Docetaxel Orion 20 mg/1 ml concentrate for solution for infusion
Docetaxel Orion 80 mg/4 ml concentrate for solution for infusion
Docetaxel Orion 160 mg/8 ml concentrate for solution for infusion

11.8.2014, version 1.1

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Docetaxel Orion is used to treat the following types of cancer: breast cancer, non-small-cell lung cancer, prostate cancer, gastric adenocarcinoma and head and neck cancer.

Breast cancer is a common form of cancer. Most of the patients (eight out of 10) are women over 50, but younger women, and in rare cases, men, can also get breast cancer. Invasive breast cancer is a type of cancer that has the ability to spread outside the breast. The most common form is invasive ductal breast cancer. Invasive ductal breast cancer accounts for about 80% of all cases of breast cancer.

Lung cancer is one of the most common and serious types of cancer. Although people who have never smoked can develop lung cancer, smoking is the main cause of it (about 90% of cases). Lung cancer mainly affects older people. It is rare in people younger than 40, but the rates of lung cancer rise sharply with age. Lung cancer is most commonly diagnosed in people aged 70-74 years.

Cancer that begins in the lungs is called primary lung cancer. There are two main types of primary lung cancer. These are classified by the type of cells in which the cancer starts. Non-small-cell lung cancer is the most common type of lung cancer, accounting for more than 80% of cases. Non-small-cell lung cancer includes squamous cell carcinoma, adenocarcinoma and large-cell carcinoma.

Prostate cancer is common among older men. It is rare in men younger than 40. Risk factors for developing prostate cancer include being over 65 years of age, family history, being African-American, and some genetic changes.

Several types of cancer can occur in the stomach. The most common type is called adenocarcinoma. It starts from one of the common cell types found in the lining of the stomach. It is a common cancer of the digestive tract worldwide and occurs most often in men over age 40. This form of gastric cancer is common in eastern Asia, parts of South America, and eastern and central Europe.

Cancers that start in the tissues and organs of the head and neck are called with general term head and neck cancers. The term covers many different types of cancer e.g. eye cancer, cancers in the nasal cavity and in the sinuses around the nose, cancer in the area that connects the back of the nose to the back of the mouth, cancers of the tongue, the gums, cheeks, lip and floor and roof of the mouth, larynx or laryngeal cancer, cancer of the food pipe or gullet, salivary gland cancer.

Using tobacco or alcohol increases risk for head and neck cancers. Approximately 85 percent of head and neck cancers are linked to tobacco use.

VI.2.2 Summary of treatment benefits

Docetaxel Orion is a generic medicine. Its benefits and risks are taken as being the same as the reference medicine's.

Docetaxel, belongs to the group of anticancer medicines known as the taxanes. Docetaxel blocks the ability of cells to destroy the internal 'skeleton' that allows them to divide and multiply. With the skeleton still in place, the cells cannot divide and they eventually die.

In clinical studies conducted with the reference product, adding docetaxel to other anticancer treatments produced increases in the number of patients whose cancer responded to treatment, how long the patients lived without their disease getting worse and how long the patients survived, in all five types of cancer. When used on its own, docetaxel was at least as effective as and sometimes more effective than the comparator medicines in breast cancer, and more effective than best supportive care (any medicines or techniques to help patients, but not other anticancer medicines) in lung cancer.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Important identified risks:		
Neutropenia - Abnormally low count of neutrophils, a type of white blood cells that help fight off infections, particularly those caused by bacteria and fungi.	Neutropenia is the most common adverse reaction of docetaxel. Lowest amount of neutrophils have been measured at a median of 7 days after the docetaxel dose but this interval may be shorter in heavily pre-treated patients. Neutropenia increases risk for severe infections.	Blood tests are taken before each treatment cycle. Lower doses are administered or treatment is discontinued, if the amount of neutrophils is too low. Patients may receive certain growth factor which helps to create new neutrophils and prevents neutropenia. Patients should be carefully monitored and doctor needs to be contacted in case of signs or symptoms of infection.
Allergic/Hypersensitivity reactions	Hypersensitivity reactions have been reported in 1-5% of patients. They have generally occurred within a few minutes following the start of the infusion of docetaxel and have	Docetaxel Orion should not be given to a patient who is allergic/hypersensitive to docetaxel or any of the excipients.

Risk	What is known	Preventability
	been usually mild or moderate. The most frequently reported symptoms were flushing, rash with or without itching, chest tightness, back pain, shortness of breath and fever or chills. Severe reactions were characterised by low blood pressure and/or spasm of airways in lungs or generalized rash/redness . Some cases of anaphylactic shock, sometimes fatal, have been reported.	Careful monitoring of the patientduring and after the infusion. Preparedness for immediate first-aid in case of acute hypersensitivity reaction.
Respiratory disorders	Different kinds of disorders in respiratory system have been reported in association with docetaxel therapy. In some cases even resulting in death of the patient.	If new or worsening respiratory/lung symptoms develop, patients should be closely monitored, promptly investigated, and appropriately treated. Interruption of docetaxel therapy is recommended until diagnosis is available. Early use of supportive care measures may help improve the condition. The benefit of resuming docetaxel treatment must be carefully evaluated.
Eye disorders	Cases of cystoid macular oedema (CMO; cyst-like swelling of macula, a special area in the center of the back surface of the eye) have been reported in patients treated with docetaxel.	Patients with impaired vision should undergo a prompt and complete ophthalmologic examination. If cystoid macular oedema is diagnosed, docetaxel treatment should be discontinued and appropriate treatment initiated.
Skin reactions	Very rare cases of severe skin	Careful monitoring of the patient. Appropriate treatment and discontinuation of docetaxel therapy, if necessary.

Risk	What is known	Preventability
	reactions (skin lupus erythematosus and bullous eruptions, that result in fluid-filled blisters or bullae, such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis), have been reported with docetaxel. In some cases concomitant factors may have contributed to the development of these effects.	
Damage/Toxic effects on heart	Heart failure has been observed in patients receiving docetaxel in combination with other cancer medication trastuzumab, particularly following anthracycline (doxorubicin or epirubicin)-containing chemotherapy. The degree of heart failure may vary from moderate to severe and has been associated with death. In patients treated with the TAC regimen (docetaxel, doxorubicin, cyclophosphamide) for node-positive breast cancer, the risk of heart failure has been shown to be higher during the first year after treatment.	Before treatment doctor should be informed of history of any previous heart problems. Patients should be monitored for symptoms of heart failure during therapy and during the follow-up period. When treatment with docetaxel in combination with trastuzumab is considered, patient's heart function should be examined before the treatment. Heart function should also be further monitored during treatment (e.g. every three months) to help to identify patients who may develop heart dysfunction.
Severe damage/toxic effects to the peripheral nervous system (the part of the nervous system that is outside the brain and spinal cord)	Cases of toxic effect on peripheral nerves have been reported. Mild to moderate neuro-sensory signs are characterised by feeling of numbness, pins and needles or pain including burning. Neuro-motor events are mainly characterised by weakness.	Before treatment doctor should be informed of history of any previous nerve damage. During the treatment doctor should be informed if any symptoms appear, which could be related to nerve damage e.g. feeling of numbness, pins and needles or muscle weakness. If symptoms appear, lower dose should be administered or, if necessary, treatment will be discontinued.

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Use in patients with hepatic impairment	Very rare cases of hepatitis, sometimes resulting in death primarily in patients with pre-existing liver disorders, have been reported. Docetaxel must not be used in patients with severe liver impairment. Reduced dose recommended in patients with mild/moderate increase in liver enzyme levels. No dosage recommendations can be given in patients with high increase in liver enzyme levels and docetaxel should be used in these patients only if strictly indicated.
Renal failure	Renal insufficiency and renal failure have been reported in association with docetaxel. In about 20% of these cases there were no risk factors for acute renal failure such as concomitant nephrotoxic medicinal products and gastrointestinal disorders. There are no data available in patients with severely impaired renal function treated with docetaxel.
Male fertility	Undesirable effects on the testis observed in rodent toxicity studies suggest that docetaxel may impair male fertility. Therefore, men being treated with docetaxel are advised not to father a child during and up to 6 months after treatment and to seek advice on conservation of sperm prior to treatment.

Missing information

Risk	**What is known**
Pregnancy and lactation	There is no information on the use of docetaxel in pregnant women. Docetaxel has been shown to be both embryotoxic and foetotoxic in rabbits and rats, and to reduce fertility in rats. As with other cytotoxic medicinal products, docetaxel may cause foetal harm when administered to pregnant women. Therefore, docetaxel must not be used during pregnancy unless clearly indicated. Women of childbearing age receiving docetaxel should be advised to avoid becoming pregnant, and to inform the treating physician immediately should this occur. Docetaxel is a lipophilic substance but it is not known whether it is excreted in human milk. Consequently, because of the potential for adverse reactions in nursing infants, breast feeding must be discontinued for the duration of docetaxel therapy. <u>Contraception in males and females</u> An effective method of contraception should be used during

Risk	What is known
	treatment.

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 Docetaxel Orion can be found in the authority's web page

This medicine has no additional risk minimisation measures

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment