ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 30 mg hard gastro-resistant capsules
Duloxetine Viatris 60 mg hard gastro-resistant capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

30 mg capsules

Each capsule contains 30 mg of duloxetine (as hydrochloride).

Excipient(s) with known effect

Each capsule contains 62.1 mg sucrose.

For the full list of excipients, see section 6.1.

60 mg capsules

Each capsule contains 60 mg of duloxetine (as hydrochloride).

Excipient(s) with known effect

Each capsule contains 124.2 mg sucrose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard gastro-resistant capsule

30 mg capsules

Opaque blue cap and opaque white body approximately 15.9 mm, imprinted in gold ink with 'MYLAN' over 'DL 30' on both the cap and the body.

60 mg capsules

Opaque blue cap and opaque yellow body approximately 21.7 mm, imprinted in white ink with 'MYLAN' over 'DL 60' on both the cap and the body.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of major depressive disorder.
Treatment of diabetic peripheral neuropathic pain.
Treatment of generalised anxiety disorder.

Duloxetine Viatris is indicated in adults.

For further information see section 5.1.

4.2 Posology and method of administration

Posology

Major depressive disorder
The starting and recommended maintenance dose is 60 mg once daily with or without food. Dosages above 60 mg once daily, up to a maximum dose of 120 mg per day have been evaluated from a safety perspective in clinical trials. However, there is no clinical evidence suggesting that patients not responding to the initial recommended dose may benefit from dose up-titrations.

Therapeutic response is usually seen after 2-4 weeks of treatment.

After consolidation of the antidepressive 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.

Generalised anxiety disorder
The recommended starting dose in patients with generalised anxiety disorder is 30 mg once daily with or without food. In patients with insufficient response the dose should be increased to 60 mg, which is the usual maintenance dose in most patients.

In patients with co-morbid major depressive disorder, the starting and maintenance dose is 60 mg once daily (please see also dosing recommendation above).

Doses up to 120 mg per day have been shown to be efficacious and have been evaluated from a safety perspective in clinical trials. In patients with insufficient response to 60 mg, escalation up to 90 mg or 120 mg may therefore be considered. Dose escalation should be based upon clinical response and tolerability.

After consolidation of the response, it is recommended to continue treatment for several months, in order to avoid relapse.

Diabetic peripheral neuropathic pain
The starting and recommended maintenance dose is 60 mg daily with or without food. Dosages above 60 mg once daily, up to a maximum dose of 120 mg per day administered in evenly divided doses, have been evaluated from a safety perspective in clinical trials. The plasma concentration of duloxetine displays large inter-individual variability (see section 5.2). Hence, some patients that respond insufficiently to 60 mg may benefit from a higher dose.

Response to treatment should be evaluated after 2 months. In patients with inadequate initial response, additional response after this time is unlikely.

The therapeutic benefit should be reassessed regularly (at least every three months) (see section 5.1).

Special populations

Elderly

No dosage adjustment is recommended for elderly patients solely on the basis of age. However, as with any medicine, caution should be exercised when treating the elderly, especially with Duloxetine Viatris

120 mg per day for major depressive disorder or generalised anxiety disorder, for which data are limited (see sections 4.4 and 5.2).

Hepatic impairment

Duloxetine Viatris must not be used in patients with liver disease resulting in hepatic impairment (see sections 4.3 and 5.2).

Renal impairment

No dosage adjustment is necessary for patients with mild or moderate renal dysfunction (creatinine clearance 30 to 80 ml/min). Duloxetine Viatris must not be used in patients with severe renal impairment (creatinine clearance <30 ml/min; see section 4.3).

Paediatric population

Duloxetine should not be used in children and adolescents under the age of 18 years for the treatment of major depressive disorder because of safety and efficacy concerns (see sections 4.4, 4.8 and 5.1).

The safety and efficacy of duloxetine for the treatment of generalised anxiety disorder in paediatric patients aged 7-17 years have not been established. Current available data are described in sections 4.8, 5.1 and 5.2.

The safety and efficacy of duloxetine for the treatment of diabetic peripheral neuropathic pain has not been studied. No data are available.

Discontinuation of treatment
Abrupt discontinuation should be avoided. When stopping treatment with Duloxetine Viatris the dose should be gradually reduced over a period of at least one to two weeks in order to reduce the risk of withdrawal reactions (see sections 4.4 and 4.8). 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, the physician may continue decreasing the dose, but at a more gradual rate.

Method of administration

For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Concomitant use of Duloxetine Viatris with nonselective, irreversible monoamine oxidase inhibitors (MAOIs) is contraindicated (see section 4.5).

Liver disease resulting in hepatic impairment (see section 5.2).

Duloxetine Viatris 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 (see section 4.5).

Severe renal impairment (creatinine clearance <30 ml/min) (see section 4.4).

The initiation of treatment with Duloxetine Viatris is contraindicated in patients with uncontrolled hypertension that could expose patients to a potential risk of hypertensive crisis (see sections 4.4 and 4.8).

4.4 Special warnings and precautions for use

Mania and seizures

Duloxetine Viatris should be used with caution in patients with a history of mania or a diagnosis of bipolar disorder, and/or seizures.

Mydriasis

Mydriasis has been reported in association with duloxetine, therefore, caution should be used when prescribing Duloxetine Viatris 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 medicinal products that may impair its metabolism (see section 4.5). For patients who experience a sustained increase in blood pressure while receiving duloxetine either dose reduction or gradual discontinuation should be considered (see section 4.8). In patients with uncontrolled hypertension duloxetine should not be initiated (see section 4.3).

Renal impairment

Increased plasma concentrations of duloxetine occur in patients with severe renal impairment on haemodialysis (creatinine clearance <30 ml/min). For patients with severe renal impairment, see section 4.3. See section 4.2 for information on patients with mild or moderate renal dysfunction.

Serotonin syndrome/Neuroleptic malignant syndrome

As with other serotonergic agents, serotonin syndrome or neuroleptic malignant syndrome (NMS), a potentially life-threatening condition, may occur with duloxetine treatment, particularly with concomitant use of other serotonergic agents (including SSRIs, SNRIs, tricyclic antidepressants, opioids (such as buprenorphine) 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 (see sections 4.3 and 4.5).

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). Serotonin syndrome in its most severe form can resemble NMS, which includes hyperthermia, muscle rigidity, elevated serum creatine kinase levels, autonomic instability with possible rapid fluctuation of vital signs and mental status changes.

If concomitant treatment with duloxetine and other serotonergic/neuroleptic agents that may affect the serotonergic and/or dopaminergic neurotransmitter systems is clinically warranted, 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 Viatris and herbal preparations containing St John's wort (*Hypericum perforatum*).

Suicide

Major depressive disorder and Generalised 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 Viatris 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 behaviour, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant medicinal products in psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.

Cases of suicidal thoughts and suicidal behaviours have been reported during duloxetine therapy or early after treatment discontinuation (see section 4.8).

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 behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Diabetic peripheral neuropathic pain
As with other medicinal products with similar pharmacological action (antidepressants), isolated cases of suicidal ideation and suicidal behaviours have been reported during duloxetine therapy or early after treatment discontinuation. Concerning risk factors for suicidality in depression, see above. Physicians should encourage patients to report any distressing thoughts or feelings at any time.

Use in children and adolescents under 18 years of age

Duloxetine Viatris should not be used in the treatment of children and adolescents under the age of 18 years. Suicide-related behaviours (suicide attempts and suicidal thoughts), and hostility (predominantly aggression, oppositional behaviour and anger), were more frequently observed in clinical trials among children and adolescents treated with antidepressants compared to those treated with placebo. If, based on clinical need, a decision to treat is nevertheless taken, the patient should be carefully monitored for the appearance of suicidal symptoms (see section 5.1). In addition, long-term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are lacking (see section 4.8).

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. Duloxetine may increase the risk of postpartum haemorrhage (see section 4.6). 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 Viatris, 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 (see section 4.8). In clinical trials adverse events seen on abrupt treatment discontinuation occurred in approximately 45% of patients treated with duloxetine and 23% of patients taking placebo. The risk of withdrawal symptoms seen with SSRI's and SNRI's may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction. The most commonly reported reactions are listed in section 4.8. 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 duloxetine should be gradually tapered when discontinuing treatment over a period of no less than 2 weeks, according to the patient's needs (see section 4.2).

Elderly

Data on the use of duloxetine 120 mg in elderly patients with major depressive disorder and generalised anxiety disorder are limited. Therefore, caution should be exercised when treating the elderly with the maximum dosage (see sections 4.2 and 5.2).

Akathisia/psychomotor restlessness

The use of duloxetine has been associated with the development of akathisia, characterised 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.

Medicinal products containing duloxetine

Duloxetine is used under different trademarks in several indications (treatment of diabetic neuropathic pain, major depressive disorder, generalised anxiety disorder and stress urinary incontinence). The use of more than one of these products concomitantly should be avoided.

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 (see section 4.8). 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 medicinal products associated with hepatic injury.

Sexual dysfunction

Selective serotonin reuptake inhibitors (SSRIs)/serotonin norepinephrine reuptake inhibitors (SNRIs) may cause symptoms of sexual dysfunction (see section 4.8). There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRIs.

Excipients

Duloxetine Viatris hard gastro-resistant capsules contain sucrose and sodium.
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
This medicinal product contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

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 Viatris before starting an MAOI (see section 4.3).

The concomitant use of Duloxetine Viatris with selective, reversible MAOIs, like moclobemide, is not recommended (see section 4.4). The antibiotic linezolid is a reversible non-selective MAOI and should not be given to patients treated with Duloxetine Viatris (see section 4.4).

Inhibitors of CYP1A2

Because CYP1A2 is involved in duloxetine metabolism, concomitant use of duloxetine with potent inhibitors of CYP1A2 is likely to result in higher concentrations of duloxetine. Fluvoxamine (100 mg once daily), a potent inhibitor of CYP1A2, decreased the apparent plasma clearance of duloxetine by about 77% and increased AUC_{0-t} 6-fold. Therefore Duloxetine Viatris should not be administered in combination with potent inhibitors of CYP1A2 like fluvoxamine (see section 4.3).

CNS medicinal products

The risk of using duloxetine in combination with other CNS-active medicinal products has not been systematically evaluated, except in the cases described in this section. Consequently, caution is advised when Duloxetine Viatris is taken in combination with other centrally acting medicinal products or substances, including alcohol and sedative medicinal products (e.g. benzodiazepines, morphinomimetics, antipsychotics, phenobarbital, sedative antihistamines).

Serotonergic agents

In rare cases, serotonin syndrome has been reported in patients using SSRIs/SNRIs concomitantly with serotonergic agents. Caution is advisable if Duloxetine Viatris is used concomitantly with serotonergic agents like SSRIs, SNRIs, tricyclic antidepressants like clomipramine or amitriptyline, MAOIs like moclobemide or linezolid, triptans, opioids like buprenorphine, tramadol or pethidine, St John's wort (*Hypericum perforatum*), and tryptophan (see section 4.4).

Effect of duloxetine on other medicinal products

Medicinal products metabolised by CYP1A2
The pharmacokinetics of theophylline, a CYP1A2 substrate, were not significantly affected by co-administration with duloxetine (60 mg twice daily).

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 Viatris 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).

Oral contraceptives and other steroidal agents
Results of *in vitro* studies demonstrate that duloxetine does not induce the catalytic activity of CYP3A. Specific *in vivo* drug interaction studies have not been performed.

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 pharmacodynamic 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.

Effects of other medicinal products on duloxetine

Antacids and H_2 antagonists
Co-administration of duloxetine with aluminium- and magnesium-containing antacids or duloxetine with famotidine had no significant effect on the rate or extent of duloxetine absorption after administration of a 40 mg oral dose.

Inducers of CYP1A2
Population pharmacokinetic analyses have shown that smokers have almost 50% lower plasma concentrations of duloxetine compared with non-smokers.

4.6 Fertility, pregnancy and lactation

Fertility

In animal studies, duloxetine had no effect on male fertility, and effects in females were only evident at doses that caused maternal toxicity.

Pregnancy

Studies in animals have shown reproductive toxicity at systemic exposure levels (AUC) of duloxetine lower than the maximum clinical exposure (see section 5.3).

Two large observational studies do not suggest an overall increased risk of major congenital malformation (one from the US including 2,500 exposed to duloxetine during the first trimester and one from the EU including 1,500 exposed to duloxetine during the first trimester). The analysis on specific malformations such as cardiac malformations shows inconclusive results.

In the EU study, maternal exposure to duloxetine during late pregnancy (at any time from 20 weeks gestational age to delivery) was associated with an increased risk for preterm birth (less than 2-fold, corresponding to approximately 6 additional premature births per 100 women treated with duloxetine late in pregnancy). The majority occurred between 35 and 36 weeks of gestation. This association was not seen in the US study.

The US observational data have provided evidence of an increased risk (less than 2-fold) of postpartum haemorrhage following duloxetine exposure within the month prior to birth.

Epidemiological data have suggested that the use of SSRIs in pregnancy, particularly in late pregnancy, may increase the risk of persistent pulmonary hypertension in the newborn (PPHN). Although no studies have investigated the association of PPHN to SNRI treatment, this potential risk cannot be ruled out with duloxetine taking into account the related mechanism of action (inhibition of the re-uptake of serotonin).

As with other serotonergic medicinal products, discontinuation symptoms may occur in the neonate after maternal duloxetine use near term. Discontinuation symptoms seen with duloxetine may include hypotonia, tremor, jitteriness, feeding difficulty, respiratory distress and seizures. The majority of cases have occurred either at birth or within a few days of birth.

Duloxetine Viatris should be used in pregnancy only if the potential benefit justifies the potential risk to the foetus. Women should be advised to notify their physician if they become pregnant, or intend to become pregnant, during therapy.

Breast feeding

Duloxetine is very weakly excreted into human milk based on a study of 6 lactating patients, who did not breast feed their children. The estimated daily infant dose on a mg/kg basis is approximately 0.14% of the maternal dose (see section 5.2). As the safety of duloxetine in infants is not known, the use of Duloxetine Viatris while breast-feeding is not recommended.

4.7 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 Viatris 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.

4.8 Undesirable effects

Summary of the safety profile

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.

Tabulated summary of adverse reactions

Table 1 gives the adverse reactions observed from spontaneous reporting and in placebo-controlled clinical trials.

Table 1: Adverse reactions
Frequency estimate: 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 (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Very common	Common	Uncommon	Rare	Very rare	Not known
Infections and infestations					
		Laryngitis			
Immune system disorders					
			Anaphylactic reaction Hyper-sensitivity disorder		
Endocrine disorders					
			Hypo-thyroidism		
Metabolism and nutrition disorders					
	Decreased Appetite	Hyperglycaemia (reported especially in diabetic patients)	Dehydration Hyponatraemia SIADH[6]		
Psychiatric disorders					
	Insomnia Agitation Libido decreased Anxiety Orgasm abnormal Abnormal dreams	Suicidal ideation[5,7] Sleep disorder Bruxism Disorientation Apathy	Suicidal behaviour[5,7] Mania Hallucinations Aggression and anger[4]		

Very common	Common	Uncommon	Rare	Very rare	Not known
Nervous system disorders					
Headache Somnolence	Dizziness Lethargy Tremor Paraesthesia	Myoclonus Akathisia[7] Nervousness Disturbance in attention Dysgeusia Dyskinesia Restless legs syndrome Poor quality sleep	Serotonin syndrome[6] Convulsion[1] Psychomotor restlessness[6] Extra-pyramidal symptoms[6]		
Eye disorders					
	Blurred vision	Mydriasis Visual impairment	Glaucoma		
Ear and labyrinth disorders					
	Tinnitus[1]	Vertigo Ear pain			
Cardiac disorders					
	Palpitations	Tachycardia Supra-ventricular arrhythmia, mainly atrial fibrillation			Stress cardiomyopathy (Takotsubo cardiomyopathy)
Vascular disorders					
	Blood pressure increase[3] Flushing	Syncope[2] Hypertension[3,7] Orthostatic hypotension[2] Peripheral coldness	Hypertensive crisis[3,6]		
Respiratory, thoracic and mediastinal disorders					
	Yawning	Throat tightness Epistaxis	Interstitial lung disease[8] Eosinophilic pneumonia[6]		
Gastrointestinal disorders					
Nausea Dry mouth	Constipation Diarrhoea Abdominal pain Vomiting Dyspepsia Flatulence	Gastrointestinal haemorrhage[7] Gastroenteritis Eructation Gastritis Dysphagia	Stomatitis Haematochezia Breath odour Microscopic colitis[9]		

Very common	Common	Uncommon	Rare	Very rare	Not known
Hepato-biliary disorders					
		Hepatitis[3] Elevated liver enzymes (ALT, AST, alkaline phosphatase) Acute liver injury	Hepatic failure[6] Jaundice[6]		
Skin and subcutaneous tissue disorders					
	Sweating increased Rash	Night sweats Urticaria Dermatitis contact Cold sweat Photo-sensitivity reactions Increased tendency to bruise	Stevens-Johnson Syndrome[6] Angio-neurotic oedema[6]	Cutaneous vasculitis	
Musculoskeletal and connective tissue disorders					
	Musculo-skeletal pain Muscle spasm	Muscle tightness Muscle twitching	Trismus		
Renal and urinary disorders					
	Dysuria Pollakiuria	Urinary retention Urinary hesitation Nocturia Polyuria Urine flow decreased	Urine odour abnormal		
Reproductive system and breast disorders					
	Erectile dysfunction Ejaculation disorder Ejaculation delayed	Gynaecological haemorrhage Menstrual disorder Sexual dysfunction Testicular pain	Menopausal symptoms Galactorrhoea Hyperprolactinaemia Postpartum haemorrhage[6]		

Very common	Common	Uncommon	Rare	Very rare	Not known
General disorders and administration site conditions					
	Falls[10] Fatigue	Chest pain[7] Feeling abnormal Feeling cold Thirst Chills Malaise Feeling hot Gait disturbance			
Investigations					
	Weight decrease	Weight increase Blood creatine phosphokinase increased Blood potassium increased	Blood cholesterol increased		

[1] Cases of convulsion and cases of tinnitus have also been reported after treatment discontinuation.
[2] Cases of orthostatic hypotension and syncope have been reported especially at the initiation of treatment.
[3] See section 4.4.
[4] Cases of aggression and anger have been reported particularly early in treatment or after treatment discontinuation.
[5] Cases of suicidal ideation and suicidal behaviours have been reported during duloxetine therapy or early after treatment discontinuation (see section 4.4).
[6] Estimated frequency of post-marketing surveillance reported adverse reactions; not observed in placebo-controlled clinical trials.
[7] Not statistically significantly different from placebo.
[8] Estimated frequency based on placebo-controlled clinical trials.
[9] Estimated frequency based on all clinical trial data.
[10] Falls were more common in the elderly (≥65 years old).

Description of selected adverse reactions

Discontinuation of duloxetine (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbances (including paraesthesia or electric shock like sensations, particularly in the head), sleep disturbances (including insomnia and intense dreams), fatigue, somnolence, agitation or anxiety, nausea and/or vomiting, tremor, headache, myalgia, irritability, diarrhoea, hyperhydrosis and vertigo are the most commonly reported reactions.

Generally, for SSRIs and SNRIs, these events are mild to moderate and self-limiting, however, in some patients they may be severe and/or prolonged. It is therefore advised that when duloxetine treatment is no longer required, gradual discontinuation by dose tapering should be carried out (see sections 4.2 and 4.4).

In the 12 week acute phase of three clinical trials of duloxetine in patients with diabetic neuropathic pain, small but statistically significant increases in fasting blood glucose were observed in duloxetine-treated patients. HbA1c was stable in both duloxetine-treated and placebo-treated patients. In the extension phase of these studies, which lasted up to 52 weeks, there was an increase in HbA1c in both the duloxetine and routine care groups, but the mean increase was 0.3% greater in the duloxetine-treated group. There

was also a small increase in fasting blood glucose and in total cholesterol in duloxetine-treated patients while those laboratory tests showed a slight decrease in the routine care group.

The heart rate-corrected QT interval in duloxetine-treated patients did not differ from that seen in placebo treated patients. No clinically significant differences were observed for QT, PR, QRS, or QTcB measurements between duloxetine-treated and placebo-treated patients.

Paediatric population

A total of 509 paediatric patients aged 7 to 17 years with major depressive disorder and 241 paediatric patients aged 7 to 17 years with generalised anxiety disorder were treated with duloxetine in clinical trials. In general, the adverse reaction profile of duloxetine in children and adolescents was similar to that seen for adults.

A total of 467 paediatric patients initially randomized to duloxetine in clinical trials, experienced a 0.1 kg mean decrease in weight at 10-weeks compared with a 0.9 kg mean increase in 353 placebo-treated patients. Subsequently, over the four- to six-month extension period, patients on average trended toward recovery to their expected baseline weight percentile based on population data from age- and gender-matched peers.

In studies of up to 9 months an overall mean decrease of 1% in height percentile (decrease of 2% in children (7-11 years) and increase of 0.3% in adolescents (12-17 years)) was observed in duloxetine-treated paediatric patients (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Cases of overdoses, alone or in combination with other medicinal products, with duloxetine doses of 5400 mg were reported. Some fatalities have occurred, primarily with mixed overdoses, but also with duloxetine alone at a dose of approximately 1000 mg. 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antidepressants. ATC code: N06AX21.

Mechanism of action

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. Duloxetine dose-dependently increases extracellular levels of serotonin and noradrenaline in various brain areas of animals.

Pharmacodynamic effects

Duloxetine normalised pain thresholds in several preclinical models of neuropathic and inflammatory pain and attenuated pain behaviour in a model of persistent pain. The pain inhibitory action of duloxetine is believed to be a result of potentiation of descending inhibitory pain pathways within the central nervous system.

Clinical efficacy and safety

Major depressive disorder
Duloxetine was studied in a clinical programme involving 3,158 patients (1,285 patient-years of exposure) meeting DSM-IV criteria for major depression. The efficacy of duloxetine at the recommended dose of 60 mg once a day was demonstrated in three out of three randomised, double-blind, placebo-controlled, fixed dose acute studies in adult outpatients with major depressive disorder. Overall, duloxetine's efficacy has been demonstrated at daily doses between 60 and 120 mg in a total of five out of seven randomised, double-blind, placebo-controlled, fixed dose acute studies in adult outpatients with major depressive disorder.

Duloxetine demonstrated statistical superiority over placebo as measured by improvement in the 17-item Hamilton Depression Rating Scale (HAM-D) total score (including both the emotional and somatic symptoms of depression). Response and remission rates were also statistically significantly higher with duloxetine compared with placebo. Only a small proportion of patients included in pivotal clinical trials had severe depression (baseline HAM-D>25).

In a relapse prevention study, patients responding to 12-weeks of acute treatment with open-label duloxetine 60 mg once daily were randomised to either duloxetine 60 mg once daily or placebo for a further 6-months. Duloxetine 60 mg once daily demonstrated a statistically significant superiority compared to placebo ($p=0.004$) on the primary outcome measure, the prevention of depressive relapse, as measured by time to relapse. The incidence of relapse during the 6-months double-blind follow-up period was 17% and 29% for duloxetine and placebo, respectively.

During 52 weeks of placebo-controlled double blind treatment, duloxetine-treated patients with recurrent MDD had a significantly longer symptom free period ($p<0.001$) compared with patients randomised to placebo. All patients had previously responded to duloxetine during open-label duloxetine treatment (28 to 34 weeks) at a dose of 60 to 120 mg/day. During the 52-week placebo-controlled double blind treatment phase 14.4% of the duloxetine-treated patients and 33.1% of the placebo-treated patients experience a return of their depressive symptoms ($p<0.001$).

The effect of duloxetine 60 mg once a day in elderly depressed patients (≥65 years) was specifically examined in a study that showed a statistically significant difference in the reduction of the HAMD17 score for duloxetine-treated patients compared to placebo. Tolerability of duloxetine 60 mg once daily in elderly patients was comparable to that seen in the younger adults. However, data on elderly patients exposed to the maximum dose (120 mg per day) are limited and thus, caution is recommended when treating this population.

Generalised anxiety disorder

Duloxetine demonstrated statistically significant superiority over placebo in five out of five studies including four randomised, double-blind, placebo-controlled acute studies and a relapse prevention study in adult patients with generalised anxiety disorder.

Duloxetine demonstrated statistically significant superiority over placebo as measured by improvement in the Hamilton Anxiety Scale (HAM-A) total score and by the Sheehan Disability Scale (SDS) global functional impairment score. Response and remission rates were also higher with duloxetine compared to placebo. Duloxetine showed comparable efficacy results to venlafaxine in terms of improvements on the HAM-A total score.

In a relapse prevention study, patients responding to 6 months of acute treatment with open-label duloxetine were randomised to either duloxetine or placebo for a further 6-months. Duloxetine 60 mg to 120 mg once daily demonstrated statistically significant superiority compared to placebo ($p<0.001$) on the prevention of relapse, as measured by time to relapse. The incidence of relapse during the 6-months double-blind follow-up period was 14% for duloxetine and 42% for placebo.

The efficacy of duloxetine 30-120 mg (flexible dosing) once a day in elderly patients (>65 years) with generalised anxiety disorder was evaluated in a study that demonstrated statistically significant improvement in the HAM-A total score for duloxetine treated patients compared to placebo treated patients. The efficacy and safety of duloxetine 30-120 mg once daily in elderly patients with generalised anxiety disorder was similar to that seen in studies of younger adult patients. However, data on elderly patients exposed to the maximum dose (120 mg per day) are limited and, thus, caution is recommended when using this dose with the elderly population.

Diabetic peripheral neuropathic pain
The efficacy of duloxetine as a treatment for diabetic neuropathic pain was established in 2 randomised, 12-week, double-blind, placebo-controlled, fixed dose studies in adults (22 to 88 years) having diabetic neuropathic pain for at least 6 months. Patients meeting diagnostic criteria for major depressive disorder were excluded from these trials. The primary outcome measure was the weekly mean of 24-hour average pain, which was collected in a daily diary by patients on an 11-point Likert scale.

In both studies, duloxetine 60 mg once daily and 60 mg twice daily significantly reduced pain compared with placebo. The effect in some patients was apparent in the first week of treatment. The difference in mean improvement between the two active treatment arms was not significant. At least 30% reported pain reduction was recorded in approximately 65% of duloxetine treated patients versus 40% for placebo. The corresponding figures for at least 50% pain reduction were 50% and 26% respectively. Clinical response rates (50% or greater improvement in pain) were analysed according to whether or not the patient experienced somnolence during treatment. For patients not experiencing somnolence, clinical response was observed in 47% of patients receiving duloxetine and 27% of patients on placebo. Clinical response rates in patients experiencing somnolence were 60% on duloxetine and 30% on placebo. Patients not demonstrating a pain reduction of 30% within 60 days of treatment were unlikely to reach this level during further treatment.

In an open label long-term uncontrolled study, the pain reduction in patients responding to 8-weeks of acute treatment of duloxetine 60 mg once daily was maintained for a further 6-months as measured by change on the Brief Pain Inventory (BPI) 24-hour average pain item.

Paediatric population

Duloxetine has not been studied in patients under the age of 7.

Two randomized, double-blind, parallel clinical trials were performed in 800 paediatric patients aged 7 to 17 years with major depressive disorder (see section 4.2). These two studies included a 10 week placebo

and active (fluoxetine) controlled acute phase followed by six months period of active controlled extension treatment. Neither duloxetine (30-120 mg) nor the active control arm (fluoxetine 20-40 mg) statistically separated from placebo on change from baseline to endpoint in the Children´s Depression Rating Scale-Revised (CDRS-R) total score. Discontinuation due to adverse events was higher in patients taking duloxetine compared with those treated with fluoxetine, mostly due to nausea. During the 10-week acute treatment period, suicidal behaviours were reported (duloxetine 0/333 [0%], fluoxetine 2/225 [0.9%], placebo 1/220 [0.5%]). Over the entire 36-week course of the study, 6 out of 333 patients initially randomized to duloxetine and 3 out of 225 patients initially randomized to fluoxetine experienced suicidal behaviour (exposure adjusted incidence 0.039 events per patient year for duloxetine and 0.026 for fluoxetine). In addition, one patient who transitioned from placebo to duloxetine experienced a suicidal behaviour while taking duloxetine.

A randomised, double-blind, placebo-controlled study was performed in 272 patients aged 7-17 years with generalised anxiety disorder. The study included a 10 week placebo-controlled acute phase, followed by an 18 week extension treatment period. A flexible dose regimen was used in this study, to allow for slow dose escalation from 30 mg once daily to higher doses (maximum 120 mg once daily). Treatment with duloxetine showed a statistically significantly greater improvement in GAD symptoms, as measured by PARS severity score for GAD (mean difference between duloxetine and placebo of 2.7 points [95% CI 1.3-4.0]), after 10 weeks of treatment. The maintenance of the effect has not been evaluated. There was no statistically significant difference in discontinuation due to adverse events between duloxetine and placebo groups during the 10 week acute treatment phase. Two patients who transitioned from placebo to duloxetine after the acute phase experienced suicidal behaviours while taking duloxetine during the extension phase. A conclusion on the overall benefit/risk in this age group has not been established (see also sections 4.2 and 4.8).

A single study has been performed in paediatric patients with juvenile primary fibromyalgia syndrome (JPFS) in which the duloxetine-treated group did not separate from placebo group for the primary efficacy measure. Therefore, there is no evidence of efficacy in this paediatric patient population. The randomised, double-blind, placebo-controlled, parallel study of duloxetine was conducted in 184 adolescents aged 13 to 18 years (mean age 15.53 years) with JPFS. The study included a 13-week double-blind period where patients were randomised to duloxetine 30 mg/60 mg, or placebo daily. Duloxetine did not show efficacy in reducing pain as measured by primary outcome measure of Brief Pain Inventory (BPI) average pain score endpoint: least squares (LS) mean change from baseline in BPI average pain score at 13 weeks was -0.97 in the placebo group, compared with -1.62 in the duloxetine 30/60 mg group ($p = 0.052$). The safety results from this study were consistent with the known safety profile of duloxetine.

The European Medicines Agency has waived the obligation to submit the results of studies with duloxetine in all subsets of the paediatric population in the treatment of major depressive disorder, diabetic neuropathic pain and generalised anxiety disorder. See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

Duloxetine is administered as a single enantiomer. Duloxetine is extensively metabolised by oxidative enzymes (CYP1A2 and the polymorphic CYP2D6), followed by conjugation. The pharmacokinetics of duloxetine demonstrate large intersubject variability (generally 50-60%), partly due to gender, age, smoking status and CYP2D6 metaboliser status.

Absorption

Duloxetine is well absorbed after oral administration with a C_{max} occurring 6 hours post dose. The absolute oral bioavailability of duloxetine ranged 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 alpha-l acid glycoprotein. Protein binding is not affected by renal or hepatic impairment.

Biotransformation

Duloxetine is extensively metabolised and the metabolites are excreted principally in urine. Both cytochromes P450-2D6 and 1A2 catalyse 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 metabolisers with respect to CYP2D6 has not been specifically investigated. Limited data suggest that the plasma levels of duloxetine are higher in these patients.

Elimination

The elimination half-life of duloxetine ranges from 8 to 17 hours (mean of 12 hours). After an intravenous dose the plasma clearance of duloxetine ranges from 22 l/hr to 46 l/hr (mean of 36 l/hr). After an oral dose the apparent plasma clearance of duloxetine ranges from 33 to 261 l/hr (mean 101 l/hr).

Special populations

Gender
Pharmacokinetic differences have been identified between males and females (apparent plasma clearance is approximately 50% lower in females). Based upon the overlap in the range of clearance, gender-based pharmacokinetic differences do not justify the recommendation for using a lower dose for female patients.

Age
Pharmacokinetic differences have been identified between younger and elderly females (≥65 years) (AUC increases by about 25% and half-life is about 25% longer in the elderly), although the magnitude of these changes is not sufficient to justify adjustments to the dose. As a general recommendation, caution should be exercised when treating the elderly (see sections 4.2 and 4.4).

Renal impairment
End stage renal disease (ESRD) patients receiving dialysis had 2-fold higher duloxetine C_{max} and AUC values compared with healthy subjects. Pharmacokinetic data on duloxetine is limited in patients with mild or moderate renal impairment.

Hepatic impairment
Moderate liver disease (Child Pugh Class B) affected the pharmacokinetics of duloxetine. Compared with healthy subjects, the apparent plasma clearance of duloxetine was 79% lower, the apparent terminal half-life was 2.3 times longer, and the AUC was 3.7 times higher in patients with moderate liver disease. The pharmacokinetics of duloxetine and its metabolites have not been studied in patients with mild or severe hepatic insufficiency.

Breast-feeding mothers
The disposition of duloxetine was studied in 6 lactating women who were at least 12-weeks postpartum. Duloxetine is detected in breast milk, and steady-state concentrations in breast milk are about one-fourth

those in plasma. The amount of duloxetine in breast milk is approximately 7 µg/day while on 40 mg twice daily dosing. Lactation did not influence duloxetine pharmacokinetics.

Paediatric population
Pharmacokinetics of duloxetine in paediatric patients aged 7 to 17 years with major depressive disorder following oral administration of 20 to 120 mg once daily dosing regimen was characterized using population modelling analyses based on data from 3 studies. The model-predicted duloxetine steady state plasma concentrations in paediatric patients were mostly within the concentration range observed in adult patients.

5.3 Preclinical safety data

Duloxetine was not genotoxic in a standard battery of tests and was not carcinogenic in rats. Multinucleated cells were seen in the liver in the absence of other histopathological changes in the rat carcinogenicity study. The underlying mechanism and the clinical relevance are unknown. Female mice receiving duloxetine for 2 years had an increased incidence of hepatocellular adenomas and carcinomas at the high dose only (144 mg/kg/day), but these were considered to be secondary to hepatic microsomal enzyme induction. The relevance of this mouse data to humans is unknown. Female rats receiving duloxetine (45 mg/kg/day) before and during mating and early pregnancy had a decrease in maternal food consumption and body weight, oestrous cycle disruption, decreased live birth indices and progeny survival, and progeny growth retardation at systemic exposure levels estimated to be at the most at maximum clinical exposure (AUC). In an embryotoxicity study in the rabbit, a higher incidence of cardiovascular and skeletal malformations was observed at systemic exposure levels below the maximum clinical exposure (AUC). No malformations were observed in another study testing a higher dose of a different salt of duloxetine. In prenatal/postnatal toxicity studies in the rat, duloxetine induced adverse behavioural effects in the offspring at exposures below maximum clinical exposure (AUC).

Studies in juvenile rats reveal transient effects on neurobehaviour, as well as significantly decreased body weight and food consumption; hepatic enzyme induction; and hepatocellular vacuolation at 45 mg/kg/day. The general toxicity profile of duloxetine in juvenile rats was similar to that in adult rats. The no-adverse effect level was determined to be 20 mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content

Sugar spheres (sucrose, maize starch)
Hypromellose
Macrogol
Crospovidone
Talc
Sucrose
Hypromellose phthalate
Diethyl phthalate

30 mg capsules

Capsule shell

Brilliant blue (E133)
Titanium dioxide (E171)

Gelatin
Gold ink

Gold ink contains

Shellac
Propylene glycol
Strong ammonia solution
Yellow iron oxide (E172)

60 mg capsules

Capsule shell

Brilliant blue (E133)
Yellow iron oxide (E172)
Titanium dioxide (E171)
Gelatin
White ink

White ink contains

Shellac
Propylene glycol
Sodium hydroxide
Povidone
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Blister packs PVC/PCTFE/Alu or PVC/PE/PVdC/Alu: 2 years.
Blister packs OPA/Alu/PVC – Alu: 3 years.
Bottle packs: 3 years.

Bottle packs only:
Once opened, use within 180 days.

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

30 mg capsules

PVC/PCTFE/Aluminium or OPA/Aluminium/PVC – Aluminium blister pack containing 7, 14, 28, 98 and multipacks containing 98 (2 packs of 49) hard gastro-resistant capsules.
PVC/PE/PVdC/Aluminium blister pack containing 7, 14, 28, 49, 98 and multipacks containing 98 (2 packs of 49) hard gastro-resistant capsules.

PVC/PCTFE/Aluminium or OPA/Aluminium/PVC – Aluminium perforated unit dose blister pack containing 7 x 1, 28 x 1 and 30 x 1 hard gastro-resistant capsules.
PVC/PE/PVdC/Aluminium perforated unit dose blister pack containing 7 x 1 and 28 x 1 hard gastro-resistant capsules.
HDPE bottle pack, with desiccant, containing 30, 100, 250 and 500 hard gastro-resistant capsules

60 mg capsules

PVC/PCTFE/Aluminium or OPA/Aluminium/PVC – Aluminium blister pack containing 14, 28, 84, 98 and multipacks containing 98 (2 packs of 49) hard gastro-resistant capsules.
PVC/PE/PVdC/Aluminium blister pack containing 14, 28, 49, 98 and multipacks containing 98 (2 packs of 49) hard gastro-resistant capsules.
PVC/PCTFE/Aluminium or OPA/Aluminium/PVC – Aluminium perforated unit dose blister pack containing 28 x 1, 30 x 1 and 100 x 1 hard gastro-resistant capsules
PVC/PE/PVdC/Aluminium perforated unit dose blister pack containing 28 x 1 hard gastro-resistant capsules.
HDPE bottle pack, with desiccant, containing 30, 100, 250 and 500 hard gastro-resistant capsules

Not all packs sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

30 mg capsules

EU/1/15/1010/001 7 hard gastro-resistant capsules
EU/1/15/1010/002 28 hard gastro-resistant capsules
EU/1/15/1010/003 98 hard gastro-resistant capsules
EU/1/15/1010/004 7 x 1 hard gastro-resistant capsules
EU/1/15/1010/005 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/006 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/007 30 hard gastro-resistant capsules
EU/1/15/1010/008 100 hard gastro-resistant capsules
EU/1/15/1010/009 250 hard gastro-resistant capsules
EU/1/15/1010/010 500 hard gastro-resistant capsules
EU/1/15/1010/021 14 hard gastro-resistant capsules
EU/1/15/1010/022 7 hard gastro-resistant capsules

EU/1/15/1010/023 14 hard gastro-resistant capsules
EU/1/15/1010/024 28 hard gastro-resistant capsules
EU/1/15/1010/025 98 hard gastro-resistant capsules
EU/1/15/1010/026 7 x 1 hard gastro-resistant capsules
EU/1/15/1010/027 28 x 1 hard gastro-resistant capsules)
EU/1/15/1010/028 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/037 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/038 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/041 7 hard gastro-resistant capsules
EU/1/15/1010/042 7 x 1 hard gastro-resistant capsules
EU/1/15/1010/043 14 hard gastro-resistant capsules
EU/1/15/1010/044 28 hard gastro-resistant capsules
EU/1/15/1010/045 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/046 49 hard gastro-resistant capsules
EU/1/15/1010/047 98 hard gastro-resistant capsules
EU/1/15/1010/048 98 hard gastro-resistant capsules (2 packs of 49)

60 mg capsules

EU/1/15/1010/011 28 hard gastro-resistant capsules
EU/1/15/1010/012 84 hard gastro-resistant capsules
EU/1/15/1010/013 98 hard gastro-resistant capsules
EU/1/15/1010/014 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/015 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/016 100 x 1 hard gastro-resistant capsules
EU/1/15/1010/017 30 hard gastro-resistant capsules
EU/1/15/1010/018 100 hard gastro-resistant capsules
EU/1/15/1010/019 250 hard gastro-resistant capsules
EU/1/15/1010/020 500 hard gastro-resistant capsules
EU/1/15/1010/029 28 hard gastro-resistant capsules
EU/1/15/1010/030 84 hard gastro-resistant capsules
EU/1/15/1010/031 98 hard gastro-resistant capsules
EU/1/15/1010/032 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/033 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/034 100 x 1 hard gastro-resistant capsules
EU/1/15/1010/035 14 hard gastro-resistant capsules
EU/1/15/1010/036 14 hard gastro-resistant capsules
EU/1/15/1010/039 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/040 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/049 14 hard gastro-resistant capsules
EU/1/15/1010/050 28 hard gastro-resistant capsules
EU/1/15/1010/051 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/052 49 hard gastro-resistant capsules
EU/1/15/1010/053 98 hard gastro-resistant capsules
EU/1/15/1010/054 98 hard gastro-resistant capsules (2 packs of 49)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 June 2015
Date of latest renewal: 13 February 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Mylan Hungary Kft
Mylan utca 1
Komárom
2900
Hungary

Mylan Germany GmbH
Zweigniederlassung Bad Homburg v. d. Hoehe, Benzstrasse 1
Bad Homburg v. d. Hoehe
Hessen, 61352,
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;

- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER CARTON FOR 30 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 30 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 30 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

7 hard gastro-resistant capsules
14 hard gastro-resistant capsules
28 hard gastro-resistant capsules
49 hard gastro-resistant capsules
98 hard gastro-resistant capsules
7 x 1 hard gastro-resistant capsules
28 x 1 hard gastro-resistant capsules
30 x 1 hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/001 7 hard gastro-resistant capsules
EU/1/15/1010/002 28 hard gastro-resistant capsules
EU/1/15/1010/003 98 hard gastro-resistant capsules
EU/1/15/1010/004 7 x 1 hard gastro-resistant capsules
EU/1/15/1010/005 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/006 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/021 14 hard gastro-resistant capsules
EU/1/15/1010/022 7 hard gastro-resistant capsules
EU/1/15/1010/023 14 hard gastro-resistant capsules
EU/1/15/1010/024 28 hard gastro-resistant capsules
EU/1/15/1010/025 98 hard gastro-resistant capsules
EU/1/15/1010/026 7 x 1 hard gastro-resistant capsules
EU/1/15/1010/027 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/028 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/041 7 hard gastro-resistant capsules
EU/1/15/1010/042 7 x 1 hard gastro-resistant capsules
EU/1/15/1010/043 14 hard gastro-resistant capsules
EU/1/15/1010/044 28 hard gastro-resistant capsules
EU/1/15/1010/045 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/046 49 hard gastro-resistant capsules
EU/1/15/1010/047 98 hard gastro-resistant capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Duloxetine Viatris 30 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER OUTER CARTON FOR MULTIPACK FOR 30 MG HARD GASTRO RESISTANT CAPSULES, WITH BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 30 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 30 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

Multipack: 98 (2 packs of 49) hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/037 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/038 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/048 98 hard gastro-resistant capsules (2 packs of 49)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Duloxetine Viatris 30 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER INNER CARTON FOR MULTIPACK FOR 30 MG HARD GASTRO RESISTANT CAPSULES, WITHOUT BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 30 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 30 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

49 hard gastro-resistant capsules
Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/037 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/038 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/048 98 hard gastro-resistant capsules (2 packs of 49)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR 30 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 30 mg hard gastro-resistant capsules
duloxetine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BOTTLE CARTON FOR 30 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 30 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 30 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

30 hard gastro-resistant capsules
100 hard gastro-resistant capsules
250 hard gastro-resistant capsules
500 hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 months after opening.

Opening date:……

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/007 30 hard gastro-resistant capsules
EU/1/15/1010/008 100 hard gastro-resistant capsules
EU/1/15/1010/009 250 hard gastro-resistant capsules
EU/1/15/1010/010 500 hard gastro-resistant capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Duloxetine Viatris 30 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL FOR 30 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 30 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 30 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

30 hard gastro-resistant capsules
100 hard gastro-resistant capsules
250 hard gastro-resistant capsules
500 hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 months after opening.

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/007 30 hard gastro-resistant capsules
EU/1/15/1010/008 100 hard gastro-resistant capsules
EU/1/15/1010/009 250 hard gastro-resistant capsules
EU/1/15/1010/010 500 hard gastro-resistant capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER CARTON FOR 60 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 60 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 60 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

14 hard gastro-resistant capsules
28 hard gastro-resistant capsules
49 hard gastro-resistant capsules
84 hard gastro-resistant capsules
98 hard gastro-resistant capsules
28 x 1 hard gastro-resistant capsules
30 x 1 hard gastro-resistant capsules
100 x 1 hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/011 28 hard gastro-resistant capsules
EU/1/15/1010/012 84 hard gastro-resistant capsules
EU/1/15/1010/013 98 hard gastro-resistant capsules
EU/1/15/1010/014 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/015 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/016 100 x 1 hard gastro-resistant capsules
EU/1/15/1010/029 28 hard gastro-resistant capsules
EU/1/15/1010/030 84 hard gastro-resistant capsules
EU/1/15/1010/031 98 hard gastro-resistant capsules
EU/1/15/1010/032 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/033 30 x 1 hard gastro-resistant capsules
EU/1/15/1010/034 100 x 1 hard gastro-resistant capsules
EU/1/15/1010/035 14 hard gastro-resistant capsules
EU/1/15/1010/036 14 hard gastro-resistant capsules
EU/1/15/1010/049 14 hard gastro-resistant capsules
EU/1/15/1010/050 28 hard gastro-resistant capsules)
EU/1/15/1010/051 28 x 1 hard gastro-resistant capsules
EU/1/15/1010/052 49 hard gastro-resistant capsules
EU/1/15/1010/053 98 hard gastro-resistant capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Duloxetine Viatris 60 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER OUTER CARTON FOR MULTIPACK FOR 60 MG HARD GASTRO RESISTANT CAPSULES, WITH BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 60 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 60 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

Multipack: 98 (2 packs of 49) hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/039 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/040 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/054 98 hard gastro-resistant capsules (2 packs of 49)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Duloxetine Viatris 60 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER INNER CARTON FOR MULTIPACK FOR 60 MG HARD GASTRO RESISTANT CAPSULES, WITHOUT BLUE BOX

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 60 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 60 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

49 hard gastro-resistant capsules
Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/039 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/040 98 hard gastro-resistant capsules (2 packs of 49)
EU/1/15/1010/054 98 hard gastro-resistant capsules (2 packs of 49)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR 60 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 60 mg hard gastro-resistant capsules
duloxetine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BOTTLE CARTON FOR 60 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 60 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 60 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

30 hard gastro-resistant capsules
100 hard gastro-resistant capsules
250 hard gastro-resistant capsules
500 hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 months after opening.

Opening date:……

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/017 30 hard gastro-resistant capsules
EU/1/15/1010/018 100 hard gastro-resistant capsules
EU/1/15/1010/019 250 hard gastro-resistant capsules
EU/1/15/1010/020 500 hard gastro-resistant capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Duloxetine Viatris 60 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL FOR 60 MG HARD GASTRO RESISTANT CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Duloxetine Viatris 60 mg hard gastro-resistant capsules
duloxetine

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 60 mg of duloxetine (as hydrochloride).

3. LIST OF EXCIPIENTS

Contains sucrose.
See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard gastro-resistant capsules

30 hard gastro-resistant capsules
100 hard gastro-resistant capsules
250 hard gastro-resistant capsules
500 hard gastro-resistant capsules

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Use within 6 months after opening.

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Viatris Limited
Damastown Industrial Park,
Mulhuddart, Dublin 15,
DUBLIN
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1010/017 30 hard gastro-resistant capsules
EU/1/15/1010/018 100 hard gastro-resistant capsules
EU/1/15/1010/019 250 hard gastro-resistant capsules
EU/1/15/1010/020 500 hard gastro-resistant capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Duloxetine Viatris 30 mg hard gastro-resistant capsules
Duloxetine Viatris 60 mg hard gastro-resistant capsules
duloxetine

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Duloxetine Viatris is and what it is used for

Duloxetine Viatris contains the active substance duloxetine. Duloxetine Viatris increases the levels of serotonin and noradrenaline in the nervous system.

Duloxetine Viatris is used in adults to treat:
- depression
- generalised anxiety disorder (chronic feeling of anxiety or nervousness)
- diabetic neuropathic pain (often described as burning, stabbing, stinging, shooting or aching or like an electric shock. There may be loss of feeling in the affected area, or sensations such as touch, heat, cold or pressure may cause pain)

Duloxetine Viatris starts to work in most people with depression or anxiety within two weeks of starting treatment, but it may take 2-4 weeks before you feel better. Tell your doctor if you do not start to feel better after this time. Your doctor may continue to give you Duloxetine Viatris when you are feeling better to prevent your depression or anxiety from returning.

In people with diabetic neuropathic pain it can take some weeks before you feel better. Talk to your doctor if you do not feel better after 2 months.

2. What you need to know before you take Duloxetine Viatris

Do not take Duloxetine Viatris if you:
- are allergic to duloxetine or any of the other ingredients of this medicine (listed in section 6)
- have liver disease
- have severe kidney disease

- are taking or have taken within the last 14 days, another medicine known as a monoamine oxidase inhibitor (MAOI) (see 'Other medicines and Duloxetine Viatris')
- are taking fluvoxamine which is usually used to treat depression, ciprofloxacin or enoxacin which are used to treat some infections
- are taking other medicines containing duloxetine (see 'Other medicines and Duloxetine Viatris')

Talk to your doctor if you have high blood pressure or heart disease. Your doctor will tell you if you should be taking Duloxetine Viatris.

Warnings and precautions
The following are reasons why Duloxetine Viatris may not be suitable for you. Talk to your doctor before you take Duloxetine Viatris if you:
- are taking other medicines to treat depression or medicines known as opioids that are used to relieve pain or to treat opioid (narcotic) addiction.
  The use of these medicines together with Duloxetine Viatris can lead to serotonin syndrome, a potentially life-threatening condition (see "Other medicines and Duloxetine Viatris").
- are taking St. John's Wort, a herbal treatment (*Hypericum perforatum*)
- have kidney disease
- have had seizures (fits)
- have had mania
- suffer from bipolar disorder
- have eye problems, such as certain kinds of glaucoma (increased pressure in the eye)
- have a history of bleeding disorders (tendency to develop bruises), especially if you are pregnant (see 'Pregnancy and breast-feeding)
- are at risk of low sodium levels (for example if you are taking diuretics, especially if you are elderly)
- are currently being treated with another medicine which may cause liver damage
- are taking other medicines containing duloxetine (see 'Other medicines and Duloxetine Viatris')

Duloxetine Viatris may cause a sensation of restlessness or an inability to sit or stand still. You should tell your doctor if this happens to you.

You should also contact you doctor:
If you experience signs and symptoms of restlessness, hallucinations, loss of coordination, fast heart beat, increased body temperature, fast changes in blood pressure, overactive reflexes, diarrhoea, coma, nausea, vomiting, as you might be suffering a serotonin syndrome.

In its most severe form, serotonin syndrome can resemble Neuroleptic Malignant Syndrome (NMS). Signs and symptoms of NMS may include a combination of fever, fast heart beat, sweating, severe muscle stiffness, confusion, increased muscle enzymes (determined by a blood test).

Medicines like Duloxetine Viatris (so called SSRIs/SNRIs) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued after stopping treatment.

Thoughts of suicide and worsening of your depression or anxiety disorder
If you are depressed and/or have anxiety disorders you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer.
You may be more likely to think like this if you:
- have previously had thoughts about killing or harming yourself
- are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in adults aged less than 25 years with psychiatric conditions who were treated with an antidepressant

If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.

You may find it helpful to tell a relative or close friend that you are depressed or have an anxiety disorder, and ask them to read this leaflet. You might ask them to tell you if they think your depression or anxiety is getting worse, or if they are worried about changes in your behaviour.

Children and adolescents under 18 years of age
Duloxetine Viatris should normally not be used for children and adolescents under 18 years. Also, you should know that patients under 18 have an increased risk of side-effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines. Despite this, your doctor may prescribe Duloxetine Viatris for patients under 18 because he/she decides that this is in their best interests. If your doctor has prescribed Duloxetine Viatris for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking Duloxetine Viatris. Also, the long-term safety effects concerning growth, maturation, and cognitive and behavioural development of Duloxetine Viatris in this age group have not yet been demonstrated.

Other medicines and Duloxetine Viatris
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

The main ingredient of Duloxetine Viatris, duloxetine, is used in other medicines for other conditions:
- diabetic neuropathic pain, depression, anxiety and urinary incontinence

Using more than one of these medicines at the same time should be avoided. Check with your doctor if you are already taking other medicines containing duloxetine.

Your doctor should decide whether you can take Duloxetine Viatris with other medicines. **Do not start or stop taking any medicines, including those bought without a prescription and herbal remedies, before checking with your doctor.**

You should also tell your doctor if you are taking any of the following:

Monoamine oxidase inhibitors (MAOIs): You should not take Duloxetine Viatris if you are taking, or have recently taken (within the last 14 days) another antidepressant medicine called a monoamine oxidase inhibitor (MAOI). Examples of MAOIs include moclobemide (an antidepressant) and linezolid (an antibiotic). Taking a MAOI together with many prescription medicines, including Duloxetine Viatris, can cause serious or even life-threatening side effects. You must wait at least 14 days after you have stopped taking an MAOI before you can take Duloxetine Viatris. Also, you need to wait at least 5 days after you stop taking Duloxetine Viatris before you take a MAOI.

Medicines that cause sleepiness: These include medicines prescribed by your doctor including benzodiazepines, strong painkillers, antipsychotics, phenobarbital and antihistamines.

Medicines that increase the level of serotonin: Triptans, tryptophan, SSRIs (such as paroxetine and fluoxetine), SNRIs (such as venlafaxine), tricyclic antidepressants (such as clomipramine, amitriptyline), St John's Wort, MAOIs (such as moclobemide and linezolid), opioids (such as buprenorphine, tramadol and pethidine). These medicines may interact with Duloxetine Viatris and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, hallucinations, coma, excessive sweating, tremor, exaggeration of reflexes, increased

muscle tension, body temperature above 38°C. Contact your doctor when experiencing such symptoms, as these might indicate a potentially life-threatening condition known as serotonin syndrome.

***Oral anticoagulants or antiplatelet agents*:** Medicines which thin the blood or prevent the blood from clotting. These medicines might increase the risk of bleeding.

Duloxetine Viatris with food, drink and alcohol
Duloxetine Viatris may be taken with or without food. Care should be taken if you drink alcohol while you are being treated with Duloxetine Viatris.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

- Tell your doctor if you become pregnant, or you are trying to become pregnant, while you are taking Duloxetine Viatris. You should use Duloxetine Viatris only after discussing the potential benefits and any potential risks to your unborn child with your doctor.

- Make sure your midwife and/or doctor knows you are on Duloxetine Viatris. When taken during pregnancy, similar drugs (SSRIs) may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the newborn (PPHN), making the baby breathe faster and appear bluish. These symptoms usually begin during the first 24 hours after the baby is born. If this happens to your baby you should contact your midwife and/or doctor immediately.

- If you take Duloxetine Viatris near the end of your pregnancy, your baby might have some symptoms when it is born. These usually begin at birth or within a few days of your baby being born. These symptoms may include floppy muscles, trembling, jitteriness, not feeding properly, trouble with breathing and fits. If your baby has any of these symptoms when it is born, or you are concerned about your baby's health, contact your doctor or midwife who will be able to advise you.

- If you take Duloxetine Viatris near the end of your pregnancy there is an increased risk of excessive vaginal bleeding shortly after birth, especially if you have a history of bleeding disorders. Your doctor or midwife should be aware that you are taking duloxetine so they can advise you.

- Available data from the use of duloxetine during the first three months of pregnancy do not show an increased risk of overall birth defects in general in the child. If Duloxetine Viatris is taken during the second half of pregnancy, there may be an increased risk that the infant will be born early (6 additional premature infants for every 100 women who take duloxetine in the second half of pregnancy), mostly between weeks 35 and 36 of pregnancy.

- Tell your doctor if you are breast-feeding. The use of Duloxetine Viatris while breast-feeding is not recommended. You should ask your doctor or pharmacist for advice.

Driving and using machines
Duloxetine Viatris may make you feel sleepy or dizzy. Do not drive or use any tools or machines until you know how Duloxetine Viatris affects you.

Duloxetine Viatris contains sucrose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Duloxetine Viatris

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Duloxetine Viatris is for oral use. You should swallow your capsule whole with a drink of water.

For depression and diabetic neuropathic pain:
The usual dose of Duloxetine Viatris is 60 mg once a day, but your doctor will prescribe the dose that is right for you.

For generalised anxiety disorder:
The usual starting dose of Duloxetine Viatris is 30 mg once a day after which most patients will receive 60 mg once a day, but your doctor will prescribe the dose that is right for you. The dose may be adjusted up to 120 mg a day based on your response to Duloxetine Viatris.

To help you remember to take Duloxetine Viatris, you may find it easier to take it at the same times every day.

Talk with your doctor about how long you should keep taking Duloxetine Viatris. Do not stop taking Duloxetine Viatris, or change your dose, without talking to your doctor. Treating your disorder properly is important to help you get better. If it is not treated, your condition may not go away and may become more serious and difficult to treat.

If you take more Duloxetine Viatris than you should
Call your doctor or pharmacist immediately if you take more than the amount of Duloxetine Viatris prescribed by your doctor. Symptoms of overdose include sleepiness, coma, serotonin syndrome (a rare reaction which may cause feelings of great happiness, drowsiness, clumsiness, restlessness, feeling of being drunk, fever, sweating or rigid muscles), fits, vomiting and fast heart rate.

If you forget to take Duloxetine Viatris
If you miss a dose, take it as soon as you remember. However, if it is time for your next dose, skip the missed dose and take only a single dose as usual. Do not take a double dose to make up for a forgotten dose. Do not take more than the daily amount of Duloxetine Viatris that has been prescribed for you in one day.

If you stop taking Duloxetine Viatris
DO NOT stop taking your capsules without the advice of your doctor even if you feel better. If your doctor thinks that you no longer need Duloxetine Viatris he or she will ask you to reduce your dose over at least 2 weeks before stopping treatment altogether.

Some patients who stop taking Duloxetine Viatris suddenly have had symptoms such as:
- dizziness, tingling feelings like pins and needles or electric shock like feelings (particularly in the head), sleep disturbances (vivid dreams, nightmares, inability to sleep), fatigue, sleepiness, feeling restless or agitated, feeling anxious, feeling sick (nausea) or being sick (vomiting), shaking (tremor), headaches, muscle pain, feeling irritable, diarrhoea, excessive sweating or vertigo.

These symptoms are usually not serious and disappear within a few days, but if you have symptoms that are troublesome you should ask your doctor for advice.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. These effects are normally mild to moderate and often disappear after a few weeks.

Very common side effects (may affect more than 1 in 10 people)
- headache, feeling sleepy
- feeling sick (nausea), dry mouth

Common side effects (may affect up to 1 in 10 people)
- lack of appetite
- trouble sleeping, feeling agitated, less sex drive, anxiety, difficulty or failure to experience orgasm, unusual dreams
- dizziness, feeling sluggish, tremor, numbness, including numbness, pricking or tingling of the skin
- blurred eyesight
- tinnitus (hearing sound in the ear when there is no external sound)
- feeling the heart pumping in the chest,
- increased blood pressure, flushing
- increased yawning
- constipation, diarrhoea, stomach pain, being sick (vomiting), heartburn or indigestion, breaking wind
- increased sweating, (itchy) rash
- muscle pain, muscle spasm
- painful urination, frequent urination
- problems getting an erection, changes in ejaculation
- falls (mostly in elderly people), fatigue
- weight loss

Children and adolescents under 18 years of age with depression treated with this medicine had some weight loss when they first start taking this medicine. Weight increased to match other children and adolescents of their age and sex after 6 months of treatment.

Uncommon side effects (may affect up to 1 in 100 people)
- throat inflammation that causes a hoarse voice
- suicidal thoughts, difficulty sleeping, grinding or clenching the teeth, feeling disorientated, lack of motivation
- sudden involuntary jerks or twitches of the muscles, sensation of restlessness or an inability to sit or stand still, feeling nervous, difficulty concentrating, changes in sense of taste, difficulty controlling movement e.g. lack of coordination or involuntary movements of the muscles, restless legs syndrome, poor sleep quality
- large pupils (the dark centre of the eye), problems with eyesight
- feeling of dizziness or “spinning” (vertigo), ear pain
- fast and/or irregular heart beat
- fainting, dizziness, lightheadedness or fainting on standing up, cold fingers and/or toes
- throat tightness, nose bleeds
- vomiting blood, or black tarry stools (faeces), gastroenteritis, burping, difficulty swallowing
- inflammation of the liver that may cause abdominal pain and yellowing of the skin or whites of the eyes
- night sweats, hives, cold sweats, sensitivity to sunlight, increased tendency to bruise
- muscle tightness, muscle twitching
- difficulty or inability to pass urine, difficulty to start urinating, needing to pass urine during the night, needing to pass more urine than normal, having a decreased urine flow

- abnormal vaginal bleeding, abnormal periods, including heavy, painful, irregular or prolonged periods, unusually light or missed periods, sexual dysfunction, pain in the testicles or scrotum
- chest pain, feeling cold, thirst, shivering, feeling hot, abnormal gait
- weight gain
- Duloxetine Viatris may cause effects that you may not be aware of, such as increases in liver enzymes or blood levels of potassium, creatine phosphokinase, sugar, or cholesterol

Rare side effects (may affect up to 1 in 1,000 people)
- serious allergic reaction which causes difficulty in breathing or dizziness with swollen tongue or lips, allergic reactions
- decreased thyroid gland activity which can cause tiredness or weight gain
- dehydration, low levels of sodium in the blood (mostly in elderly people; the symptoms may include feeling dizzy, weak, confused, sleepy or very tired, or feeling or being sick, more serious symptoms are fainting, fits or falls), syndrome of inappropriate secretion of anti-diuretic hormone (SIADH)
- suicidal behaviour, mania (over activity, racing thoughts and decreased need for sleep), hallucinations, aggression and anger
- "Serotonin syndrome" (a rare reaction which may cause feelings of great happiness, drowsiness, clumsiness, restlessness, feeling of being drunk, fever, sweating or rigid muscles), fits
- increased pressure in the eye (glaucoma)
- inflammation of the mouth, passing bright red blood in your stools, bad breath, inflammation of the large intestine (leading to diarrhoea)
- liver failure, yellowing of the skin or whites of the eyes (jaundice)
- Stevens-Johnson syndrome (serious illness with blistering of the skin, mouth, eyes and genitals), serious allergic reaction which causes swelling of the face or throat (angioedema)
- contraction of the jaw muscle
- abnormal urine odour
- menopausal symptoms, abnormal production of breast milk in men or women
- coughing, wheezing and shortness of breath which may be accompanied by a high temperature
- excessive vaginal bleeding shortly after birth (postpartum haemorrhage)

Very rare side effects (may affect up to 1 in 10,000 people)
- inflammation of the blood vessels in the skin (cutaneous vasculitis)

Frequency not known (cannot be estimated from the available data)
- signs and symptoms of a condition called "stress cardiomyopathy" which may include chest pain, shortness of breath, dizziness, fainting, irregular heartbeat.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Duloxetine Viatris

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton.

Store in the original package in order to protect from moisture.

Bottle packs only:
Use within 6 months of opening.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Duloxetine Viatris contains
The active substance is duloxetine.
Each capsule contains 30 mg or 60 mg of duloxetine (as hydrochloride).

The other ingredients are:
Capsule content: Sugar spheres (sucrose, maize starch), hypromellose, Macrogol, Crospovidone, talc, sucrose, hypromellose phthalate, diethyl phthalate.

Capsule shell: Brilliant blue (E133), yellow iron oxide (E172) (60 mg only), titanium dioxide (E171), gelatin and edible gold ink (30 mg only) or edible white ink (60 mg only).
Edible gold ink: shellac, propylene glycol, strong ammonia solution, yellow iron oxide (E172).
Edible white ink: shellac, propylene glycol, sodium hydroxide, povidone, titanium dioxide (E171).

What Duloxetine Viatris looks like and contents of the pack
Duloxetine Viatris is hard gastro-resistant capsule. Each capsule of Duloxetine Viatris contains pellets of duloxetine hydrochloride with a covering to protect them from stomach acid.

Duloxetine Viatris is available in 2 strengths: 30 mg and 60 mg.
The 30 mg capsules have an opaque blue cap and opaque white body, imprinted in gold ink with 'MYLAN' over 'DL 30' on both the cap and the body.
The 60 mg capsules have an opaque blue cap and opaque yellow body, imprinted in white ink with 'MYLAN' over 'DL 60' on both the cap and the body.

Duloxetine Viatris 30 mg is available in blister packs of 7, 14, 28, 49, 98 and in a multipack of 98 comprising 2 cartons, each containing 49 capsules, in perforated blister packs containing 7 x1, 28 x 1, 30 x 1 capsules and in bottles containing 30, 100, 250, 500 capsules and a desiccant. Do not eat the desiccant.
Duloxetine Viatris 60 mg is available in blister packs of 14, 28, 49, 84, 98 and in a multipack of 98 comprising 2 cartons, each containing 49 capsules, in perforated blister packs containing 28 x 1, 30 x 1, and 100 x 1capsules and bottles containing 30, 100, 250 and 500 capsules and a desiccant. Do not eat the desiccant.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Viatris Limited, Damastown Industrial Park, Mulhuddart, Dublin 15, DUBLIN, Ireland

Manufacturers

Mylan Hungary Kft., Mylan utca 1, Komárom 2900, Hungary

Mylan Germany GmbH, Zweigniederlassung Bad Homburg v. d. Hoehe, Benzstrasse 1, Bad Homburg v. d. Hoehe, Hessen, 61352, Germany

For any further information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Viatris
Tél/Tel: + 32 (0)2 658 61 00

България
Майлан ЕООД
Тел: +359 2 44 55 400

Česká republika
Viatris CZ s.r.o.
Tel: +420 222 004 400

Danmark
Viatris ApS
Tlf: +45 28 11 69 32

Deutschland
Viatris Healthcare GmbH
Tel: +49 800 0700 800

Eesti
Viatris OÜ
Tel: +372 6363 052

Ελλάδα
Viatris Hellas Ltd
Τηλ: +30 2100 100 002

España
Viatris Pharmaceuticals, S.L.
Tel: + 34 900 102 712

France
Viatris Santé
Tél: +33 4 37 25 75 00

Lietuva
Viatris UAB
Tel: +370 5 205 1288

Luxembourg/Luxemburg
Viatris
Tél/Tel: + 32 (0)2 658 61 00
(Belgique/Belgien)

Magyarország
Viatris Healthcare Kft.
Tel.: + 36 1 465 2100

Malta
V.J. Salomone Pharma Ltd.
Tel: + 356 21 22 01 74

Nederland
Mylan BV
Tel: +31 (0)20 426 3300

Norge
Viatris AS
Tlf: +47 66 75 33 00

Österreich
Viatris Austria GmbH
Tel.: +43 1 86390

Polska
Viatris Healthcare Sp. z o.o.
Tel: + 48 22 546 64 00

Portugal
Mylan, Lda.
Tel: + 351 214 127 200

Hrvatska
Viatris Hrvatska d.o.o.
Tel: +385 1 23 50 599

Ireland
Viatris Limited
Tel: +353 1 8711600

Ísland
Icepharma hf.
Sími: +354 540 8000

Italia
Viatris Italia S.r.l.
Tel: +39 02 612 46921

Κύπρος
CPO Pharmaceuticals Limited
Τηλ: +357 22863100

Latvija
Viatris SIA
Tel: + 371 676 055 80

România
BGP Products SRL
Tel: + 4 0372 579 000

Slovenija
Viatris d.o.o.
Tel: +386 1 23 63 180

Slovenská republika
Viatris Slovakia s.r.o.
Tel: +421 2 32 199 100

Suomi/Finland
Viatris Oy
Puh/Tel: +358 20 720 9555

Sverige
Viatris AB
Tel: + 46 (0)8 630 19 00

This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.