Duzalta®
(DULOXETINE HCl USP)

ڈُزالٹا

COMPOSITION
DUZALTA® 20mg
Each capsule contains……. Duloxetine 20mg
(as enteric coated pellets of Duloxetine hydrochloride)
DUZALTA® 30mg
Each capsule contains……. Duloxetine 30mg
(as enteric coated pellets of Duloxetine hydrochloride)
DUZALTA® 40mg
Each capsule contains……. Duloxetine 40mg
(as enteric coated pellets of Duloxetine hydrochloride)
DUZALTA® 60mg
Each capsule contains…….Duloxetine 60mg
(as enteric coated pellets of Duloxetine hydrochloride)
(USP Specs.)

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS
Data indicates that antidepressants increase the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term use. Data does not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there is a reduction in risk with antidepressant use in patients aged 65 and older.
[see Warnings and Precautions]
In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber [see WARNINGS AND PRECAUTIONS]
Note: *This warning is only applicable to the use of Duloxetine in Major Depressive Disorder*

DESCRIPTION
DUZALTA (Duloxetine) is a selective serotonin and noradrenaline reuptake inhibitor (SSNRI) for oral administration with antidepressant, anxiolytic and central pain inhibitory effects. The chemical name of Duloxetine is (+)-(S)-N-methyl-γ-(1-naphthyloxy)-2 thiophenepropylamine hydrochloride. It has a molecular formula of $C_{18}H_{19}NOS•HCl$.

Clinical Pharmacology

Mechanism of Action

Major Depressive Disorder
Duloxetine is a combined serotonin (5-HT) and noradrenaline (NA) reuptake inhibitor. It weakly inhibits dopamine reuptake, with no significant affinity for histaminergic, dopaminergic, cholinergic, and adrenergic receptors. Increased nor-adrenergic and serotonergic neurotransmission is responsible for its antidepressant, anxiolytic and central pain inhibitory effects.

Stress Urinary Incontinence:
Increased levels of 5-HT and NE in the sacral spinal cord lead to increased urethral tone via enhanced pudendal nerve stimulation to the urethral striated sphincter muscle only during the storage phase of the micturition cycle. This results in stronger urethral closure during urine storage with physical stress that could explain the efficacy of duloxetine in the treatment of women with SUI.

Pharmacodynamics:
Major Depressive Disorder:
Duloxetine is a potent inhibitor of neuronal serotonin and norepinephrine reuptake and a less potent inhibitor of dopamine reuptake. Duloxetine has no significant affinity for dopaminergic, adrenergic, cholinergic, histaminergic, opioid, glutamate, and GABA receptors. Duloxetine does not inhibit monoamine oxidase (MAO). Duloxetine is in a class of drugs known to affect urethral resistance. If symptoms of urinary hesitation develop during treatment with Duloxetine, consideration should be given to the possibility that they might be drug-related.
Stress Urinary Incontinence:
Data indicates that increased levels of 5-HT and NE in the sacral spinal cord, lead to increased urethral tone via enhanced pudendal nerve stimulation to the urethral striated sphincter muscle only during the storage phase of the micturition cycle. A similar mechanism in women is believed to result in stronger urethral closure during urine storage with physical stress that could explain the efficacy of duloxetine in the treatment of women with SUI.
Pharmacokinetics
Absorption:
Duloxetine is well absorbed after oral administration, with a Cmax occurring 6 hours post-dose. The absolute oral bioavailability of duloxetine ranges from 32% to 80% (mean of 50%). Food delays the time to reach the peak concentration from 6 to 10 hours and it marginally decreases the extent of absorption (approximately 11%). These changes do not have any clinical significance.
Distribution:
Duloxetine is approximately 96% bound to human plasma proteins. Duloxetine binds to both albumin and alpha1-acid glycoprotein. Protein binding is not affected by renal or hepatic impairment.
Metabolism:
Duloxetine is extensively metabolized and the metabolites are excreted principally in urine. Both cytochromes P450-2D6 and 1A2 catalyze the formation of the two major metabolites, glucuronide conjugate of 4-hydroxy duloxetine and sulfate conjugate of 5-hydroxy, 6-methoxy duloxetine. Based upon in vitro studies, the circulating metabolites of duloxetine are considered pharmacologically inactive. The pharmacokinetics of duloxetine in patients who are poor metabolizers with respect to CYP2D6 has not been specifically investigated. Limited data suggest that the plasma levels of duloxetine are higher in these patients.
Elimination:
Duloxetine has an elimination half-life of about 12 hours (range 8 to 17 hours) and its pharmacokinetics is dose proportional over the therapeutic range. Steady-state plasma concentrations are typically achieved after 3 days of dosing. Elimination of duloxetine is mainly through hepatic metabolism involving two P450 isozymes, CYP1A2 and CYP2D6.

INDICATIONS
DUZALTA is indicated for the treatment of:
- Major Depressive Disorder
- Generalized Anxiety Disorder
- Diabetic Peripheral Neuropathic pain
- Fibromyalgia
- Chronic Musculoskeletal Pain
- Treatment of moderate to severe Stress Urinary Incontinence (SUI) [20 and 40 mg strengths] in women.

DOSAGE AND ADMINISTRATION

Indications	Starting Dose	Target Dose	Maximum Dose
Major Depressive disorder	40 mg/day to 60 mg/day	**Acute Treatment:** 40 mg/day (20 mg twice daily) to 60 mg/day (once daily or as 30 mg twice daily) **Maintenance Treatment:** 60 mg/day	120 mg/day
Generalized Anxiety disorder Adults Elderly Children and Adolescents (7 to 17 years of age)	 30-60 mg/day 30 mg/day 30 mg/day	 60 mg/day (once daily) 60 mg/day (once daily) 30 to 60 mg/day (once daily)	 120 mg/day 120 mg/day 120 mg/day
Diabetic Peripheral Neuropathy	60 mg/day	60 mg/day (once daily)	60 mg/day
Fibromyalgia	30 mg/day	60 mg/day (once daily)	60 mg/day
Chronic Musculoskeletal Pain	30 mg/day	60 mg/day (once daily)	60 mg/day
Stress Urinary Incontinence	40mg twice daily	20mg twice daily for two weeks	40 mg

Major Depressive Disorder:
In major depressive disorder therapeutic response is usually seen after 2-4 weeks of treatment. After consolidation of the anti-depressive response, it is recommended to continue treatment for several months, in order to avoid relapse. In patients responding to duloxetine, and with a history of repeated episodes of major depression, further long-term treatment at a dose of 60 to 120 mg/day could be considered.
In patients with generalized anxiety disorder, after consolidation of the anxiolytic response, it is recommended to continue treatment for several months, in order to avoid relapse.
Stress Urinary Incontinence:
After 2-4 weeks of treatment, patients should be re-assessed in order to evaluate the benefit and tolerability of the therapy. Dose escalation may decrease, though not eliminate, the risk of nausea and dizziness.
In SUI, the efficacy of duloxetine has not been evaluated for longer than 3 months. The benefit of treatment should be re-assessed at regular intervals. Combining Duloxetine with a pelvic floor muscle training (PFMT) programme may be more effective than either treatment alone. It is recommended that consideration be given to concomitant PFMT.

Dosing considerations in special populations
Renal Impairment: Do not use in patients with severe renal impairment, GFR <30 mL/min. No dosage adjustment is necessary for patients with mild or moderate renal dysfunction (creatinine clearance 30 to 80 ml/min)
Hepatic Impairment: Do not use in patients with chronic liver disease or cirrhosis.
Paediatric population: The safety and efficacy of duloxetine 40 mg for the treatment of stress urinary incontinence has not been studied. No data are available.
Elderly: Caution should be exercised when treating the elderly.
Administration requirements
Swallow DUZALTA whole. Do not chew or crush. Do not open the capsule and sprinkle its contents on food or mix with liquids. All of these might affect the enteric coating. DUZALTA can be given without regard to meals. If a dose of DUZALTA is missed, take the missed dose as soon as it is remembered. If it is almost time for the next dose, skip the missed dose and take the next dose at the regular time. Do not take two doses of DUZALTA at the same time.

CONTRAINDICATIONS

- Hypersensitivity to Duloxetine.
- Monoamine Oxidase Inhibitors (MAOIs): The use of MAOIs intended to treat psychiatric disorders with Duloxetine or within 5 days of stopping treatment. Duloxetine is contraindicated because of an increased risk of serotonin syndrome. The use of duloxetine within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated. Starting duloxetine in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome.
- Liver disease resulting in hepatic impairment.
- Duloxetine should not be used in combination with fluvoxamine, ciprofloxacin or enoxacin (i.e., potent CYP1A2 inhibitors), since the combination results in elevated plasma concentrations of duloxetine.
- Severe renal impairment (creatinine clearance <30 ml/min).
- The initiation of treatment with duloxetine is contraindicated in patients with uncontrolled hypertension that could expose patients to a potential risk of hypertensive crisis

WARNINGS AND PRECAUTIONS
Mania and Seizures
Duloxetine should be used with caution in patients with a history of mania or a diagnosis of bipolar disorder, and/or seizures. Activation of mania and hypomania has been reported in trials of patients with major depressive disorder treated with duloxetine. No activation of mania or hypomania was reported in clinical trials of patients with diabetic neuropathic pain, fibromyalgia or chronic musculoskeletal pain. Activation of mania or hypomania has been reported in a small proportion of patients with mood disorders (including bipolar disorder) who were treated with other antidepressants. In patients with bipolar disorder, antidepressants may induce a maniac episode. Caution is required in prescribing duloxetine for the treatment of depressive episode to patients with bipolar disorder.

Mydriasis
Mydriasis has been reported in association with duloxetine; therefore, caution should be used when prescribing duloxetine to patients with increased intraocular pressure or those at risk of acute narrow-angle glaucoma.

Blood Pressure and Heart Rate
Duloxetine has been associated with an increase in blood pressure, and clinically significant hypertension in some patients. This may be due to the noradrenergic effect of duloxetine. Cases of hypertensive crisis have been reported with duloxetine, especially in patients with pre-existing hypertension. Therefore, in patients with known hypertension and/or other cardiac disease, blood pressure monitoring is recommended, especially during the first month of treatment. Duloxetine should be used with caution in patients whose conditions could be compromised by an increased heart rate or by an increase in blood pressure. Caution should also be exercised when duloxetine is used with other drugs that may impair its metabolism. For patients who experience a sustained increase in blood pressure while receiving duloxetine, either dose reduction or gradual discontinuation should be considered. In patients with uncontrolled hypertension, duloxetine should not be initiated.

Renal Impairment
Increased plasma concentrations of duloxetine occur in patients with severe renal impairment on haemodialysis (creatinine clearance <30 ml/min).

Serotonin syndrome
As with other serotonergic agents, serotonin syndrome, a potentially life-threatening condition, may occur with duloxetine treatment, particularly with concomitant use of other serotonergic agents (including SSRIs, SNRIs, tricyclic antidepressants or triptans), with agents that impair metabolism of serotonin such as MAOIs, or with antipsychotics or other dopamine antagonists that may affect the serotonergic neurotransmitter systems.
It is also possible during concomitant use with fentanyl, lithium, tramadol, tryptophan, buspirone and amphetamines. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea).
If concomitant treatment with duloxetine and other serotonergic agents that may affect the serotonergic and/or dopaminergic neurotransmitter systems is clinically warranted. It is also possible during concomitant use with fentanyl, lithium, tramadol, tryptophan, buspirone and amphetamines. Careful observation of the patient is advised, particularly during treatment initiation and dose increases.

St John's Wort
Adverse reactions may be more common during concomitant use of duloxetine and herbal preparations containing St John's Wort (Hypericum perforatum).

Suicide
Major Depressive Disorder and Generalized Anxiety Disorder: Depression is associated with an increased risk of suicidal thoughts, self-harm, and suicide (suicide-related events). 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.
Other psychiatric conditions for which Duloxetine is prescribed can also be associated with an increased risk of suicide-related events. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.
Patients with a history of suicide-related events or those exhibiting a significant degree of suicidal thoughts prior to commencement of treatment, are known to be at greater risk of suicidal thoughts or suicidal behavior, and should receive careful monitoring during treatment. Close supervision of patients, and in particular those at high risk, should accompany medicinal product therapy, especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behavior or thoughts, and unusual changes in behavior, and to seek medical advice immediately if these symptoms present.

Use in Children and Adolescents Under 18 Years of Age
Duloxetine should not be used in children and adolescents for the treatment of major depressive disorder. Duloxetine can be used in the treatment of children and adolescents 7-17 years of age with generalized anxiety disorder but caution should be implemented. Suicide-related behaviors (suicide attempts and suicidal thoughts) and hostility (predominantly aggression, oppositional behavior, and anger) were more frequently observed in clinical trials among children and adolescents treated with antidepressants compared to those treated with placebo. The patient should be carefully monitored for the appearance of suicidal symptoms. In addition, long-term safety data in children and adolescents concerning growth, maturation, and cognitive and behavioral development are lacking.

Haemorrhage
There have been reports of bleeding abnormalities, such as ecchymoses, purpura, and gastrointestinal haemorrhage, with selective serotonin reuptake inhibitors (SSRIs) and serotonin/noradrenaline reuptake inhibitors (SNRIs), including duloxetine. Caution is advised in patients taking anticoagulants and/or medicinal products known to affect platelet function (e.g., NSAIDs or acetylsalicylic acid (ASA)), and in patients with known bleeding tendencies.

Hyponatraemia
Hyponatraemia has been reported when administering duloxetine, including cases with serum sodium lower than 110 mmol/l. Hyponatraemia may be due to a syndrome of inappropriate anti-diuretic hormone secretion (SIADH). The majority of cases of hyponatraemia were

reported in the elderly, especially when coupled with a recent history of, or condition pre-disposing to, altered fluid balance. Caution is required in patients at increased risk for hyponatraemia, such as elderly, cirrhotic, or dehydrated patients, or patients treated with diuretics.

Discontinuation of Treatment
Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt. The risk of withdrawal symptoms seen with SSRIs and SNRIs may be dependent on several factors, including the duration and dose of therapy and the rate of dose reduction. Symptoms 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, the 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 duloxetine should be gradually tapered when discontinuing treatment over a period of no less than 2 weeks, according to the patient's needs.

Akathisia/Psychomotor Restlessness
Duloxetine has been associated with the development of akathisia, characterised by an 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.

Hepatitis/Increased Liver Enzymes
Cases of liver injury, including severe elevations of liver enzymes (>10-times upper limit of normal), hepatitis, and jaundice have been reported with duloxetine. Most of them occurred during the first months of treatment. The pattern of liver damage was predominantly hepatocellular. Duloxetine should be used with caution in patients treated with other drugs associated with hepatic injury.

Severe Skin Reactions
Severe skin reactions, including erythema multiform and Stevens - Johnson syndrome (SJS), can occur with duloxetine. Duloxetine should be discontinued at the first appearance of blisters, peeling rash, mucosal erosions or any other sign of hypersensitivity if no other etiology can be identified.

Orthostatic Hypotension, Falls and Syncope
Orthostatic hypotension, falls and syncope have been reported with Duloxetine. These tend to occur within the first week of therapy but may occur any time during treatment, particularly after dose increases. The risk of falling appears to be related to the degree of orthostatic decrease in blood pressure as well as other factors that may increase the risk of falls. The risk of blood pressure decreases may be greater in patients taking concomitant medications that induce orthostatic hypotension (such as antihypertensives) or are potent CYP1A2 inhibitors (see DRUG INTERACTIONS) and in patients taking Duloxetine at doses above 60 mg daily. Discontinuation of duloxetine should be considered in patients who experience symptomatic orthostatic hypotension, falls and/or syncope during therapy. Risk of falls is higher in the elderly.

Urinary Hesitation and Retention
Duloxetine is in a class of drugs known to affect urethral resistance. In post marketing experience, cases of urinary retention have been observed. In some instances of urinary retention associated with Duloxetine use, hospitalization and/or catheterization has been needed. This property is useful in women with Stress Urinary Incontinence (SUI)

Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. Duloxetine may be associated with sedation and dizziness. Patients should be instructed that if they experience sedation or dizziness they should avoid potentially hazardous tasks such as driving or operating machinery.

ADVERSE REACTIONS
The most commonly reported adverse reactions in patients treated with duloxetine were nausea, headache, dry mouth, somnolence and dizziness. However, the majority of common adverse reactions were mild to moderate; they usually started early in therapy, and most tended to subside even as therapy was continued.
Infections and infestations
Uncommon: Laryngitis
Immune system disorders
Rare: Anaphylactic reaction, Hyper-sensitivity disorder
Endocrine disorders
Rare: Hypo-thyroidism
Metabolism and nutrition disorders
Common: Decreased appetite
Uncommon: Hyperglycaemia (reported especially in diabetic patients)
Rare: Dehydration, Hyponatraemia
Psychiatric disorders
Common: Insomnia, Agitation, Libido decreased, anxiety, orgasm abnormal, abnormal dreams
Uncommon: Suicidal ideation, sleep disorder, bruxism, disorientation, apathy,
Rare: Suicidal behavior, mania, hallucinations, aggression and anger
Nervous system disorders
Very common: Headache, Somnolence
Common: Dizziness, Lethargy, Tremor, Paraesthesia
Uncommon: Myoclonus, Akathisia, Nervousness, Disturbance in attention, Dysgeusia, Dyskinesia, Restless legs syndrome, Poor quality sleep
Rare: Serotonin syndrome, Convulsion, Psychomotor restlessness, Extra-pyramidal symptoms
Eye disorders
Common: Blurred vision
Uncommon: Mydriasis, Visual impairment
Rare: Glaucoma,
Ear and labyrinth disorders
Common: Tinnitus
Uncommon: Vertigo, Ear pain
Cardiac disorders
Common: Palpitations
Uncommon: Tachycardia, Supra-ventricular arrhythmia, mainly atrial fibrillation
Vascular disorders
Common: Blood pressure increase, Flushing,
Uncommon: Syncope, Hypertension, Orthostatic hypotension, Peripheral coldness
Rare: Hypertensive crisis
Respiratory, thoracic and mediastinal disorders
Common: Yawning
Uncommon: Throat tightness, Epistaxis
Gastrointestinal disorders
Very common: Nausea, Dry mouth
Common: Constipation, Diarrhoea, Abdominal pain, Vomiting, Dyspepsia, Flatulence
Uncommon: Gastrointestinal haemorrhage, Gastroenteritis, Eructation, Gastritis, Dysphagia
Rare: Stomatitis, Haematochezia, breath odour, microscopic colitis
Hepato-biliary disorders
Uncommon: Hepatitis, Elevated liver enzymes (ALT, AST, alkaline phosphatase), acute liver injury
Rare: Hepatic failure, Jaundice
Skin and subcutaneous tissue disorders
Common: Sweating increased, Rash
Uncommon: Night sweats, urticaria, Dermatitis contact, Cold sweat, Photo-sensitivity reactions, increased tendency to bruise,
Rare: Stevens - Johnson syndrome, Angio-neurotic oedema
Very rare: Cutaneous vasculitis
Musculoskeletal and connective tissue disorders
Common: Musculo-skeletal pain, Muscle spasm
Uncommon: Muscle tightness, Muscle twitching
Rare: Trismus
Renal and urinary disorders
Common: Dysuria, Pollakiuria
Uncommon: Urinary retention, Urinary hesitation, Nocturia, Polyuria, Urine flow decreased
Rare: Urine odour abnormal
Reproductive system and breast disorders
Common: Erectile dysfunction, Ejaculation disorder, Ejaculation delayed
Uncommon: Gynaecological haemorrhage, menstrual disorder, Sexual dysfunction, Testicular pain,
Rare: Menopausal symptoms, Galactorrhoea, Hyperprolactinaemia
General disorders and administration site conditions
Common: Falls, fatigue
Uncommon: Chest pain, feeling abnormal, feeling cold, thirst, chills, malaise, feeling hot, gait disturbance
Investigations
Common: Weight decrease
Uncommon: Weight increase, blood creatine phosphokinase increased, blood potassium increased
Rare: Blood cholesterol increased

DRUG INTERACTIONS

Monoamine Oxidase Inhibitors (MAOIs)
Due to the risk of serotonin syndrome, duloxetine should not be used in combination with non-selective, irreversible monoamine oxidase inhibitors (MAOIs) or within at least 14 days of discontinuing treatment with an MAOI. Based on the half-life of duloxetine, at least 5 days should be allowed after stopping duloxetine before starting an MAOI.
The concomitant use of duloxetine with selective, reversible MAOIs, like moclobemide, is not recommended. The antibiotic linezolid is a reversible non-selective MAOI and should not be given to patients treated with duloxetine.
Inhibitors of CYP1A2
CYP1A2 is involved in duloxetine metabolism; concomitant use of duloxetine with potent inhibitors of CYP1A2 is likely to result in higher concentrations of duloxetine. Therefore, duloxetine should not be administered in combination with potent inhibitors of CYP1A2 such as fluvoxamine, cimetidine, ciprofloxacin and enoxacin.
Serotonergic agents
In rare cases, serotonin syndrome has been reported in patients using SSRIs/SNRIs concomitantly with serotonergic agents. Caution is advisable if duloxetine is used concomitantly with serotonergic agents like SSRIs, SNRIs, tricyclic antidepressants like clomipramine or amitriptyline, MAOIs like moclobemide or linezolid, St John's Wort (Hypericum perforatum) or triptans, tramadol, pethidine, and tryptophan.

Effect of Duloxetine on Other Medicinal Products

Medicinal products metabolised by CYP2D6: Duloxetine is a moderate inhibitor of CYP2D6. When duloxetine was administered at a dose of 60 mg twice daily with a single dose of desipramine, a CYP2D6 substrate, the AUC of desipramine increased 3-fold. The co-administration of duloxetine (40 mg twice daily) increases steady-state AUC of tolterodine (2 mg twice daily) by 71%, but does not affect the pharmacokinetics of its active 5-hydroxyl metabolite and no dosage adjustment is recommended. Caution is advised if duloxetine is co-administered with medicinal products that are predominantly metabolised by CYP2D6 (risperidone, tricyclic antidepressants [TCAs], such as nortriptyline, amitriptyline, and imipramine), particularly if they have a narrow therapeutic index (such as flecainide, propafenone, and metoprolol).

Anticoagulants and antiplatelet agents: Caution should be exercised when duloxetine is combined with oral anticoagulants or antiplatelet agents due to a potential increased risk of bleeding attributable to a pharmacodynamics interaction. Furthermore, increases in INR values have been reported when duloxetine was co-administered to patients treated with warfarin. However, concomitant administration of duloxetine with warfarin under steady-state conditions, in healthy volunteers, as part of a clinical pharmacology study, did not result in a clinically significant change in INR from baseline or in the pharmacokinetics of R- or S-warfarin.

USE IN SPECIAL POPULATIONS

US FDA Pregnancy Category C
Duloxetine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. Women should be advised to notify their physician if they become pregnant, or intend to become pregnant, during therapy.
Neonates exposed during pregnancy to serotonin - norepinephrine reuptake inhibitors (SNRIs) or selective serotonin reuptake inhibitors (SSRIs) have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding which can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of the SNRIs or SSRIs, or possibly, a drug discontinuation syndrome. In some cases, the clinical picture is consistent with serotonin syndrome.
Nursing mothers
Duloxetine is very weakly excreted into human milk. The safety of duloxetine in infants is not known, the use of duloxetine while breast-feeding is not recommended. However, if use is required the developmental and health benefits of human milk feeding should be considered along with the mother's clinical need for Duloxetine and any potential adverse effects on the milk-fed child from the drug or from the underlying maternal condition and caution should be implemented.
Gender
Duloxetine's half-life is similar in men and women. Dosage adjustment based on gender is not necessary.
Pediatrics
Safety and effectiveness in the pediatric population have not been established. Anyone considering the use of Duloxetine in a child or adolescent must balance the potential risks with the clinical need
Smoking Status
Dosage modifications are not recommended for smokers.
Race
No specific pharmacokinetic study was conducted to investigate the effects of race.
Hepatic Impairment
Patients with clinically evident hepatic impairment have decreased duloxetine metabolism and elimination. Duloxetine must not be used in active liver disease and hepatic impairment.

Severe Renal Impairment
Limited data are available on the effects of duloxetine in patients with end-stage renal disease (ESRD). Duloxetine must not be used in severe renal impairment (creatinine clearance <30 ml/min). No dosage adjustment is necessary for patients with mild or moderate renal dysfunction (creatinine clearance 30 to 80 ml/min).

OVER DOSAGE
Signs and symptoms of overdose (duloxetine alone or in combination with other medicinal products) included somnolence, coma, serotonin syndrome, seizures, vomiting and tachycardia.
No specific antidote is known for duloxetine, but if serotonin syndrome ensues, specific treatment (such as with cyproheptadine and/or temperature control) may be considered. A free airway should be established. Monitoring of cardiac and vital signs is recommended, along with appropriate symptomatic and supportive measures. Gastric lavage may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal may be useful in limiting absorption. Duloxetine has a large volume of distribution and forced diuresis, haemoperfusion, and exchange perfusion are unlikely to be beneficial.

PRESENTATION

Duzalta® 20 mg:
Pack of 14 capsules

Duzalta® 30 mg:
Pack of 14 capsules

Duzalta® 40 mg:
Pack of 14 capsules

Duzalta® 60 mg:
Pack of 10 capsules

INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, report at pharmacovigilance@pharmevo.biz

For more information on our products call PharmAssist helpline 0800-82222 Monday to Friday 9:00 am to 6:00 pm or email us at : pharmassist@pharmevo.biz

ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔
روشنی، گرمی اور نمی سے محفوظ، 30°C سے کم درجہ حرارت پر رکھیں۔
دوا کے مکمنہ منفی اثرات کے متعلق pharmacovigilance@pharmevo.biz پر مطلع کریں۔

ہماری ادویات کی مزید معلومات کے لئے فارم اسسٹ کی ہیلپ لائن نمبر 0800-82222 پر کال کریں۔
پیر تا جمعہ صبح 9:00 بجے تا شام 6:00 بجے

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