VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Tumours of the testis

Testicular cancer is a disease in which malignant (cancer) cells form in the tissues of one or both testicles. It is the most common cancer in men 15-34 years of age. Approximately 0.4 percent of men will be diagnosed with testis cancer at some point during their lifetime. There has been a steady increase in incidence over previous decades in industrialised countries. If the tumour is diagnosed early, over 95% of men are cured (>95% of people survive 5 Years or more after being diagnosed with testis cancer).

A certain form of lung cancer (small cell lung cancer)

Small cell lung cancer is a disease in which malignant (cancer) cells form in the tissues of the lung. Approximately 6.6 percent of men and women will be diagnosed with lung and bronchus cancer at some point during their lifetime. Lung cancer is more common in men than women. Tobacco smoking is the most common cause of lung cancer. Lung cancer is the leading cause of death from cancer in the U.S. 17,4% of people survive 5 Years or more after being diagnosed with Small cell lung cancer. If the cancer is found only in the part of the body where it started (localised), 54.8% of people survive 5 Years or more after being diagnosed with Small cell lung cancer.

Certain types of cancer of the blood (acute myeloid leukaemia, AML)

Leukemia is cancer of the blood cells. The type of leukemia depends on the type of blood cell that has become cancerous. Acute myeloid leukemia (AML) is a type of cancer in which the bone marrow makes abnormal myeloblasts (a type of white blood cell), red blood cells, or platelets.
Although leukemia is among the most common childhood cancers, it most often occurs in older adults. Leukemia occurs most often in adults older than 55 years. Acute leukemia is a fast-growing cancer that usually gets worse quickly. Acute myeloid leukaemia is not common. In the European Union, 5 to 8 cases will be diagnosed among 100,000 people every year.

VI.2.2 Summary of treatment benefits

Etoposide is a cancer chemotherapy drug which slows the process of cell division. Etoposide belongs to a class of drugs known as podophyllotoxin derivatives; it slows or stops the growth of cancer cells in the body.

Based on the available data from clinical studies and clinical experience of several years, etoposide represents an effective drug in the treatment of:

- Tumours of the testis in combination with other products against cancer.

- A certain form of lung cancer (small cell lung cancer), in combination with other products against cancer.

- Certain types of cancer of the blood (acute myelomonocytic and monocytic leukaemia; in combination with other products against cancer.)

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

VI.2.3 Unknowns relating to treatment benefits

There are no adequate and well-controlled studies in pregnant women and in paediatric population.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Haematological toxicity (Blood toxicity)	The following was reported with etoposide: bone marrow suppression (myelosuppression), especially a reduction of the number of white blood cells (leucopenia) and platelets (thrombocytopenia) which makes infections more likely and increases the risk of bleeding or bruising, reduction of red blood cells which can make the skin pale and cause weakness or breathlessness (anaemia).	Etoposide should not be used if you have severe suppression of the functioning of the bone marrow, unless when this is caused by your disease. If you have bone marrow depression caused by radiation therapy or chemotherapy, your doctor will not restart the treatment until your blood tests shows that this is justified. Also tell your doctor if you think that you have infections.
Anaphylactic reaction (severe allergic reaction)	Hypersensitivity (anaphylactoid) reactions characterised by fever, flushing, increased heart rate (tachycardia), contraction of the airways (bronchospasms), breathing difficulties and low blood pressure (hypotension). Also temporarily stopping with breathing (apnoea) followed by spontaneous return of breathing after withdrawal of etoposide infusion, increase in blood pressure. The reactions can be managed by discontinuing the etoposide infusion and administration of blood pressure increasing products, corticosteroids, antihistamines and/or volume enlarging products as appropriate. Anaphylactoid-type reactions can occur after the first intravenous administration of etoposide. Redness of the skin (erythema), swelling (oedema) of the face and tongue, coughing, perspiring, blue discolouration of the lips, tongue, skin and mucous membranes due to a lack of oxygen in the blood (cyanosis), spasms (convulsions), vocal cord spasm (laryngospasms) and high blood pressure (hypertension) were also observed. The blood pressure	If you think that you might have an allergic reaction causing flushing, fast heartbeat, difficulty in breathing and a severe reduction in blood pressure (anaphylactic reaction). Tell your doctor immediately of these symptoms, you may need urgent medical attention.

Risk	What is known	Preventability
	generally normalises within a few hours after ending the infusion. Anaphylactoid reactions were more often reported in children who received doses that were higher than recommended.	
Hypotension (drop in blood pressure) **following rapid intravenous administration**	Drop in blood pressure after an etoposide infusion is administered too rapidly.	Can be prevented by reducing the rate of the infusion.
Injection site reactions	Leaking of fluid outside the vessel (extravasation) was reported following etoposide injection administration.	Etoposide should be only administered in a vein. If you have a stinging or burning sensation at the place where you have been injected with etoposide, it may be due to leaking of etoposide out of the vein. If this happens please tell your doctor as they will start treatment from a different vein and will monitor the affected area carefully.
Secondary leukemia	Blood cancer (secondary leukemia) and a certain form of blood cancer (Acute promyelocytic leukaemia) were reported with etoposide.	The total (cumulative) dose of etoposide has been associated to the higher risk. Etoposide is only used under strict supervision of a doctor experienced with the use of cytostatics. Tell your doctor if you have previously been treated with products against cancer or if you have received radiation therapy.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Mutagenic potential in germ cells (changes in human reproductive egg or the sperm cell)	During and for 6 months after the use of etoposide both men and women must use products to prevent pregnancy. Because etoposide can cause infertility, men can have their sperm frozen at the sperm bank before the treatment with etoposide starts.
Concurrent use of live vaccines	Patients should not use etoposide if they will receive yellow fever vaccine or other live vaccines. Etoposide may reduce the effectiveness of the immune system, therefore yellow fever vaccine or other live vaccines should not be used in immunosuppressed patients

Missing information

Risk	What is known
Paediatric use	Safety and effectiveness of etoposide in paediatric patients have not been investigated.
Geriatric use	The safety and efficacy of etoposide in elderly people have not been established.

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 information leaflet (PIL). The measures in these documents are known as routine risk minimisation measures.

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

Not applicable. This is the pre-approval Teva RMP version for etoposide.