DULOXETINE ORION, CAPSULES

PUBLIC SUMMARY OF RISK MANAGEMENT PLAN

DATE: 23-04-2015, VERSION 1.3

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Duloxetine Orion is a medicine that is used to treat adults with the following diseases:

Major depressive disorder

Major depressive disorder or major depression is a disease where a person has persistent low mood or loss of interest in things they used to enjoy. In addition the person may experience loss of energy or changes in appetite and sleep.

Estimates in various countries across the world (Belgium, France, Germany, Italy, the Netherlands, Spain, and the United States) suggest that approximately 17.5% of people have major depressive disorder.

Generalised anxiety disorder

Generalised anxiety disorder is long-term anxiety or nervousness about everyday matters. The cause of generalised anxiety disorder is not clear although it is believed to be related to both genetic factors and life experiences.

The number of people affected by this condition varies between different countries and cultures. Regardless of geography, however, women are more likely to be affected than men. There also appear to be more cases of generalised anxiety disorder among older people up until the age of 60, when the number of cases begins to decline. Among those aged 18 to 64 years, it is estimated that 6.2% (7.7% of women and 4.6% of men) will have generalised anxiety disorder over their lifetimes.

Diabetic peripheral neuropathic pain

Diabetic peripheral neuropathic pain is pain that results from damage to nerve endings in the extremities and is caused by diabetes.

Approximately 16% to 26% of people with diabetes have diabetic peripheral neuropathic pain.

VI.2.2 Summary of treatment benefits

For major depression, duloxetine has been compared with placebo (a dummy treatment) in eight main studies involving a total of 2,544 patients. Six of the studies looked at the treatment of depression and measured the change in symptoms over up to six months. The other two studies looked at how long it took for symptoms to return in patients who had initially responded to duloxetine, including 288 patients with a history of repeated episodes of depression for up to five years. Although the results of the depression studies varied, duloxetine was more effective than placebo in four of the studies. In the two studies where the approved dose of duloxetine was compared with placebo, duloxetine was more effective. It also took longer for symptoms to return in patients taking duloxetine than in those taking placebo.

For neuropathic pain, duloxetine has been compared with placebo in two 12-week studies in 809 diabetic adults. The main measure of effectiveness was the change in the severity of pain each week.

These studies showed that duloxetine was more effective at reducing pain than placebo. In both studies, pain reduction was seen from the first week of treatment for up to 12 weeks.

For generalised anxiety disorder, duloxetine has been compared with placebo in five studies involving a total of 2,337 patients. Four studies looked at the treatment of the disorder by measuring the reduction in symptoms after nine to 10 weeks. The fifth study looked at how long it took for symptoms to return in 429 patients who had initially responded to duloxetine. Duloxetine was shown to be more effective than placebo at treating the disorder and preventing symptoms returning.

VI.2.3 Unknowns relating to treatment benefits

Duloxetine should not be used in patients under 18 years old as its benefit has not been demonstrated. In studies specifically involving patients aged above 65 years with depression or anxiety, no difference in response was seen compared with younger patients, but some older people may be more sensitive to duloxetine.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Problems with the liver (hepatic risks)	Problems with the liver including hepatitis, elevated liver enzymes and acute (short-term) liver injury, are uncommon and may affect up to 1 in 100 people. Liver failure or yellowing of skin or eyes (jaundice) is rare and may affect up to 1 in 1,000 people.	Liver problems are not preventable because they cannot be predicted. Patients with liver disease or patients who drink a lot of alcohol should not take duloxetine. Patients and those who care for them should watch for signs of problems with the liver such as yellowing of the skin or eyes. If these are seen, patients should tell their doctor immediately.

Risk	What is known	Preventability
Suicide attempts and thoughts about committing suicide (suicidality)	Suicide attempts and thoughts about committing suicide are uncommon and may affect up to 1 in 100 people.	This risk is not preventable. Patients should contact their doctor or go to a hospital straightaway if they have thoughts of harming or killing themselves at any time. Patients may find it helpful to tell a relative or close friend that they are depressed or have an anxiety disorder and ask them to read the patient leaflet. Patients might ask family or friends to tell them if they think the depression or anxiety symptoms are getting worse or if they are worried about changes in the patient's behaviour.

Risk	What is known	Preventability
		Patients with a history of suiciderelated behaviours should be carefully monitored during treatment.

Risk	What is known	Preventability
High blood sugar levels (hyperglycaemia)	High blood sugar levels are uncommon and may affect up to 1 in 100 people.	Patients should tell their doctor if they have diabetes. Patients and those who care for them should watch for symptoms of high blood sugar levels such as urinating a lot more than usual, drinking a lot more than usual, and feeling weak.

Risk	What is known	Preventability
Serious illness with blistering of the skin, mouth, eyes and other parts of the body (Stevens-Johnson syndrome)	This illness is rare and may affect up to 1 in 1,000 people.	Patients who have had this illness could have it again, but it is not predictable. Doctors should be aware of this risk, and patients and those who care for them should watch for symptoms of blistering of the skin, mouth, eyes, and other parts of the body and should notify the doctor/seek medical attention immediately if these are seen.

Risk	What is known	Preventability
Bleeding in the stomach and intestine (gastrointestinal tract bleeding)	This risk is uncommon and may affect up to 1 in 100 people.	This risk is not preventable. Doctors should be aware of this risk. Duloxetine should be used with caution in patients taking anticoagulants (blood thinners such as warfarin) and/or medicines known to affect platelet function (such as non-steroidal anti-inflammatory drugs [NSAIDs]) and in patients with known bleeding tendencies.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Heart and blood vessel problems (cardiovascular events) including heart attack, heart failure and stroke	Small increases in blood pressure and heart rate have been seen in duloxetine clinical trials. The long-term effects of small increases of blood pressure and heart rate are not known for duloxetine. Patients who have high blood pressure and take blood pressure medication

Risk	What is known (Including reason why it is considered a potential risk)
	together with an NSAID may be at risk for increased blood pressure when combined with duloxetine treatment. Potential heart effects to watch out for are signs of a heart attack, stroke, and heart failure; all are very rarely reported events. In patients with a sustained increase in blood pressure while receiving duloxetine, dose reduction or gradual discontinuation should be considered.

Risk	What is known (Including reason why it is considered a potential risk)
Kidney failure (renal failure)	Kidney problems were very rarely reported in clinical trials and in reports from everyday clinical experience. There was no indication in clinical trials that the risk of kidney failure was higher in duloxetine-treated patients than in placebotreated patients.

Missing information

Risk	What is known
Risk of exposure to duloxetine during pregnancy (prospective data about potential risks of exposure to duloxetine during pregnancy)	There is limited information about the use of duloxetine in women who are pregnant; therefore the potential risk to unborn babies is unknown. Women and their doctors should think carefully about whether duloxetine is needed during pregnancy.

Risk	What is known
Use of duloxetine 120 mg in elderly patients	There is not much information about duloxetine use in elderly patients. The dose of duloxetine does not need to be adjusted for patients in this age group, but elderly patients may be more sensitive to duloxetine and caution should be used in treating such patients with the maximum possible dose (120 mg per day) of duloxetine.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures. The Summary of Product Characteristics and the Package leaflet for Duloxetine Orion can be found in the national authority's web page.
This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan (if applicable)

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable.