# Questa® 10mg Tablets
(Escitalopram)

# کوئیسٹا ۱۰ ملی گرام ٹیبلیٹس
(ایسیٹالوپرام)

**WARNING: Suicidality and Antidepressant Drugs**
Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Escitalopram or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Escitalopram is not approved for use in pediatric patients less than 18 years of age.

**QUALITATIVE AND QUANTITATIVE COMPOSITION**
**Questa 10mg Tablets**
Each film coated tablet contains:
Escitalopram Oxalate USP eq. to
Escitalopram.....10mg
(Product specs: USP)

**PHARMACEUTICAL FORM**
Film-coated tablets

**CLINICAL PARTICULARS**
**THERAPEUTIC INDICATIONS:**

Questa tablets are indicated for the following indications:
- Treatment of major depressive episodes.
- Treatment of panic disorder with or without agoraphobia.
- Treatment of social anxiety disorder (social phobia).
- Treatment of generalized anxiety disorder.
- Treatment of obsessive-compulsive disorder.

**POSOLOGY AND METHOD OF ADMINISTRATION**
Posology
Safety of daily doses above 20mg has not been demonstrated.

Major depressive episodes
Usual dosage is 10mg once daily. Depending on individual patient response, the dose may be increased to a maximum of 20mg 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 5mg is recommended for the first week before increasing the dose to 10mg daily. The dose may be further increased, up to a maximum of 20mg daily, dependent on individual patient response.
Maximum effectiveness is reached after about 3 months. The treatment lasts several months.

Social anxiety disorder
Usual dosage is 10mg once daily. Usually 2-4 weeks are necessary to obtain symptom relief. The dose may subsequently, depending on individual patient response, be decreased to 5mg or increased to a maximum of 20mg 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.

Generalized anxiety disorder
Initial dosage is 10mg once daily. Depending on the individual patient response, the dose may be increased to a maximum of 20mg daily. Long term treatment of responders can be considered for at least 6 months in patients receiving 20mg/day. Treatment benefits and dose should be re-evaluated at regular intervals.

Obsessive-Compulsive Disorder
Initial dosage is 10mg once daily. Depending on the individual patient response, the dose may be increased to a maximum of 20mg daily.
As OCD is a chronic disease, patients should be treated for a sufficient period to ensure that they are symptom free. Treatment benefits and dose should be re-evaluated at regular intervals.

**Pediatric population**
It should not be used in the treatment of children and adolescents under the age of 18 years.

**Elderly patients (> 65 years of age)**
Initial dosage is 5mg once daily. Depending on individual patient response the dose may be increased to 10mg daily. The efficacy in social anxiety disorder has not been studied in elderly patients.

**Reduced renal function**
Dosage adjustment is not necessary in patients with mild or moderate renal impairment. Caution is advised in patients with severely reduced renal function (CrCl less than 30mL/min).

**Reduced hepatic function**
An initial dose of 5mg daily for the first two weeks of treatment is recommended in patients with mild or moderate hepatic impairment. Depending on individual patient response, the dose may be increased to 10mg daily. Caution and extra careful dose titration are advised in patients with severely reduced hepatic function.

Poor metabolizers of CYP2C19
For patients who are known to be poor metabolizers with respect to CYP2C19, an initial dose of 5mg daily during the first two weeks of treatment is recommended. Depending on individual patient response, the dose may be increased to 10mg daily.

Discontinuation symptoms seen when stopping treatment
Abrupt discontinuation should be avoided. When stopping treatment with escitalopram the dose should be gradually reduced over a period of at least one to two weeks in order to reduce the risk of discontinuation symptoms. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, continue decreasing the dose, but at a more gradual rate.

Method of administration
Questa tablet is administered as a single daily dose and may be taken with or without food.

**CONTRAINDICATIONS:**
- Hypersensitivity to the active substance
- Concomitant treatment with non-selective, irreversible monoamine oxidase inhibitors (MAO-inhibitors) is contraindicated due to the risk of serotonin syndrome with agitation, tremor, hyperthermia etc.
- The combination with reversible MAO-A inhibitors (e.g. moclobemide) or the reversible non-selective MAO-inhibitor linezolid is contraindicated due to the risk of onset of a serotonin syndrome.
- It is contraindicated in patients with known QT interval prolongation or congenital long QT syndrome.
- It is contraindicated together with medicinal products that are known to prolong the QT interval.

**Special warnings and precautions for use**
The following special warnings and precautions apply to the therapeutic class of SSRIs (Selective Serotonin Re-Uptake Inhibitors).

Pediatric population
It should not be used in the treatment of pediatric population. If, based on clinical need, a decision to treat is nevertheless taken, the patient should be carefully monitored for the appearance of suicidal symptoms. In addition, long-term safety data in the pediatric population concerning growth, maturation and cognitive and behavioral development are lacking.

Paradoxical anxiety
Some patients with panic disorder may experience increased anxiety symptoms at the beginning 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 an anxiogenic effect.

Seizures
It should be discontinued if a patient develops seizures for the first time, or if there is an increase in seizure frequency (in patients with a previous diagnosis of epilepsy). SSRIs should be avoided in patients with unstable epilepsy and with controlled epilepsy should be closely monitored.

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

Diabetes
In patients with diabetes, treatment with an SSRI may alter glycemic control (hypoglycemia or hyperglycemia). Insulin and/or oral hypoglycemic dosage may need to be adjusted.

Suicide/suicidal thoughts or clinical worsening
This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.
Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are known to be at greater risk of suicidal thoughts or suicide attempts.

Akathisia/psychomotor restlessness
The use of SSRIs/SNRIs has been associated with the development of akathisia, characterized by a subjectively unpleasant or distressing restlessness and need to move often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Hyponatremia
Hyponatremia, probably due to inappropriate antidiuretic hormone secretion (SIADH), has been reported rarely with the use of SSRIs and generally resolves on discontinuation of therapy. Caution should be exercised in patients at risk, such as the elderly, or patients with cirrhosis, or if used in combination with medications which may cause hyponatremia.

Hemorrhage
Caution is advised in patients taking SSRIs, particularly in concomitant use with oral anticoagulants, with medicinal products known to affect platelet function (e.g. atypical antipsychotics and phenothiazines, most tricyclic antidepressants, acetylsalicylic acid and non-steroidal anti-inflammatory medicinal products (NSAIDs), ticlopidine and dipyridamole) and in patients with known bleeding tendencies.

ECT (electroconvulsive therapy)
Caution is advisable with concurrent administration of SSRIs and ECT.

Serotonin syndrome
Caution is advisable if it is used concomitantly with medicinal products with serotonergic effects such as triptans (including sumatriptan), opioids (including tramadol), and tryptophan.
In rare cases, serotonin syndrome has been reported in patients using SSRIs concomitantly with serotonergic medicinal products. A combination of symptoms, such as agitation, tremor, myoclonus and hyperthermia may indicate the development of this condition. If this occurs treatment with the SSRI and the serotonergic medicinal product should be discontinued immediately and symptomatic treatment initiated.

St. John's wort
Concomitant use of SSRIs and herbal remedies containing St. John's wort (*Hypericum perforatum*) may result in an increased incidence of adverse reactions.

Discontinuation symptoms seen when stopping treatment
Discontinuation symptoms when stopping treatment are common, particularly if discontinuation is abrupt.

The risk of discontinuation symptoms may be dependent on several factors including the duration, dose of therapy and the rate of dose reduction. Dizziness, sensory disturbances (including paraesthesia and electric shock sensations), sleep disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor, confusion, sweating, headache, diarrhea, palpitations, emotional instability, irritability, and visual disturbances are the most commonly reported reactions.
Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity.
They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that escitalopram should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient's needs.

Sexual dysfunction
(SSRIs)/(SNRIs) may cause symptoms of sexual dysfunction. There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRI.

Coronary heart disease
Due to limited clinical experience, caution is advised in patients with coronary heart disease

QT interval prolongation
Escitalopram has been found to cause a dose-dependent prolongation of the QT interval. Cases of QT interval prolongation and ventricular arrhythmia including Torsade de Pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalemia, or with pre-existing QT interval prolongation or other cardiac diseases.
Caution is advised in patients with significant bradycardia; or in patients with recent acute myocardial infarction or uncompensated heart failure.
Electrolyte disturbances such as hypokalemia and hypomagnesaemia increase the risk for malignant arrhythmias and should be corrected before starting treatment.
If patients with stable cardiac disease are treated, an ECG review should be considered before treatment is started.
If signs of cardiac arrhythmia occur during treatment, the treatment should be withdrawn and an ECG should be performed.

Angle-Closure Glaucoma
SSRIs including escitalopram may have an effect on pupil size resulting in mydriasis. This mydriatic effect has the potential to narrow the eye angle resulting in increased intraocular pressure and angle closure glaucoma, especially in patients pre-disposed. It should therefore be used with caution in patients with angle-closure glaucoma or history of glaucoma.

**Fertility, pregnancy, and Lactation**

Pregnancy
It should not be used during pregnancy unless clearly necessary and only after careful consideration of the risk/benefit.
Neonates should be observed if maternal use continues into the later stages of pregnancy, particularly in the third trimester. Abrupt discontinuation should be avoided during pregnancy.

Lactation
It is expected that it will be excreted into human milk. Consequently, breast-feeding is not recommended during treatment

Fertility
Impact on human fertility has not been observed so far.

**Effects on ability to drive and use machines:**
Patients should be cautioned about the potential risk of an influence on their ability to drive a car and operate machinery.

**Undesirable effects**
Adverse reactions listed below are classified according to frequency and System Organ Class (SOC). Frequency categories are defined according to the following convention: Very common (≥ 1/10), Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), Not known.

| System organ class | Adverse reaction | Frequency |
|---|---|---|
| Blood and lymphatic system disorders | Thrombocytopenia | Not known |
| Immune system disorders | Anaphylactic reaction | Rare |
| Endocrine disorders | Inappropriate ADH secretion | Not known |
| Metabolism and nutrition disorders | Decreased appetite, increased appetite, weight increased | Common |
| | Weight decreased | Uncommon |
| | Hyponatremia, anorexia | Not known |
| Psychiatric disorders | Anxiety, restlessness, abnormal dreams, libido decreased Female: anorgasmia | Common |
| | Bruxism, agitation, nervousness, panic attack, confusional state | Uncommon |
| | Aggression, depersonalization, hallucination | Rare |
| | Mania, suicidal ideation, suicidal behaviour | Not known |
| Nervous system disorders | Headache | Very common |
| | Insomnia, somnolence, dizziness, paraesthesia, tremor | Common |
| | Taste disturbance, sleep disorder, syncope | Uncommon |
| | Serotonin syndrome | Rare |
| | Dyskinesia, movement disorder, convulsion, psychomotor restlessness/akathisia | Not known |
| Eye disorders | Mydriasis, visual disturbance | Uncommon |
| Ear and labyrinth disorders | Tinnitus | Uncommon |
| Cardiac disorders | Tachycardia | Uncommon |
| | Bradycardia | Rare |
| | Electrocardiogram QT prolonged, ventricular arrhythmia including Torsade de Pointes | Not known |
| Vascular disorders | Orthostatic hypotension | Not known |
| Respiratory, thoracic and mediastinal disorders | Sinusitis, yawning | Common |
| | Epistaxis | Uncommon |
| Gastrointestinal disorders | Nausea | Very common |
| | Diarrhea, constipation, vomiting, dry mouth | Common |
| | Gastrointestinal hemorrhages (including rectal hemorrhage) | Uncommon |
| Hepatobiliary disorders | Hepatitis, liver function test abnormal | Not known |
| Skin and subcutaneous tissue disorders | Sweating increased | Common |
| | Urticaria, alopecia, rash, pruritus | Uncommon |
| | Ecchymosis, angioedemas | Not known |
| Musculoskeletal and connective tissue disorders | Arthralgia, myalgia | Common |
| Renal and urinary disorders | Urinary retention | Not known |
| Reproductive system and breast disorders | Male: ejaculation disorder, impotence | Common |
| | Female: metrorrhagia, menorrhagia | Uncommon |
| | Galactorrhea Male: priapism Postpartum hemorrhage | Not known |
| General disorders and administration site conditions | Fatigue, pyrexia | Common |
| | Oedema | Uncommon |

**Overdose**
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.
ECG monitoring is advised in case of overdose in patients with congestive heart failure/bradyarrhythmia, in patients using concomitant medications that prolong the QT interval, or in patients with altered metabolism, e.g. liver impairment.

**PHARMACOLOGICAL PROPERTIES**
**Pharmacodynamic Properties**
Pharmacotherapeutic group: antidepressants, selective serotonin reuptake inhibitors
ATC code: N06AB10

Mechanism of action
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.
It has no or low affinity for a number of receptors including 5-$HT_{1A}$, 5-$HT_2$, DA $D_1$ and $D_2$ receptors, $\alpha_1$-, $\alpha_2$-, β-adrenoceptors, histamine $H_1$, muscarine cholinergic, benzodiazepine, and opioid receptors.
The inhibition of 5-HT re-uptake is the only likely mechanism of action explaining the pharmacological and clinical effects of escitalopram.

**PHARMACOKINETIC PROPERTIES**
Absorption
Absorption is almost complete and independent of food intake. (Mean time to maximum concentration (mean Tmax) is 4 hours after multiple dosing). As with racemic citalopram, the absolute bio-availability of escitalopram is expected to be about 80%.

Distribution
The apparent volume of distribution ($V_{d,\beta/F}$) after oral administration is about 12 to 26 L/kg. The plasma protein binding is below 80% for escitalopram and its main metabolites.

Biotransformation
Escitalopram is metabolized in the liver to the demethylated and didemethylated metabolites. Both of these are pharmacologically active. Alternatively, the nitrogen may be oxidized to form the N-oxide metabolite. Both parent substance and metabolites are partly excreted as glucuronides. After multiple dosing the mean concentrations of the demethyl and didemethyl metabolites are usually 28-31% and <5%, respectively, of the escitalopram concentration. Biotransformation of escitalopram to the demethylated metabolite is mediated primarily by CYP2C19. Some contribution by the enzymes CYP3A4 and CYP2D6 is possible.

Elimination
The elimination half-life ($t_{½\beta}$) after multiple dosing is about 30 hours and the oral plasma clearance (Cloral) 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.

Linearity/non-linearity
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.

**Special populations**
Elderly
It appears to be eliminated more slowly in elderly patients compared to younger patients. Systemic exposure (AUC) is about 50 % higher in elderly compared to young healthy ones.

Renal impairment
With racemic citalopram, a longer half-life and a minor increase in exposure have been observed in patients with reduced kidney function (CLcr 10-53 mLmin). Plasma concentrations of the metabolites have not been studied, but they may be elevated.

Hepatic impairment
In patients with mild or moderate hepatic impairment (Child-Pugh Criteria A and B), the half-life of escitalopram is about twice as long and the exposure is about 60% higher than in subjects with normal liver function.

Polymorphism
It has been observed that poor metabolisers with respect to CYP2C19 have twice as high a plasma concentration of escitalopram as extensive metabolisers. No significant change in exposure was observed in poor metabolisers with respect to CYP2D6.

**PHARMACEUTICAL PARTICULARS**
**Incompatibilities**
Not applicable

**Shelf life:** 02 years

**Special precautions for storage**
Protect from heat, sunlight & moisture, store below 30°C.
The expiration date refers to the product correctly stored at the required condition.
Keep out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.

**NATURE AND CONTENTS OF CONTAINER/PRESENTATION**
Questa 10mg Tablets: Cold form & Cold seal Alu Alu blister pack of 14 Tablets

**MARKETING AUTHORIZATION HOLDER**
**Head Office:**
Bosch Pharmaceuticals (Pvt.) Ltd.,
8, Modern Society, Tipu Sultan Road, Karachi-75350, (Pakistan).

**Manufacturer:**
Bosch Pharmaceuticals (Pvt.) Ltd.,
Plot No. 221-223, Sector 23, Korangi Industrial Area Karachi, Pakistan

**MARKETING AUTHORIZATION / REGISTRATION NUMBER**
047212

**DATE FROM WHICH MARKETING IS AUTHORIZED/RENEWAL OF AUTHORIZATION**
02-11-2007/01-11-2022

**DATE OF REVISION OF THE TEXT**
07-02-2024

ہدایات:-
دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
**Bosch Pharmaceuticals (Pvt) Ltd.**
221-223, Sector 23, Korangi Industrial Area,
Karachi - Pakistan