VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Testicular cancer

Testicular cancer is the 16th most common cancer among men in the UK (2011), accounting for 1% of all new cases of cancer in males. In 2011, there were 2,207 new cases of testicular cancer in the UK. The crude incidence rate shows that there are 7 new testicular cancer cases for every 100,000 males in the UK. Although the incidence of testicular cancer is low throughout the world, it is estimated to have doubled in the last 40 years and there is appreciable variation between countries. The highest rates of testicular cancer are reported for white Caucasian populations in industrialised countries, particularly in western and northern Europe and Australia/New Zealand, while the disease is generally rare in non-Caucasian populations - the New Zealand Maoris being the

exception.

Ovarian cancer:

Ovarian cancer is the 5th most common cancer among women in the UK (2011), accounting for 4% of all new cases of cancer in females. In 2011, there were 7,116 new cases of ovarian cancer in the UK. The crude incidence rate shows that there are 22 new ovarian cancer cases for every 100,000 females in the UK. Ovarian cancer is the fifth most common cancer in Europe for females, and the 13th most common cancer overall, with around 65,600 new cases diagnosed in 2012 (4% of female cases and 2% of the total). In Europe (2012), the highest World age-standardised incidence rate for ovarian cancer are in Latvia; the lowest are in Albania. UK ovarian cancer incidence rates are estimated to be the ninth highest in Europe.

Bladder cancer:

Bladder cancer is the seventh most common cancer in the UK (2011), accounting for 3% of all new cases. In males, it is the fourth most common cancer, whilst it is the 13th most common cancer in females. In 2011, there were 10,399 new cases of bladder cancer in the UK: 7,452 in men and 2,947 in women, giving a male: female ratio of around 25:10. The crude incidence rate shows that there are 24 new bladder cancer cases for every 100,000 males in the UK, and 9 for every 100,000 females. Bladder cancer is the 5th most common cancer in Europe, with more than 151,000 new cases diagnosed in 2012. In Europe, the highest World age-standardised incidence rates for bladder cancer are in Belgium for men and Hungary for women; the lowest rates are in the United Kingdom for men and the Ukraine for women.

Advanced non-small-cell lung carcinoma (NSCLC):

Lung cancer is one of the most common cancers worldwide, with 1.35 million new cases diagnosed every year. Non-small cell lung cancer accounts for 85% of all lung cancer cases. It is estimated that lung cancer accounts for an average of 20% of all cancer deaths. Almost half of the cases of lung cancer occur in developing countries, with men being affected more than women (globally, 36 per 100,000 men compared with 12 per 100,000 women). The incidence differs considerably across different countries in Europe. The rates vary from 22 to 63 per 100 000 and from 5 to 33/100 000 per year in men and women,

respectively. In most European countries, the incidence continues to rise in women but decreases in men. This trend seems to occur later in Southern and Eastern Europe than in the Northern regions.

Metastatic or recurrent head and neck cancer:

Head and neck cancers are common in several regions of the world where tobacco use and alcohol consumption is high. Overall, head and neck cancer accounts for more than 550,000 cases annually worldwide. Males are affected significantly more than females with a ratio ranging from 2:1 to 4:1. The incidence rate in males exceeds 20 per 100,000 in regions of France, Hong Kong, the Indian subcontinent, central and Eastern Europe, Spain, Italy, Brazil and among African Americans in the Unites States. The major risk factors include tobacco or betel quid chewing, cigarette or bidi smoking, and alcohol consumption.

Small cell lung cancer (SCLC):

Globally, lung cancer is the most frequent malignancy in men and the fifth most common cancer in women. An estimated 1.6 million new lung cancers are diagnosed worldwide each year. The highest occurence rates in males are observed in Central/Eastern and Southern Europe (57 and 49 per 100 000, respectively), whereas in women the highest rates are found in Northern Europe (36 per 100 000). Virtually all patients have a history of tobacco use. Therefore, smoking habits are closely linked to incidence, which varies across different populations. There was a decrease of SCLC incidence over time and by birth in both sexes. The decrease in SCLC was more marked than that in all lung cancers. The decrease in SCLC occurence rates may reflect decreases in the prevalence of cigarette smoking, and changes in the type of cigarettes smoked.

Cervical cancer:

Cervical cancer is the 12th most common cancer among females in the UK (2011), accounting for around 2% of all new cases of cancer in females. In 2011, there were 3,064 new cases of cervical cancer in the UK. The crude incidence rate shows that there are around 10 new cervical cancer cases for every 100,000 females in the UK. Cervical cancer

is the sixth most common cancer in Europe for females, and the 16th most common cancer overall, with around 58,400 new cases diagnosed in 2012 (4% of female cases and 2% of the total). In Europe (2012), the highest World age-standardised incidence rates for cervical cancer are in Romania; the lowest are in Switzerland. UK cervical cancer incidence rates are estimated to be the 12th lowest in Europe. These data are broadly in line with Europe-specific data available elsewhere.

VI.2.2 Summary of treatment benefits

Cisplatin can destroy cells in body that may cause certain types of cancer (tumour of testis, tumour of ovary, tumour of the bladder, head and neck epithelial tumour, lung cancer and for cervical cancer in combination with radiotherapy).

Accord has not done any studies to evaluate the expected benefits of Cisplatin Accord considering its similarity to the currently marketed product.

VI.2.3 Unknowns relating to treatment benefits

The efficacy of Cisplatin Accord is applicable to all patients in the target population based on demographics.

VI.2.4 Summary of safety concerns

Important identified risks:

Risk	**What is known**	**Preventability**
Toxic effect on kidneys (Nephrotoxicity)	Agents to treat high blood pressure (antihypertensives containing furosemide, hydralazine, diazoxide, and propranolol) may increase the toxic effect of cisplatin on kidneys.	Yes Patients are advised not to take Cisplatin if they have kidney problems (renal dysfunction) Doctor will carry out tests in order to determine the kidney

Risk	What is known	Preventability
	Cisplatin toxicity may severely affect the kidneys when administered simultaneously with agents that may cause side effects in the kidneys, such as those for the prevention/ treatment of certain infections (antibiotics: cephalosporins, aminoglycosides, and/or amphotericin B) and contrast agents. Giving a drug that increases the amount urine the body produces (loop diuretics) in combination with cisplatin may damage the kidneys An unknown number of patients may experience kidney dysfunction, such as failure to produce urine (anuria) and urine poisoning of the blood (uraemia).	functionality. In order to avoid, or reduce, kidney problems, patients are advised to drink large amounts of water for a period of 24 hours following treatment with Cisplatin.
Nerve damage (Neuropathies)	Administration of cisplatin prior to treatment with paclitaxel or in combination with docetaxel may result in severe nerve damage. Patients may rarely experience sensory nerve demage (bilateral, sensory neuropathy), characterised by tickling, itching or tingling	Yes Patients are advised not to take Cisplatin if they have previously suffered from nervous disorders caused by cisplatin

Risk	What is known	Preventability
	without cause and sometimes characterised by a loss of taste, touch, sight, sudden shooting pains from the neck through the back into the legs when bending forwards.	
Damage to the ear (Ototoxicity)	Cisplatin may damage a patient's hearing, especially when given at the same time as drugs that affect hearing (e.g. aminoglycosides). Giving a drug that increases the amount urine the body produces (loop diuretics) in combination with cisplatin may damage patient's hearing. Cisplatin given in combination with ifosphamide may result in hearing impairment. Uncommonly patients may experience damage to the ear (ototoxicity). Rarely, patients may not be able to hold normal conversation, loss of hearing (in particular among children and elderly patients). An unknown number of patients may experience loss of hearing combined with tinnitus (ringing in	Yes Patients are advised not to take Cisplatin if their hearing is impaired Patient's hearing will be tested prior to each treatment with Cisplatin.

Risk	What is known	Preventability
	ears)	
Allergy (Hypersensitivity reactions)	Uncommonly patients may experience hypersensitivity reactions, including rash, eczema with severe itching and lump formation (urticaria), redness and inflammation of the skin (erythema) or itching (pruritus), (anaphylactoid reactions) with symptoms such as swelling of the face and fever, low blood pressure (hypotension), accelerated heartbeat (tachycardia), breathing difficulties (dyspnoea), distress as a result of muscle cramps in the airways (bronchospasms)	Yes Patients are advised not to take cisplatin if they are allergic (hypersensitive) to cisplatin or to any of the other ingredients of cisplatin or any other medicine that contains platina compounds Patient may be administered agents (antihistamines, such as buclizine, cyclizine, loxapine, meclozine, phenothiazines, thioxanthenes and/or trimethobenzamides) to treat hypersensitivity.
Decreased ability or inability of the bone marrow to produce blood cells (Bone marrow depression)	Simultaneous use of medicines that inhibit the bone marrow function or radiation can potentiate the adverse effects of cisplatin on the bone marrow Very commonly patients may experience suppression of the bone marrow characterised by a severe decrease of white blood cells, which makes infections more likely (leukopenia), reduction in blood platelets, which increases	Yes Patients are advised not to take Cisplatin if they suffer from severe suppression of bone marrow functionality, symptoms may be: extreme tiredness, easy bruising or bleeding, occurrence of infections

Risk	What is known	Preventability
	the risk of bruising and bleeding (thrombocytopenia), as well as reduction in red blood cells, which can make the skin pale and cause weakness or breathlessness (anaemia)	
Drug interaction with live vaccines, including yellow fever vaccine	Yellow fever vaccine is strictly contraindicated because of the risk of life-threatening vaccinal disease. In view of the risk of generalised illness, it is advisable to use an inactive vaccine if available.	Yes Patients are advised not to take Cisplatin combined with live vaccines, including yellow fever vaccine
Drug interaction with phenytoin	Cisplatin may reduce the absorption of phenytoin resulting in reduced epilepsy control when phenytoin is given as current treatment.	Yes Patients are advised not to take Cisplatin combined with phenytoin

Important potential risks

Risk	What is known
Injection site reactions	Patients may commonly experience inflammation of a vein (phlebitis) at injection site. At an unknown frequency patient may experience pain, redness and inflammation of the skin (erythema, skin

Risk	What is known
	ulcer) at the area of injection. If cisplatin is injected outside the blood vessels, the administration must be stopped immediately. Infiltration of cisplatin in the skin can result in tissue damage (cellulitis, fibrosis and necrosis).
Ability to produce secondary cancers (Secondary carcinoma)	Rarely, Cisplatin, like other similar medicines, increases the risk of leukaemia (acute leukaemia).
Birth defects (Teratogenicity)	Cisplatin may be toxic to the foetus when administered to a pregnant woman. Cisplatin must not be used during pregnancy unless clearly indicated by doctor. Patients must use effective contraception during and at least 6 months after treatment with cisplatin.
Infertility	Male patients treated with cisplatin are advised not to father a child during treatment and for up to 6 months after treatment. Further, men are advised to seek counseling on sperm preservation before starting treatment. An unknown number of patients may experience impaired sperm production and impaired egg production .
Inflammation of the eye nerve combined with pain and reduced nerve function (optic neuritis)	An unknown number of patients may experience inflammation of the eye nerve combined with pain and reduced nerve function.
Use in lactating females	Cisplatin is excreted in breast milk. Patients treated with

Risk	What is known
	cisplatin must not breastfeed.

Missing information

Risk	What is known
None	-

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.

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
3.0	24 July 2014	No changes are made in safety concerns	The Overview of disease epidemiology (Part VI.2.1) and Summary of safety concerns (Part VI.2.4) have

Version	Date	Safety Concern	Comment
			been revised.
2.0	24 June 2014	Following safety concerns are added: Important identified risks: • Drug interaction with live vaccines, including yellow fever vaccine • Drug interaction with phenytoin Important potential risk: • Optic neuritis • Use in lactating females	The Overview of disease epidemiology (Part VI.2.1) has been revised.