VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Estrogen receptor-positive breast cancer:
Breast cancer is the most common cancer in women. Incidence rates vary greatly worldwide from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. Some of the factors associated with breast cancer are female gender, age, family history, genetics, obesity, physical inactivity, alcohol or hormone replacement therapy. One type of breast cancer is estrogen receptor positive (ER+) type in which the cancer cells, like normal breast cells, may receive signals from estrogen that could promote their growth. About 75% of all breast cancers are “ER+”. Breast cancer tumours that are ER+ are likely to respond to endocrine therapy. Endocrine therapies are usually taken after surgery, chemotherapy, and/or radiation. Such therapy helps prevent recurrence of the disease by blocking the effects of estrogen.

VI.2.2 Summary of treatment benefits

Based on available data from clinical studies and clinical experience, fulvestrant represents an effective drug in the treatment of locally advanced breast cancer (the cancer has started to spread) or metastatic breast cancer (the cancer has already spread to other parts of the body) in women who have been through the menopause. It is used for cancer that is “oestrogen-receptor positive” (when the cancer cells have receptors for the hormone oestrogen on their surface). Fulvestrant is used when the disease has returned during or after treatment with an “anti-oestrogen” (a type of medicine used to treat breast cancer), or when the disease has got worse during treatment with an anti-oestrogen.

If administered as indicated in the Summary of Product Characteristics and taking into account the contraindications, the warnings and precautions, fulvestrant can be considered effective in the approved indication.

VI.2.3 Unknowns relating to treatment benefits

Limited or no information is available in the treatment of:

- paediatric population (children aged 0 to 18 years),
- patients with severe hepatic impairment,
- patients with severe renal impairment.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Injection site reactions	Fulvestrant may cause reactions at the injection site such as pain and/or inflammation. Injection site reactions, such as pain and/or inflammation are very common side effects (may affect more than 1 in 10 people).	If the patients get injection site reactions, such as pain and/or inflammation, they should talk to their doctor, pharmacist or nurse.
Increased risk of bleeding at the injection site	Bruising and bleeding at the site of injection can occur due to the injection of the drug directly into a muscle (intramuscular route). Therefore, fulvestrant should be	The patients should tell to their doctor, pharmacist, or nurse before using fulvestrant if they have low numbers of platelets (which help blood clotting), bleeding disorders, previous problems with

Risk	What is known	Preventability
	used with caution if treating patients with bleeding problems, low blood platelet count (thrombocytopenia) or those taking medicines to prevent blood clots. Bruising and bleeding at the site of injection is an uncommon side effects (may affect up to 1 in 100 people).	blood clots, or if they are using anticoagulants (medicines to prevent blood clots). If the patients get bruising and bleeding at the site of injection, they should inform their doctor, pharmacist or nurse.
Increased risk of blood clots within a vein (venous thromboembolic events)	Increased risk of blood clots (thromboembolism) is commonly seen in women with advanced breast cancer. However, the exact role of fulvestrant cannot be assessed since the cancer patients are at higher risk of developing venous thromboembolic events.	The patients may need immediate medical treatment if they experience thromboembolism (increased risk of blood clots). The patients should tell to their doctor, pharmacist, or nurse before using fulvestrant if they have bleeding disorders or previous problems with blood clots.
Allergic (hypersensitivity) reactions	Allergic reactions such as swelling of the face, lips, tongue and/or throat and itching skin and skin rash such as hives may occur with fulvestrant.	The patients should not get fulvestrant if they are allergic to fulvestrant or any of the other ingredients of this medicine. The patients should tell to their doctor, pharmacist, or nurse before getting fulvestrant if they have allergic reactions, including swelling of the face, lips, tongue and/or throat. The patients should inform their doctor, pharmacist, or nurse immediately if they experience allergic (hypersensitivity) reactions, including swelling of the face, lips, tongue and/or throat.
Liver and bile disorders (hepatobiliary disorders)	Abnormal levels of liver enzymes (in blood tests) are a very common side effect of fulvestrant (may affect more than 1 in 10 people). Elevation of bile pigment produced by the liver (bilirubin) is common side effect (may affect up to 1 in 10 people). Increase of gamma-GT (a liver enzyme seen in a blood test) is an uncommon side effect (may affect up to 1 in 100 people). Patients may also develop inflammation of the liver (hepatitis) and liver failure.	Patients should consult their doctor, pharmacist or nurse before using fulvestrant if they have any liver problems. Patients with severe liver problems should not use fulvestrant. The patients should inform their doctor, pharmacist, or nurse immediately if they experience inflammation of the liver (hepatitis), or liver failure. If the patients get abnormal levels of liver enzymes, increase of bilirubin (bile pigment produced by the liver) or increase of gamma-GT (a liver enzyme seen in a blood test), they should talk to their doctor, pharmacist or nurse.

Important potential risks

Risk	What is known (including reason why it is considered a potential risk)
Reduced bone mineral density	There are no long-term data on the effect of fulvestrant on bone. Due to the mechanism of action of fulvestrant, there is a potential risk of osteoporosis. The

Risk	What is known (including reason why it is considered a potential risk)
(osteopenia) and loss of bone density (osteoporosis)	patients should talk to their doctor, pharmacist, or nurse before using fulvestrant if they have osteoporosis.
Ischaemic heart and blood vessels problems (cardiovascular events)	The patients treated with fulvestrant may be at a potential risk of developing ischaemic cardiovascular events. However, the exact mechanism by which fulvestrant may cause heart problems is not well-understood.
Abnormal changes of the endometrium (endometrial dysplasia)	There is possibility of abnormal changes of the inner mucous membrane of the uterus (endometrium) due to fulvestrant therapy. Animal data do not suggest that fulvestrant would have that effect on the uterus of postmenopausal women. Current data in breast cancer patients treated with fulvestrant did not result in clinically significant changes in endometrial thickness. There is no evidence of uterus thickness change in the breast cancer patients studied.
Joint disorders	The patients treated with fulvestrant may be at a potential risk of developing joint disorders. However, a mechanism by which fulvestrant might cause them is not known.
Disease that inflames or scars the lungs (interstitial lung disease)	The patients treated with fulvestrant may be at a potential risk of developing interstitial lung disease. However, a mechanism by which fulvestrant might cause this event is not known.
Inflammation of blood vessels (vasculitis)	The patients treated with fulvestrant may be at a potential risk of developing vasculitis. However, a mechanism by which fulvestrant might cause this event is not known.
Oily solution gets into the lung (pulmonary microembolism of oily solutions)	As the product contains castor oil as an ingredient, it must not be administered into a vein. The oily solutions must be injected strictly intramuscularly and very slowly. Pulmonary microembolism of oily solutions could lead to signs and symptoms such as cough, shortness of breath (dyspnoea) or chest pain. These reactions may occur during or immediately after the injection and are reversible.

Missing information

Risk	What is known
Treatment of children aged 0 to less than 18 years	Fulvestrant is not indicated in children and adolescents under 18 years, as safety and efficacy have not been established in this group of patients.
Use in pregnant or breastfeeding women	Fulvestrant must not be used in pregnant women. Studies in animals have shown toxicity in the animal foetuses (reproductive toxicity) including an increased incidence of foetal abnormalities and deaths. Animal studies have shown excretion of fulvestrant in breast milk. It is not known whether fulvestrant is excreted in human milk. Considering the potential for serious adverse reactions, fulvestrant should not be used during lactation. If the patients can become pregnant, they should use effective contraception while being treated with fulvestrant.
Use in patients with severe liver	The patients must not get fulvestrant if they have severe liver problems, since there are no data for this patient group. Fulvestrant should be used with caution

Risk	What is known
problems (hepatic impairment)	in patients with mild to moderate liver problems, since the exposure may be increased. The patients should talk to their doctor, pharmacist, or nurse before getting fulvestrant if they have liver problems, or suffer from alcoholism.
Use in patients with severe kidney problems (renal impairment)	Fulvestrant should be used with caution in patients with severe renal impairment. The patients should talk to their doctor, pharmacist, or nurse before getting fulvestrant if they have kidney problems.
Reproductive toxicity (reprotoxicity)	Fulvestrant must not be used in pregnant women. Studies in animals have shown toxicity in the animal foetuses (reproductive toxicity) including an increased incidence of foetal abnormalities and deaths. If the patients can become pregnant, they should use effective contraception while being treated with fulvestrant.

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 Patient Information Leaflet (PIL). The measures in these documents are known as routine risk minimisation measures.

No additional risk minimisation measures are proposed.

VI.2.6 Planned post authorisation development plan

Not applicable.

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

Not applicable.