VI.2. Elements for a Public Summary

VI.2.1. Overview of Disease Epidemiology

Acute lymphocytic leukaemia (ALL) occurs more commonly in children, and, in Europe, ALL is diagnosed in around 3.59 children (ages 0 to 14 years) per 100,000, and in 1.28 out of every 100,000 adults a year. Deaths per 100,000 among children with ALL ages 0 to 14 years occur up to 4 times more often compared to those without ALL.[115] As a result of toxicity from chemotherapy regimens, patients with ALL have an increased chance of heart complications such as heart attack, congestive heart failure, disease of the lining surrounding the heart and problems with the heart muscle.[116] Other complications from treatment include cerebrovascular (e.g. stroke) and thrombotic events (e.g. blood clots).[117]

In Europe, AML is diagnosed in 3.7 out of every 100,000 adults a year, and in 0.7 among children ages 0 to 14 years, and 0.8 among ages 15 to 24 years. [118] New cases of AML are rising in the population over age 60 years. The diagnosis rate is 9.2 per 100,000 and 10.2 in men and women, aged 65 to 74 years, and even higher among adults aged 75 to 84 years (16.9 and 16.8 in men and women, respectively).[119] Mortality due to AML is higher in adults

than in children, ranging from 4 to 6 deaths per 100,000 cases in adults compared to 0.2 in children under 20.[120,121] Patients treated for AML are likely to suffer fatal complications such as multi-organ failure from bacterial and fungal infections.[122,123] Elderly patients with AML are at risk for serious central nervous system toxicities that lead to death.[124]

In Europe, breast cancer is diagnosed in 62.8 women out of every 100,000 each year, and among new cases, 20% to 25% have locally advanced breast cancer.[125,126] Among every 100,000 women who are diagnosed with breast cancer in the EU, approximately 22.4 will die each year.[127] Women who are diagnosed with breast cancer at an advanced age may be more likely than younger women to die of breast cancer. Breast cancer patients are more likely to have other medical conditions such as hypertension, heart conditions, stroke, emphysema/ asthma/chronic obstructive pulmonary disease, Crohn's Disease, arthritis of the hip, and diabetes.[128]

VI.2.2. Summary of Treatment Benefits

Idarubicin is a cancer drug (chemotherapy drug) belonging to a drug class called anthracyclines. Idarubicin works by killing rapidly dividing cells and interferes with ways in which the cells of the human body grow and increase in number, such as cancer cells. This action can affect normal cells as well.

Acute myelogenous (non-lymphocytic) leukaemia in adults:

Three controlled clinical studies were conducted to evaluate the efficacy and safety of a treatment containing idarubicin as compared to a treatment not containing it in untreated adult patients with acute myeloid leukaemia, a type of blood cancer. In these studies, 70% to 80% of the patients receiving treatment with idarubicin obtained a complete response, as compared to 58% to 60% of those who received the comparator treatment. Duration of response and overall survival were (on average) longer in patients receiving the treatment containing idarubicin compared with comparators.[129,130,131]

Acute lymphocytic leukaemia in adults and children:

Idarubicin showed significant activity against acute lymphocytic leukaemia in patients who were previously treated for acute leukaemia and did not respond to treatment. Following treatment with idarubicin, all signs of cancer disappeared in 50% to 60% of patients and the duration of response was better than the alternative treatment.[132,133,134]

Breast cancer:

Idarubicin was more effective in inducing regression of advanced breast cancer than the comparator treatments. The duration of response in advanced breast cancer patients receiving idarubicin varied from 2 to 6 months. The response rate of idarubicin in patients with breast cancer was comparable to alternative treatment, which consisted of a variety of treatments selected by the treating physician.[135,136,137]

Considering the efficacy and safety reported in various clinical trials of idarubicin for the approved indications, the overall benefit-risk profile of idarubicin remains favourable.

VI.2.3. Unknowns Relating to Treatment Benefits

No major differences in treatment benefit with idarubicin were seen across age, gender or ethnicity. Investigators continue to actively study the drug in a controlled clinical setting in different protocols in order to optimize its therapeutic benefit for its approved indications.

VI.2.4. Summary of Safety Concerns

Table 36. Important Identified Risks

Risk	What is Known	Preventability
Heart rhythm changes which may include irregular, slow or rapid heartbeat. (Acute cardiotoxicity)	Common side effects in patients receiving idarubicin (may affect up to 1 in 10 people) may include an increase or decrease in heart rate, or irregular heart beat/pulse. An uncommon side effect (may affect up to 1 in 100 people) may include ECG changes.	Physician supervision and care. Before starting and during treatment you will need regular checks including heart tests.
Heart muscle disease and the heart does not pump properly (Cardiomyopathy)	Congestive heart failure is the most severe form of heart muscle disease and the heart does not pump properly (cardiomyopathy) caused by idarubicin and sometimes limits how many treatments patients can receive. Common side effects in patients receiving idarubicin (may affect up to 1 in 10 people) may include heart failure.	Physician supervision and care. Before starting, during and after treatment you will need regular checks including heart tests.
Abnormally low number of white blood cells, red blood cells or part of the blood that cause clots in the bloodstream (Severe myelosuppression, increased susceptibility to severe infections and haemorrhages)	A decrease in the number of red blood cells, white blood cells or abnormally low amount of the part of the blood that causes clots (platelets) may affect more than 1 in 10 patients receiving idarubicin (very common). A decrease in the number of white blood cells can make someone more susceptible to infections.	Physician supervision and care. Before starting and during treatment you will need regular checks including blood tests.
Cancer of the blood caused by medication to treat cancer (Secondary leukaemia)	Though used to treat cancer, idarubicin can sometimes cause new cancers, including cancers of blood such as leukaemia.. These may occur many years after treatment and may affect up to 1 in 100 patients (uncommon).	Physician supervision and care.
Abnormal opening in the stomach or intestines (Gastrointestinal perforation/ haemorrhage)	Occasionally, episodes of serious gastrointestinal events (perforation or bleeding) have been observed in patients receiving oral idarubicin.	It is not known how to prevent the development of abnormal opening in the stomach or intestines (hole).
A serious condition when cancer treatment causes cancer cells to die quickly (Tumour lysis syndrome)	Tumour lysis syndrome can occur when the dying cancer cells break down and release material into the bloodstream, resulting in damage to the kidneys. Symptoms include nausea, shortness of breath, irregular heartbeat, muscular cramps, seizures (convulsions), clouding of urine and decreased amount of urine and tiredness (frequency cannot be estimated from the available	Physician supervision and care.

Table 36. Important Identified Risks

Risk	What is Known	Preventability
	data). Frequency cannot be estimated from the available data.	

Table 37. Important Potential Risks

Risk	What is Known	Preventability
May experience more and/or severe toxic reactions if your liver does not work properly (Increased toxicity in patients with hepatic impairment)	Idarubicin has not been fully evaluated in patients who have liver problems. The dose may need to be decreased in patients with mild liver problems. Idarubicin should not be used in patients with severe liver disease. Frequency cannot be estimated from the available data.	Physician supervision and care. Regular medical examinations and periodic blood tests to check liver function.
May experience more and/or severe toxic reactions if your kidneys do not work properly (Increased toxicity in patients with renal impairment)	Idarubicin has not been fully evaluated in patients who have kidney problems. The dose may need to be decreased in patients with mild kidney problems. Idarubicin should not be used in patients with severe kidney disease. Frequency cannot be estimated from the available data.	Physician supervision and care. Regular medical examinations and periodic blood tests to check kidney function.

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 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

There are no post-authorisation studies planned.

VI.2.7. Studies that are a Condition of the Marketing Authorisation

There are no studies that are conditions of the Marketing Authorisation.

VI.2.8. Summary of Changes to the Risk Management Plan Over Time

Major changes to the Risk Management Plan over time are shown in **Table 38**

Table 38. Major Changes to the Risk Management Plan Over Time

Version	Date	Safety Concerns	Comment
1.0	22 May 2015	Initial RMP	-
1.1	17 March 2016	1) Missing information deleted 2) Important potential risks added 3) Pivotal trial information added to Summary of Treatment Benefits 4) Footnote added for Indications in the Product Overview regarding advanced breast cancer	This update is in response to WS procedure DE/H/xxxx/WS/281 Day 55
1.2	09 June 2016	1) Two important identified risks were revised (Severe Myelosuppression and Increased Susceptibility to Severe Infections and Haemorrhages; ~~Mucositis/stomatitis/esophagitis (complication including~~ Gastrointestinal haemorrhage/perforation~~)~~ 2) Revised language in Section VI.2. Elements for a public summary	This update is in response to WS procedure DE/H/xxxx/WS/281 Day 60.

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