Belexa

(Escitalopram USP)

(USP Specifications)
10mg Tablets

بیلیکسا

(ایسیٹالوپرام یو ایس پی)

۱۰ ملی گرام ٹیبلیٹس

USP Specs.

Composition:

Each film coated tablet contains:

Escitalopram as oxalate USP....10mg

PHARMACOLOGICAL CLASSIFICATION:

Psychoanaleptics (antidepressants) 5HT reuptake inhibitor.

PHARMACOLOGICAL ACTION:

Mechanism of action

Escitalopram is a selective serotonin reuptake inhibitor (SSRI) and belongs to a group of medicines known as antidepressants. These medicines help to normalize the levels of serotonin in the brain. Disturbances in the serotonin, system of the brain are key factors in the development of depression and related disorders. Escitalopram has minimal effect on noradrenaline (NA), dopamine (DA) and gamma aminobutyric acid (GABA) uptake. Escitalopram has no or very low affinity for a series of rt receptors including 5-HT1A, 5-HT2, DA D1 and D2 receptors, alpha1-,alpha2-, (beta-adrenoceptors, histamine H1, muscarine cholinergic, benzodiazepine, and opioid receptors.

INDICATIONS:

Belexa (Escitalopram) is used for the treatment of depression generalized anxiety, social anxiety and panic disorders. This disease is characterized by low/depressed mood, lack of energy, melancholia feelings of little or no worth and sleeping disorders. Depression may also be accompanied by suicidal thoughts.Depressed patients may further suffer from symptoms of anxiety. Belexa (Escitalopram) is also used for the treatment of panic disorder. This disease is characterized by patient's development unexpected attacks of intense panic or anxiety when faced with particular situations or due to the fear of experiencing new attacks precisely what triggers the attacks varies from patient to patient. The attacks recur when the patient faces the same situation again.

Children: as safety and efficacy have not been established in this population.

Monoamine Oxidase Inhibitors- Cases of serious reactions have been reported in patients receiving an SSRI such as (Escitalopram) in combination with a monoamine oxidase inhibitor (MAOI), and in patients who have recently discontinued an (Escitalopram) should not be used in combination with an MAOI.

(Escitalopram) may be started 14 days after discontinuing treatment with an MAOI.

At least 7 days should elapse after discontinuing (Escitalopram) treatment before starting an MAOI.

PHARMACOKINETICS:

Absorption

Absorption is independent of food intake (mean Tmax is 4 hours after multiple dosing).

Distribution

The apparent volume of distribution (Vd,beta/F) after oral administration is about 12 to 26 L/kg.

The plasma protein binding of escitalopram is approximately 55%.

Biotransformation

Escitalopram is metabolised in the liver to the demethylated and di-demethylated metabolites.

Alternatively, the nitrogen may be oxidised to form the N-oxide metabolite. Both parent and metabolites are partialy excreted as glucuronides. Unchanged escitalopram is the predominant compound in plasma. After multiple dosing the mean concentrations of the demethyl and di-demethyl metabolites are usually 28-31% and <5% of the escitalopram concentration, respectively. Biotransformation of escitalopram to the demethylated metabolite is mediated by a combination of CYP2C19, CYP3A4 and CYP2D6.

Elimination

The elimination half-life after multiple dosing is about 30 hours and the oral plasma clearance (cloral) is about 0.60 L/min. Escitalopram and major metabolites are excreted like racemic citalopram- assumed to be eliminated both by the hepatic (metabolic) and the renal routes with the major part of the dose excreted as metabolites in urine. Hepatic clearance is mainly by the P450 enzyme system. CYP2C19 is the primary isoenzyme involved in the demethylation of escitalopram, followed by CYP3A4 and CYP2D6. There is linear pharmacokinetics. 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.

Elderly patients (> 65 years of age)

A longer half-life (about 50%) and decreased clearance values, due to a reduced rate of metabolism, have been demonstrated in the elderly.

Reduced hepatic function

Escitalopram is eliminated more slowly in patients with reduced hepatic function. The half-life of escitalopram is approximately twice as long in patients with hepatic impairment and steady state escitalopram concentrations at a given dose will be approximately twice as high as in patients with normal liver function.

Reduced renal function

Escitalopram is eliminated more slowly in patients with mild to moderate reduction of renal function with no major impact on the escitalopram concentrations in serum. At present no information is available for the treatment of patients with severely reduced renal function (creatinine clearance < 30 mL/min).

Polymorphism

Based on in-vitro results with escitalopram and in-vivo results with the racemic citalopram, genetic polymorphism with respect to CYP2D6 is not known, with respect to CYP2C19, it may be of clinical relevance, as shown in limited numbers.

WARNINGS AND SPECIAL PRECAUTIONS:

Mania- (Escitalopram) should be discontinued in any patient entering a manic phase. (Escitalopram) should be used with caution in patients with a history of mania/hypomania.

Paradoxical anxiety- Some patients with panic disorder may experience increased anxiety symptoms at the start of treatment with antidepressants. This paradoxical reaction usually subsides within two weeks during continued treatment. A low starting dose is advised to reduce the likelihood of a paradoxical anxiogenic effect.

Seizures- (Escitalopram) should be discontinued in any patient who develops seizures. (Escitalopram) should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored.

(Escitalopram) should be discontinued if there is an increase in seizure frequency.

Diabetes mellitus- In patients with diabetes mellitus treatment with (Escitalopram) may alter glycaemic control, possibly due to improvement of depressive symptoms. Insulin and/or oral hypoglycaemic dosage may need to be adjusted.

Suicide- As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored during this period. The possibility of a suicide attempt is inherent in depression and may persist until significant therapeutic effect is achieved.

Haemorrhage- There have been reports of cutaneous bleeding abnormalities, such as ecchymoses and purpura, with (Escitalopram). Caution is advised in patients taking (Escitalopram), particularly in concomitant use with medicines known to affect platelet function (e.g. atypical antipsychotics and phenothiazines, most tricyclic antidepressants, aspirin and non-steroidal anti-inflammatory medicines (NSAIDs), as well as in patients with a history of bleeding disorders.

ECT (electroconvulsive therapy) - There is limited published clinical experience of concurrent administration of (Escitalopram) and ECT, therefore caution is advisable.

Effects on ability to drive and use machines

(Escitalopram) does not impair intellectual function or psychomotor performance. Nevertheless, patients who are depressed and require treatment may have an impaired ability to drive or operate machinery. They should be warned of the possibility and advised to avoid such tasks if so affected. Risk of Serotonin syndrome When stopping (Escitalopram) therapy, gradual dose reduction should be considered.

INTERACTIONS:

Escitalopram has a low potential for clinically significant medicine interactions. In vitro studies have shown that the biotransformation of escitalopram to its demethylated metabolites depends on three parallel pathways (cytochrome P450 (CYP) 2C19, 3A4 and 2D6). Escitalopram is a very weak inhibitor of isoenzyme CYP1A2, 2C9, 2C19, 2E1, and 3A, and weak inhibitor of 2D6.

Effects of other medicinal products on BELEXA (ESCITALOPRAM) in vivo

Ritonavir:

The pharmacokinetics of single doses of (Escitalopram) was not changed by co-administration with a single dose of ritonavir (CYP3A4 inhibitor).

Ketoconazole:

Co-administration with ketoconazole (potent CYP3A4 inhibitor) did not change the pharmacokinetics of racemic citalopram.

Cimetidine:

Co-administration of racemic citalopram with cimetidine (potent CYP2D6, 3A4 and 1A2 inhibitor) resulted in increased plasma concentrations of the racemate (43% increase in AUC, 39% increase in C_{max}). Thus, caution should be exercised at the upper end of the dose range of (Escitalopram) when used concomitantly with high doses of cimetidine.

Monoamine Oxidase inhibitors (MAOI), Sumatriptan & Tramadol:

Co-administration with MAO inhibitors may cause serotonin syndrome. Co-administration with other serotonergic medicines (e.g. tramadol, sumatriptan) as well as other antidepressants with serotonergic properties may lead to an enhancement of serotonin associated effects, e.g. the serotonin syndrome. There have been reports of enhanced effects when (Escitalopram) has been given with lithium or tryptophan and therefore concomitant use of (Escitalopram) with these medicines should be undertaken with caution.

Effects of BELEXA (ESCITALOPRAM) on other medicinal products in vivo

Desipramine:

Co-administration with a single dose of desipramine (a CYP2D6 substrate) resulted in a two fold increase in plasma levels of desipramine. Therefore, caution is advised when (Escitalopram) and desipramine are co-administered. A similar increase in plasma levels of desipramine, after administration of imipramine, was seen when given together with racemic citalopram.

Some cases presented with features resembling serotonin syndrome.

Metoprolol:

Co-administration with a single dose of metoprolol 100 mg (a CYP2D6 substrate) resulted in a two fold increase in the C_{max} and a 52% increase of the AUC of metoprolol. However, the combination had no clinically significant effects on blood pressure and heart rate.

Selegiline:

Racemic citalopram increased the AUC of selegiline by 29%.

Other:

Pharmacokinetic interaction studies with racemic citalopram have demonstrated no clinically important interactions with carbamazepine (CYP3A4 substrate), triazolam (CYP3A4 substrate), theophylline (CYP1 A2 substrate) (single dose), warfarin (CYP3A4 and CYP2C9 substrate), levomepromazine (CYP2D6 inhibitor), lithium and digoxin. However, prothrombin time was slightly increased after a single dose of 25mg warfarin. The International Normalised Ratio (INR) needs to be carefully monitored in patients on the combination.

PREGNANCY AND LACTATION:

The safety of (Escitalopram) in pregnant and lactating women has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Doses of Escitalopram used in the treatment of generalised anxiety disorder & social anxiety disorder.

Adults

Major depressive episodes

(Escitalopram) should be administered as a single oral dose of 10 mg daily in otherwise healthy adults. Depending on individual patient response, the dose may be increased to a maximum of 20 mg daily.

Usually 2-4 weeks are necessary for an antidepressant response.

Panic disorder

A single oral dose of 5 mg is recommended for the first week before increasing the dose to 10 mg daily. The dose may be further increased, up to a maximum of 20 mg daily, dependent on individual patient response.

Elderly patients (> 65 years of age)

A longer half-life and a decreased clearance have been demonstrated in the elderly, therefore a lower initial and maximum dose should be considered.

Reduced renal function

Dosage adjustment is not necessary in patients with mild or moderate renal impairment. No information is available on the treatment of patients with severely reduced renal function (creatinine clearance < 30 mL/min.).

Reduced hepatic function

Dosages should be halved to the lower end of the dose range in patients with hepatic insufficiency. (Escitalopram) is administered as a single daily dose.

(Escitalopram) may be taken without regard to food intake

SIDE EFFECTS:

Adverse reactions observed with (Escitalopram) are most frequent during the first one or two weeks of treatment and may decrease in intensity and frequency with continued treatment.

After prolonged administration abrupt cessation of (Escitalopram) may produce withdrawal reactions in some patients.

Common (>1/100, <1/10)

Both genders:

Nausea, insomnia, somnolence, sweating increased, diarrhoea, constipation, dizziness, fatigue, appetite decreased, sinusitis, libido decreased, pyrexia, yawning.

Gender specific:

Ejaculation disorder, impotence, abnormal orgasm (female).

Uncommon (>1/1000, <1/100)

Sleep disorder, taste disturbance

SSRI - Class Reactions

The following adverse reactions apply to the therapeutic class of SSRIs.

Cardiovascular disorders - Postural hypotension

Disorders of metabolism and nutrition - Hyponatraemia, inappropriate ADH secretion.

Disorders of the eye - Abnormal vision

Gastrointestinal disorders - Nausea, vomiting, dry mouth, diarrhoea, anorexia.

General disorders - Insomnia, dizziness, fatigue, drowsiness, anaphylactoid reactions.

Hepato-biliary disorders - Abnormal liver function tests.

Musculoskeletal disorders - Arthralgia, myalgia.

Neurological disorders - Seizures, tremor, movement disorders, serotonin syndrome (typically characterized by a rapid onset of changes in mental state, with confusion, mania, agitation, hyperactivity, shivering, fever, tremor, ocular movements, myoclonus, hyperreflexia, and incoordination).

Psychiatric disorders - Hallucinations, mania, confusion, agitation, anxiety, depersonalisation, panic attacks, nervousness.

Renal and urinary disorders - Urinary retention.

Reproductive disorders - Galactorrhoea, sexual dysfunction such as ejaculation disorder and anorgasmia.

Skin disorders - Rash, ecchymoses, pruritus, angioedema, sweating.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Doses of 190 mg have been taken without any symptoms being reported.

Treatment

There is no specific antidote. Treatment is supportive and symptomatic. Gastric lavage should be carried out as soon as possible after oral ingestion. Cardiac and vital signs monitoringa re recommended along with general symptomatic supportive measures.

Dosage & Instructions:

Store at room temperature (25ºC - 30ºC). Protect from sunlight, heat & moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Belexa 10mg Tablets available in 2x10's Packs

Manufactured by:
LISKO
Lisko Pakistan (Pvt.) Ltd.
L-10-D Block-21 Shaheed Rashid Minhas Road, F.B. Industrial Area,Karachi.

Marketed by:
ORGANIC Pharmaceuticals