dose or discontinue if severe side-effects occur. Consult product literature. (BNF 827)

5- Storing Everolimus

Keep out of the reach and sight of children.
Store below25°C and Protect from light and moisture.
Do not use Everolimus after the expiry date which is stated on the box after "Exp.".
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6- Further information

What Everolimuscontains
Medicinally active substance:
1 Tablet contains5 mg and 10 mgeverolimus.
Other ingredients:
Lactose monohydrate, Crospovidone,Lactose anhydrous,Magnesium Stearate,ButylatedHydroxytoluene,Ascorbic acid,Hypromellose.
Contains of the pack:
Each box contains 4 blister cards of 7 tablets each.

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EVGT-0000-LF-00

Sobhan Oncology Co.	
Leaflet	Everolimus
Color	Pantone 185 C & 295 C
Size	350x290 Tolerance: ±1mm
File name	EVGT-0000-LF-00
Date	02.02.1398