PUBLIC SUMMARY OF RISK MANAGEMENT PLAN (RMP)

FLUOXETINE ORION 20 MG HARD CAPSULE

ORION CORPORATION

DATE: 27-09-2016, VERSION 1.1

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Major depressive episodes

Depression is a medical illness that involves the brain. It is a very common condition that affects around one in every five people. Many factors can cause depression, including the genes (DNA), brain chemistry, and environmental factors like stress. Depression is different from feeling sad or down every now and then. People with depression constantly feel sad, with lack of energy, feel tired, and have difficulty enjoying routine activities almost every day. Not everyone with depression feels sad or down. Other symptoms of depression include: changes in sleeping habits such as sleeping poorly or sleeping more than usual, losing interest in usual activities such as favourite hobbies, time with family members, or evenings out with friends, not eating as much or eating more, whether or not you are hungry, strong feelings of despair, worthlessness, or hopelessness, finding it hard to think or concentrate, feelings of excessive or inappropriate guilt, and thoughts of suicide. Depression is a serious, but treatable, problem that should not be ignored. Depression is treated with medicines, talk therapy (talking with a trained professional about thoughts and feelings, sometimes called "psychotherapy" or "counselling"), or a combination of the two.

Obsessive-compulsive disorder (OCD)

Obsessive-compulsive disorder (OCD) is a condition in which people have unwanted and repeated thoughts, feelings, ideas, sensations (obsessions), or behaviours that make them feel driven to do something (compulsions). This problem can be accompanied by eating disorders, other anxiety disorders, or depression. It strikes men and women in roughly equal numbers. Common obsessions include the following: contamination, safety, doubting one's memory or perception, need to do the right thing, need for order or symmetry, unwanted, intrusive sexual/aggressive thoughts. Common compulsions include the following: cleaning/washing, checking (e.g. locks, stove, iron, safety of children), counting/repeating actions a certain number of times or until it feels right, arranging objects, confessing/seeking reassurance. One-third of adults with OCD develop symptoms as children, and research indicates that OCD might run in families. Both pharmacological and behavioural treatments can benefit the person with OCD.

Bulimia nervosa

Bulimia nervosa is an eating disorder that is characterised by episodes of binging and purging the food (compensation by means of self-induced vomiting and/or excessive ingestion of laxatives to induce diarrhoea) and or associated calories. Bulimia is a significant public-health problem, both because of the physical and mental health effects it can have. While there is no known specific cause for bulimia, family history and environmental stressors are thought to contribute to the development of the illness. Adolescents are most at risk for developing bulimia, as statistics show that about three-quarters of people who develop the illness do so before they reach 22 years of age, most often at 15 to 16 years of age. Cognitive behavioural therapy is thought to be somewhat superior to other forms of psychotherapy in treating this

eating disorder. Medication, nutritional counseling, and family therapy are also often part of the treatment for bulimia.

VI.2.2 Summary of treatment benefits

Fluoxetine Orion is a prescription medicine used for the treatment of major depressive episodes, obsessive-compulsive disorder and bulimia nervosa. It belongs to class of medicines known as selective serotonin reuptake inhibitors (SSRI).

The efficacy of fluoxetine for the treatment for major depressive episodes was established in several studies as compared to placebo.

For the treatment of obsessive-compulsive disorder, fluoxetine was found to be more effective than placebo in short-term trials (under 24 weeks).

In short term trials (under 16 weeks), in out-patients for bulimia nervosa, fluoxetine 60 mg/day was shown to be significantly more effective than placebo for the reduction of binging, vomiting and purging activities.

VI.2.3 Unknowns relating to treatment benefits

Animal data have shown that fluoxetine may affect sperm quality. Human case reports with some SSRI's have shown that an effect on sperm quality is reversible. Impact on human fertility has not been observed so far.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Suicide/suicidal thoughts or clinical worsening of the disease	If patient is depressed and/or has anxiety disorders he/she can sometimes have thoughts of harming or killing himself/herself. These may be increased when first starting antidepressants, since these medicines all take time to work, usually about two weeks but sometimes longer.	Doctor should be contacted if patient has thoughts of harming or killing himself/herself at any time.
Abnormality in the heart's electrical system (QT prolongation)	Cases of QT interval prolongation (an abnormality in the heart's electrical system) and ventricular arrhythmia including torsades de pointes (abnormal very fast and dangerous heart rhythms) have been reported during the postmarketing period. Use of fluoxetine with following medicines may affect the heart's rhythm, *e.g.* Class IA and III antiarrhythmics, antipsychotics (*e.g.* phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants, certain antimicrobial agents (*e.g.* sparfloxacin, moxifloxacin, erythromycin IV, pentamidine), anti-malaria treatment particularly halofantrine or certain	Fluoxetine should be used with caution in patients with conditions such as congenital long QT syndrome, a family history of QT prolongation or other clinical conditions that predispose to arrhythmias (abnormal heart rhythms). Patients should inform their doctor or pharmacist if they are taking, have recently taken or might take any other medicines.

Risk	What is known	Preventability
	antihistamines (astemizole, mizolastine). Combination with these medicines may increase the risk of changes in the electrical activity of the heart.	
Abnormal elevated or irritable mood state (Activation of mania)	Abnormal elevated or irritable mood (mania) was commonly reported in paediatric trials. Antidepressants should be used with caution in patients with a history of mania/hypomania.	Regular monitoring for the occurrence of mania is recommended. Fluoxetine should be discontinued in any patient entering a manic phase.
Bleeding (Haemorrhage)	There have been reports of skin bleeding abnormalities such as ecchymosis (discoloration of the skin resulting from bleeding underneath, typically caused by bruising) and purpura (rash of purple spots on the skin caused by internal bleeding from small blood vessels) with selective serotonin re-uptake inhibitors (SSRI's). Ecchymosis has been reported as an infrequent event during treatment with fluoxetine. Other bleeding manifestations (*e.g*. vaginal bleeding, stomach bleeding, bleeding in stools) have been reported rarely.	Caution is advised in patients taking SSRI's, particularly in concomitant use with oral anticoagulants (medicines used to thin blood), drugs known to affect platelet function (*e.g.* atypical antipsychotics such as clozapine, phenothiazines, most TCA's, acetylsalisylic acid, NSAID's) or other drugs that may increase risk of bleeding as well as in patients with a history of bleeding disorder.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Use in pregnancy and lactation	In babies whose mothers took fluoxetine during the first few months of pregnancy, there have been some studies describing an increased risk of birth defects affecting the heart. In the general population, about 1 in 100 babies are born with a heart defect. This increased to about 2 in 100 babies in mothers who took fluoxetine. When taken during pregnancy, particularly in the last 3 months of pregnancy, medicines like fluoxetine may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the newborn (condition in whiuch there is increased ling pressure), 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, doctor should be contacted immediatley. It is preferable not to use this treatment during pregnancy unless the potential benefit outweighs the potential risk. Caution should be exercised when used during pregnancy, especially during late pregnancy or just before giving birth since the following effects have been reported in new born children: irritability, tremor, muscle weakness, persistent crying, and difficulty in sucking or in sleeping. Fluoxetine is excreted in breast milk therefore, it may cause side effects in the baby. If treatment with fluoxetine is considered

Risk	What is known (Including reason why it is considered a potential risk)
	necessary, discontinuation of breastfeeding should be considered; however, if breastfeeding is continued, the lowest effective dose of fluoxetine should be prescribed.
Effect on fertility	Fluoxetine has shown to reduce sperm count in animal studies. Theoretically, this could affect fertility, but effect on human fertility has not been observed as yet.

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 Fluoxetine 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.