7.2 Part VI.2 Elements for a Public Summary

7.2.1 Part VI.2.1 Overview of disease epidemiology

Breast cancer is by far the most frequent cancer among women with an estimated 1.38 million new cancer cases diagnosed in 2008 (23% of all cancers). New diagnosed cases vary from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe, and are high (> 80/100,000 women) in developed regions of the world (except Japan) and low (less than 40/100,000 women) in most of the developing regions.
The range of mortality rates is much less (approximately 6-19/100,000) because of the more favourable survival of breast cancer in developed regions. As a result, breast cancer ranks as the fifth cause of death from cancer overall, but it is still the most frequent cause of cancer death in women in both developing and developed regions, where the estimated number of deaths is almost equal to the estimated number of deaths from lung cancer. [Ferlay et al., 2010]

7.2.2 Part VI.2.2 Summary of treatment benefits

In a study, 848 advanced breast cancer patients received 250 mg fulvestrant / month and were followed-up for 9 months. 62.7% had no cancerprogression after ≥ 24 weeks, in 74% the disease was . Approximately 89% of the patients survived 9 months. The patients whose cancer was stable at 3 months benefitted from continued fulvestrant therapy. No new or unexpected safety issues arose; 90% of the patients and physicians rated fulvestrant tolerability as "very good" or "good". [Warm et al., 2011]

In another study, 83 patients with metastatic breast cancers which respond to hormones (HR MBC) were enrolled whose MBC had progressed after Tamoxifen, a drug which acts against oestrogen activity in the breast tissue, or Aromatase Inhibitors, drugs which act against oestrogen production. Six, 32, 33 and 12 patients received Fulvestrant 250 mg/month as 1st, 2nd, 3rd and 4th Hormone therapy for MBC, respectively. Fulvestrant resulted in an overall clinical benefit in 38.6% of the patients,Overall survival was 20.1 months (15.8-24.4 months). Overall, the treatment was well tolerated. Joint pain, swelling, and muscle pain were the most common side effects, all were mild to moderate. It was concluded that Fulvestrant is an active treatment in extensively pre-treated patients with HR MBC with an optimal safety profile. [De Angelis et al., 2013]

7.2.3 Part VI.2.3 Unknowns relating to treatment benefits

The safety and efficacy of Fulvestrant in children from birth to 18 years of age have not been established.

7.2.4 Part VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Increased risk of blood clots (Thromboembolic events)	Thromboembolism (formation of a blood clot that plugs the blood vessel; blood clots may break loose and travel to another place, such as the lung) is a common side effect of Fulvestrant 250 mg/	This risk should be taken into consideration when prescribing Fulvestrant 250 mg/ 5 ml Solution for injection to patients at risk.

Risk	What is known	Preventability
	5 ml Solution for injection (may affect up to 1 in 10 people). The exact role of the product cannot be assessed due to the underlying disease. Thromboembolism may need immediate medical treatment.	
Liver problems (Hepatic events)	Increase of gamma-GT, a liver enzyme seen in a blood test, inflammation of the liver (hepatitis) and liver failure are uncommon side effects of Fulvestrant 250 mg/ 5 ml Solution for injection (may affect up to 1 in 100 people). Hepatitis and Liver failure may need immediate medical treatment. Abnormal levels of liver enzymes (in blood tests) are observed very commonly under therapy with Fulvestrant 250 mg/ 5 ml Solution for injection (may affect more than 1 in 10 people). The exact role of Fulvestrant cannot be assessed due to the underlying disease. Increase of bilirubin (bile pigment produced by the liver) is observed commonly (may affect up to 1 in 10 people).	The doctor should be informed if a patient has liver problems. The drug should not be used if a patient has severe liver problems.
Injection site reactions	Injection site reactions, such as pain and/or inflammation are very common side effects (may affect more than 1 in 10 people), bruising and bleeding at the site of injection uncommon side effects (may affect up to 1 in 100 people) of Fulvestrant 250 mg/ 5 ml Solution for injection.	The doctor, pharmacist, or nurse should be informed if the patient notices injection site reactions.
Hypersensitivity (allergic) reactions	Allergic (hypersensitivity) reactions, including swelling of the face, lips, tongue and/or throat are common side effects (may affect up to 1 in 10 people) of Fulvestrant 250 mg/ 5 ml Solution for injection. A patient may need immediate medical treatment if he/she experiences allergic (hypersensitivity) reactions, including swelling of the face, lips, tongue and/or throat.	This product must not be used if a patient is allergic to fulvestrant or to any of the other ingredients of this medicine.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Bone thinning (Osteoporosis / Osteopenia)	There are no long-term data on the effect of fulvestrant on bone. But due to the mechanism of action of fulvestrant, there is a potential risk of bone thinning. The doctor should be informed if a patient has bone thinning.
Foetal abnormalities and loss of pregnancy	In studies with animals, foetal abnormalities and loss of pregnancy occurred. Hence, if pregnancy occurs while taking Fulvestrant 250 mg/ 5 ml Solution for injection, there is a potential hazard to the foetus and potential risk for loss of pregnancy. Fulvestrant 250 mg/ 5 ml Solution for injection must not be used if a woman is pregnant. If she can become pregnant, she should use effective methods to prevent a pregnancy while being treated with this drug.
Events due to poor blood supply which involve heart, blood vessels or both (Ischaemic cardiovascular events)	Currently there is no sufficient data to assess the causality of Fulvestrant to events due to poor blood supply which involve heart, blood vessels or both.
Abnormal cells of the lining of the womb (Endometrial dysplasia)	Currently there is no sufficient data to assess the causality of Fulvestrant to abnormal cells of the lining of the womb.
Joint disorder	Currently there is no sufficient data to assess the causality of Fulvestrant to joint disorders.
Lung disease of the tissue and space around the air sacs of the lungs (Interstitial lung disease)	Currently there is no sufficient data to assess the causality of Fulvestrant to lung disease of the tissue and space around the air sacs of the lungs.
Inflammation (swelling and redness) of the blood vessels (Vasculitis)	Currently there is no sufficient data to assess the causality of Fulvestrant to inflammation of the blood vessels.
Formation of micro-clots of oily solutions that plug the blood vessels in the lung (Pulmonary microembolism of oily solutions)	Currently there is no sufficient data to assess the causality of Fulvestrant to formation of micro-clots of oily solutions that plug the blood vessels in the lung.

Missing information

Risk	What is known
Safety and efficacy in children and adolescents	The safety and efficacy of fulvestrant in children from birth to 18 years of age have not been established. Fulvestrant 250 mg/ 5 ml Solution for injection is not indicated in children and adolescents under 18 years.
Patients with severely decreased liver function (Patients with severe hepatic impairment)	There are no data in patients with severely decreased liver function. The drug should not be used if a patient has severe liver problems. The doctor should be informed if a patient has severe liver problems.
Patients with severely decreased kidney function (Patients with severe renal impairment)	The doctor should be informed if a patient has severe kidney problems. This medicinal product should be used with caution in patients with severe kidney problems.
Use during pregnancy and breast feeding	Fulvestrant 250 mg/ 5 ml Solution for injection must not be used if a woman is pregnant. If she can become pregnant,

Risk	What is known
(Use in pregnancy and lactation)	she should use effective methods to prevent a pregnancy while being treated with the drug. It is not known whether fulvestrant is excreted in human milk. A woman must not breast-feed while on treatment with this drug.

7.2.5 Part VI.2.5 Summary of additional 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.

This medicine has no additional risk minimisation measures.

7.2.6 Part VI.2.6 Planned post authorisation development plan

N/A

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

N/A. This is the first RMP.