GRIP Tablets*

گرِپ ٹیبلٹس

COMPOSITION: *Each tablet contains:* Escitalopram (as oxalate)*.....10 mg
DESCRIPTION: Escitalopram is a selective serotonin (5-HT) re-uptake inhibitor. Escitalopram is the pure S-enantiomer (single isomer) of the racemic bicyclic phthalane derivative citalopram. Escitalopram oxalate is designated S- (+)-1-[3-(dimethyl-amino) propyl]-1-(p-fluorophenyl)-5-phthalancarbonitrile oxalate. The molecular formula is $C_{20}H_{21}FN_2O \cdot C_2H_2O_4$ and the molecular weight is 414.40. **PHARMACOLOGY**: *Pharmacodynamics:* Escitalopram is a selective inhibitor of serotonin (5-HT) re-uptake with high affinity for the primary binding site. It also binds to an allosteric site on the serotonin transporter, with a 1000-fold lower affinity. The inhibition of 5-HT re-uptake is the only likely mechanism of action explaining the pharmacological and clinical effects of escitalopram. *Pharmacokinetics:* Absorption is almost complete and independent of food intake. Mean time to maximum concentration (mean T_{max}) is 4 hours after multiple dosing. The apparent volume of distribution after oral administration is about 12 to 26 L/kg. The plasma protein binding is below 80% for escitalopram and its main metabolites. Escitalopram is metabolised in the liver to the pharmacologically active demethylated and didemethylated metabolites. Both of these are pharmacologically active. Biotransformation of escitalopram to the demethylated metabolite is mediated primarily by CYP2C19. Some contribution by the enzymes CYP3A4 and CYP2D6 is possible. The elimination half-life after multiple dosing is about 30 hours and the oral plasma clearance is about 0.6 L/min. The major metabolites have a significantly longer half-life. Escitalopram and major metabolites are assumed to be eliminated by both the hepatic (metabolic) and the renal routes, with the major part of the dose excreted as metabolites in the urine. Steady state plasma levels are achieved in about 1 week. Average steady-state concentrations of 50 nmol/L (range 20 to 125 nmol/L) are achieved at a daily dose of 10 mg. **INDICATIONS:** *GRIP Tablets are indicated for the treatment of:* • Major depressive episodes. • Panic disorder with or without agoraphobia. • Social anxiety disorder (social phobia). • Generalised anxiety disorder. • Obsessive-compulsive disorder **CONTRAINDICATIONS:** • Hypersensitivity to escitalopram or to any of the excipients. • Concomitant treatment with non-selective, irreversible monoamine oxidase inhibitors. **POSSIBLE ADVERSE EFFECTS:** Adverse reactions are most frequent during the first or second week of treatment and usually decrease in intensity and frequency with continued treatment. The most frequently encountered adverse effects are nausea, diarrhea/constipation, vomiting, dry mouth, decreased/increased appetite, anxiety, restlessness, abnormal dreams, insomnia/somnolence, dizziness, paresthesias, sexual dysfunction, sinusitis, yawning, arthalgia, myalgia, fatigue and pyrexia. **DRUG INTERACTIONS:** *Non-selective& Selective MAOIs:* Escitalopram is contra-indicated in combination with non-selective MAOIs. In combination with selective MAOIs like moclobemide & selegiline caution is required due to the risk of developing serotonin syndrome. *Serotonergic Medicinal Products:* Co-administration with serotonergic medicinal products (e.g., tramadol, sumatriptan and other triptans) may lead to serotonin syndrome. *Medicinal Products Lowering the Seizure Threshold:* SSRIs can lower the seizure threshold. Caution is advised when concomitantly using other medicinal products capable of lowering the seizure threshold (e.g., antidepressants (tricyclics, SSRIs), neuroleptics (phenothiazines, thioxanthenes and butyrophenones), mefloquin, bupropion and tramadol). *Lithium, Tryptophan:* There have been reports of enhanced effects when SSRIs have been given together with lithium or tryptophan, therefore concomitant use of SSRIs with these medicinal products should be undertaken with caution. *Oral Anticoagulants:* Altered anti-coagulant effects may occur when escitalopram is combined with oral anticoagulants. *CYP2C19 Inhibitors:* Caution should be exercised when used concomitantly with CYP2C19 inhibitors (e.g., omeprazole, esomeprazole, fluvoxamine, lansoprazole, ticlopidine) or cimetidine. A reduction in the dose of escitalopram may be necessary based on monitoring of side-effects during concomitant treatment. *Drugs Metabolised by CYP2D6:* Caution is recommended when escitalopram is co-administered with medicinal products that are mainly metabolized by this enzyme, e.g., flecainide, propafenone and metoprolol desipramine, clomipramine and nortriptyline or antipsychotics like risperidone, thioridazine and haloperidol. Dosage adjustment may be warranted. **WARNINGS:** *Use in Children & Adolescents Under 18 Years of Age:* Escitalopram should not be used in the treatment of children and adolescents under the age of 18 years due to suicide related behaviours and hostility. *Paradoxical Anxiety:* Some patients with panic disorder may experience increased anxiety symptoms at the beginning of treatment with antidepressants. A low starting dose is advised to reduce the likelihood of an anxiogenic effect. *Seizures:* Escitalopram should be discontinued in any patient who develops seizures. SSRIs should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. *Mania:* SSRIs should be used with caution in patients with a history of mania/hypomania. *Diabetes:* In patients with diabetes, treatment with an SSRI may alter glycaemic control (hypoglycaemia or hyperglycaemia). Insulin and/or oral hypoglycaemic dosage may need to be adjusted. *Suicide/Suicidal Thoughts:* Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. In addition, there is a possibility of an increased risk of suicidal behaviour in young adults. *Akathisia/Psychomotor Restlessness:* The use of SSRIs/SNRIs has been associated with the development of akathisia. So in patients who develop these symptoms, increasing the dose may be detrimental. *Hyponatraemia:*

Hyponatraemia, probably due to inappropriate antidiuretic hormone secretion (SIADH), has been reported rarely with the use of SSRIs and generally resolves on discontinuation of therapy. *Haemorrhage:* There have been reports of cutaneous bleeding abnormalities, such as ecchymoses and purpura, with SSRIs. Caution is advised in patients taking SSRIs, particularly in concomitant use with oral anticoagulants and in patients with known bleeding tendencies. *ECT (Electroconvulsive Therapy):* There is limited clinical experience of concurrent administration of SSRIs and ECT. Therefore caution is advisable. *Non-selective MAOIs:* Escitalopram is contra-indicated in combination with non-selective MAOIs. *Serotonin Syndrome:* Co-administration with selective MAOIs and serotogenic medicinal products may lead to Serotonin Syndrome, characterized by agitation, tremors, myoclonus, and hyperthermia, which indicates immediate discontinuation of treatment. *Effects on Ability to Drive a Vehicle or Operate Machinery:* Patients should be cautioned about the potential risk of an influence on their ability to drive a vehicle or operate machinery. *Pregnancy:* Escitalopram should not be used during pregnancy unless clearly necessary and only after careful consideration of the risk/benefit. *Lactation:* Breast-feeding is not recommended during treatment with escitalopram. **DOSAGE & ADMINISTRATION:** GRIP Tablets are administered as a single daily dose and may be taken with or without food. *Major Depressive Episodes:* Usual dosage is 1 tablet of GRIP 10 mg once daily. The dose may be increased to a maximum of 2 tablets of GRIP 10 mg (20 mg) daily. Usually 2-4 weeks are necessary to obtain antidepressant response. After the symptoms resolve, treatment for at least 6 months is required for consolidation of the response. *Panic Disorder with or without Agoraphobia:* An initial dose of 1/2 tablet of GRIP 10 mg (5 mg) is recommended for the first week before increasing the dose to 1 tablet of GRIP 10 mg daily. The dose may be further increased, up to a maximum of 2 tablets of GRIP 10 mg (20 mg) daily. Maximum effectiveness is reached after about 3 months. The treatment lasts several months. *Social Anxiety Disorder:* Usual dosage is 1 tablet of GRIP 10 mg once daily. Usually 2-4 weeks are necessary to obtain symptom relief. The dose may be decreased to1/2 tablet of GRIP 10 mg (5 mg) or increased to a maximum of 2 tablets of GRIP 10 mg (20 mg) daily. Social anxiety disorder is a disease with a chronic course, and treatment for 12 weeks is recommended to consolidate response. Long-term treatment of responders for 6 months can be considered on an individual basis to prevent relapse. Treatment benefits should be re-evaluated at regular intervals. *Generalised Anxiety Disorder:* Initial dosage is 1 tablet of GRIP 10 mg once daily. The dose may be increased to a maximum of 2 tablets of GRIP 10 mg (20 mg) daily. Long term treatment of responders has been studied for at least 6 months in patients receiving 20 mg/day. Treatment benefits and dose should be re-evaluated at regular intervals. *Obsessive-Compulsive Disorder:* Initial dosage is 1 tablet of GRIP 10 mg once daily. The dose may be increased to a maximum of 2 tablets of GRIP 10 mg (20 mg) daily. As OCD is a chronic disease, patients should be treated for a sufficient period to ensure that they are symptom free. *Elderly Patients (> 65 years of age):* Initial treatment with half the usually recommended dose and a lower maximum dose should be considered. *Reduced Renal Function:* Caution is advised in patients with severely reduced renal function (CLCR less than 30ml/min). *Reduced Hepatic Function:* An initial dose of 5 mg daily for the first 2 weeks of treatment is recommended in patients with mild or moderate hepatic impairment. Caution and extra careful dose titration is advised in patients with severely reduced hepatic function. *Poor Metabolisers of CYP2C19:* For patients who are known to be poor metabolisers with respect to CYP2C19, an initial dose of 5 mg daily during the first 2 weeks of treatment is recommended. **SPECIAL INSTRUCTIONS TO THE PHYSICIAN:** *Abrupt Discontinuation of Treatment:* Abrupt discontinuation should be avoided. When stopping treatment with escitalopram the dose should be gradually reduced over a period of at least 1 to 2 weeks in order to reduce the risk of discontinuation symptom. *Switching Treatment with MAOIs:* Escitalopram is contra-indicated in combination with non-selective MAOIs. Escitalopram may be started 14 days after discontinuing treatment with an irreversible MAOI and at least one day after discontinuing treatment with the reversible MAOI moclobemide. At least 7 days should elapse after discontinuing escitalopram treatment, before starting a non-selective MAOI. *Overdosage:* There is no specific antidote. Establish and maintain an airway, ensure adequate oxygenation and respiratory function. Gastric lavage and the use of activated charcoal should be considered. Gastric lavage should be carried out as soon as possible after oral ingestion. Cardiac and vital signs monitoring are recommended along with general symptomatic supportive measures. **STORAGE/PRECAUTIONS:** Store in a cool, dry and dark place between 15-30 °C. Keep all medicines out of the childrenís reach. **PRESENTATION:** GRIP Tablets are available in packing containing 10 & 14 tablets respectively. *Scotmann Specs.

عمومی خوراک: ڈاکٹر کی ہدایت کے مطابق۔ احتیاط: دوا صرف مستند ڈاکٹر کے زیرِ ہدایت استعمال کریں۔ روشنی، نمی اور گرمی سے بچائیں۔ 15 سے 30 ڈگری سینٹی گریڈ کے درمیان محفوظ کریں۔ تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

Complete Medical Information available only for doctors on request.

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Manufactured by: **Scotmann Pharmaceuticals,** 5-D, I-10/3 Industrial Area, Islamabad-Pakistan.