VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Small-cell bronchial carcinoma (a tumour in airways, type of lung cancer):

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Small cell lung cancer (a tumour in airways) is an aggressive subtype of lung cancer. Without treatment, in a few weeks it could lead to death. It is important to determine if the cancer is limited or is at an extensive stage. Limited-stage cancer can be treated with chemotherapy and radiation. Extensive-stage cancer is treated with chemotherapy alone. These cancers occur in individuals aged 60-80 years. Globally, lung cancer is the most frequent malignancy in men (in Europe, lung cancer is second only to prostate cancer) and the fifth most common cancer in women.

Hodgkin's disease (a type of cancer originating from white blood cells called lymphocytes)**:**

Hodgkin lymphoma (a certain type of lymph tumour) is one of the most common cancers among older children and adolescents. In UK, there is higher frequency in males compared with females. It is the third most commonly diagnosed cancer in people aged 15-29 years, and the sixth most commonly diagnosed cancer in children under 15. Infectious agents may be involved in the manner of development of the disease. Patients with HIV infection have a higher frequency compared with the population without HIV infection.

Non-Hodgkin's lymphoma (NHL, a type of cancer originating from white blood cells called lymphocytes)**:**

Non-Hodgkin lymphoma (NHL, a certain type of lymph tumour) is the fifth most common cancer in the UK (2009), accounting for 4% of all new cases. It is the fifth most common cancer among men (2009) in the UK and the seventh most common cancer among women (2009).

Acute myeloid leukaemia in adults (a malignant disease of the white blood cells)**:**

The frequency of Acute Myeloid Leukemia (a malignant disease of the white blood cells) varies with gender and race. In the first few years of life, the frequency of Acute Myeloid Leukaemia in whites is 3-fold higher than in blacks; however, blacks have slightly higher rates of Acute Myeloid Leukaemia among children age ≥3 years.

Testicular tumours (cancer of testis)**:**

Testicular cancer (cancer of testis) is a relatively rare cancer and is responsible for just over 1% of all male cancers. Testicular cancer rarely occurs before teenage but it is the most common cancer in men aged 15-44 years.

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Large increases in frequency of testicular cancer have been reported in many countries around the world over the last 40 years including the USA, Canada, Europe, Nordic countries, Australia and the UK.

VI.2.2 Summary of treatment benefits

Accord has not conducted any studies for etoposide on expected benefit considering the similarities of active ingredient and the route of administration to the currently marketed product (ETO-cell® 20 mg/ml Injection manufactured/marketed by Cell Pharm GmbH). Accord's Etoposide is expected to be beneficial for:

- The treatment of the small-cell bronchial carcinoma (a tumour in airways, type of lung cancer),
- Hodgkin's disease
- Non-Hodgkin's lymphoma (a type of cancer originating from white blood cells called lymphocytes)
- Re-induction therapy after the failure of standard therapies in acute myeloid leukaemia (a malignant disease of the white blood cells)
- Testicular tumours (cancer of testis)

The medical benefits to be expected from Accord's etoposide are similar to those of existing etoposide formulations.

VI.2.3 Unknowns relating to treatment benefits

Safety and effectiveness in children and adolescents have not been established.

VI.2.4 Summary of safety concerns

Important identified risks

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Risk	What is known	Preventability
Occurrence of secondary acute leukaemia (severe blood cancer)	Acute leukemia can occur in patient after the treatment of etoposide.	Yes Talk to your doctor or pharmacist before you start to use etoposide. Before the start of therapy, during the therapy, and before each course of treatment, a peripheral blood panel (white blood cells, platelets, haemoglobin), should be checked.
Myelosuppression (A condition in which bone marrow activity is decreased resulting in production of fewer blood cells and platelets)	Myelosuppression is very common side effect of etoposide. Concurrent use of other myelosuppressive (inhibiting bone marrow activity) medicines may have additive or synergetic effects.	Yes. Tell your doctor or pharmacist, if you are using other medicines, have recently used other medicines, or intend to use other medicines, eg. other myelosuppressive (inhibiting bone marrow activity) medicines.

Important potential risks

Risk	What is known
Teratogenicity (affecting the development of foetus) following use during	Etoposide should not normally be administered to pregnant women. If used during pregnancy, the patient must be told of

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Risk	What is known
pregnancy	the potential risk to the foetus.
Anaphylactic (Severe allergy) reaction to polysorbate 80	Etoposide Injection must not be used inpatients allergic to etoposide, podophyllotoxin, podophyllotoxin derivatives or any of the other ingredients of this medicine (anhydrous citric acid, benzyl alcohol, polysorbate 80, polyethylene glycol 300 (Macrogol 300) and anhydrous ethanol).-
Risk of toxic reactions in infant and children associated to the excipient polysorbate 80 (Risk of life threatening syndrome of liver, cholestatis and kidney failure, lung deterioration, thrombocytopenia and ascites associated to the excipient polysorbate 80 in newborn infants)	Etoposide Accord contains polysorabte 80. It must not be given to newborn babies. It may cause toxic reactions in infant and children.

Missing information

Risk	What is known
Nil	

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

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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.

VI.2.6 Planned post authorisation development plan

No studies planned.

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

Version	Date	Safety Concern	Comment
5.0	04 October 2017	"Myelosuppression" was added as important identified risk.	RMP has been updated as per CMS (FR) Day-55 assessment report
4.0	**03 April 2014**	**Following safety concern was modified:** The risk of Allergic reaction/ Anaphylactic reaction to etoposide, or any other ingredients of Etoposide Accord was modified to Allergic reaction/Anaphylactic reaction to polysorbate 80.	The language and information provided in part "Elements for a public summary" has been simplified in lay terms
3.0	**04 March 2014**	**Following safety concerns were deleted:** **Important identified risks:**	The language and information provided in part "Elements for a

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		Myelosuppression **Important potential risk:** Infusion site reactions including extravasation The risk of Anaphylactic reaction has been updated to Anaphylactic reaction to etoposide, or any other ingredients of Etoposide Accord. Due to the updation of product information, following safety concerns are revised: • Risk of toxicities in patients with hepatic or renal dysfunction and Risk of metabolic acidosis associated to the excipient benzyl alcohol have been deleted. • Risk of life threatening syndrome of liver and renal failure, pulmonary deterioration, thrombocytopenia and ascites associated to the excipient polysorbate 80 in premature infants has been updated to risk of life threatening syndrome of liver, cholestatis and renal	public summary" has been simplified in lay terms

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		failure, pulmonary deterioration, thrombocytopenia and ascites associated to the excipient polysorbate 80 in newborn infants.	
2.0	14 October 2013	Following safety concerns are added: **Important identified risks:** Occurrence of acute leukaemia, Myelosuppression **Important potential risk:** Risk of toxicities in patients with hepatic or renal dysfunction Teratogenicity following use during pregnancy Infusion site reactions including extravasation Anaphylactic reaction Risk of metabolic acidosis associated to the excipient benzyl alcohol Risk of life threatening syndrome of liver and renal failure, pulmonary deterioration, thrombocytopenia and ascites associated to the excipient polysorbate 80 in premature infants Paediatric population removed as	-

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		Missing Information Part VI has been updated with these safety concerns.	

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