VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Gefitinib is a medicine used for the treatment of adult patients with locally spread or metastatic (spread to other parts of the body) non-small cell lung cancer (NSCLC) with activating mutations (change in gene pattern) in one of the proteins in body. NSCLC is a disease in which malignant (cancer) cells form in the tissues of the lung.

Lung cancer is the most common cancer in the world and fourth most common cancer in Europe.1.8 million new cases were diagnosed in 2012. NSCLC accounts for approximately 85% of all lung cancers. The highest incidence of lung cancer was in Northern America and Europe; and the lowest incidence in Africa and, Latin America and Caribbean. Hungary had the highest rate of lung cancer, followed by Serbia and Democratic People's Republic of Korea. Smoking is the biggest risk factor for the development of lung cancer.

VI.2.2 Summary of treatment benefits

Gefitinib is a type of drug called a tyrosine kinase inhibitor (TKI), also known as a cancer growth inhibitor. Kinases are proteins in the body that regulate how the cells grow and divide. Gefitinib helps blocking a protein called 'Epidermal Growth Factor Receptor' (EGFR), which is involved in the growth and spread of cancer cells. These proteins can be found on the surface of cancer cells, such as EGFR on the surface of non-small cell lung cancer cells. EGFR is involved in the growth and spread of cancer cells. By blocking EGFR, gefitinib helps to slow down the growth and spread of the cancer. Gefitinib works only in non-small cell lung cancer cells that have a gene modification (mutation) in their EGFR.

VI.2.3 Unknowns relating to treatment benefits

Data concerning the effectiveness of gefitinib in population below 18 years of age, in pregnant and breast feeding women and patients with severe kidney impairment are missing. Therefore, the use of gefitinib in these population groups is not recommended.

VI.2.4 Summary of safety concerns

Table 11: Important Identified Risk(s)

Risk(s)	What is known	Preventability
Breathlessness, possibly with a cough or fever called Interstitial Lung Disease (ILD)	In 1.3% of the patients in clinical trials experience serious breathlessness or sudden worsening breathlessness, possibly with cough of fever. This may affect about 1 in 100 patients taking gefitinib and can be life-threatening.	If patients experience worsening of respiratory symptoms such as dyspnoea, cough and fever, gefitinib should be interrupted and the patient should be promptly investigated. If ILD is confirmed, gefitinib should be discontinued and the patient should be treated appropriately.
Inflammation of liver (Hepatitis)	In clinical studies, an average of 3.1-fold increase in exposure to gefitinib in patients with moderate and severe liver injuries was observed. It may occur very commonly affecting more than 1 in 10 people to uncommon occurrence affecting up to 1 in 100 people.	The product information for gefitinib contains a recommendation that patients should undergo periodic liver function testing when taking gefitinib. Gefitinib should be used cautiously in the presence of mild to moderate changes in liver function
Gastrointestinal perforation	Gastrointestinal perforation has been reported in patients taking gefitinib. In most cases this is associated with other known risk factors, including associated	This is a known risk factor for gefitinib as per product information.

Risk(s)	What is known	Preventability
	medications such as steroids or pain killers (NSAIDs), underlying history of gastrointestinal ulceration, age, smoking or bowel metastases (cancer spread in bowels) at sites of perforation. It may occur uncommonly i.e. in up to 1 in 100 people.	
Drug drug interaction	Some other medicines as phenytoin or carbamazepine (for seizures/ fits), rifampicin (for tuberculosis), itraconazole, ketoconazole (for fungal infections), medicines taken for ulcers, indigestion and heartburn may decrease the action of gefitinib in body.	. Also patients should tell their doctors about the medicines they consume along with gefitinib.

Table 12: Important Potential Risk(s)

Risk(s)	What is known
Haemorrhage events (including gastrointestinal haemorrhage and tumour haemorrhage)	Gefitinib could lead to bleeding episodes such as nose bleed or blood in urine or any other bleeding at the tumour location
Cerebrovascular events	There were few cases of bleeding seen in brain when gefitinib was tested in clinical trials.
Drug-drug interactions: interactions with oral anticoagulants	Gefitinib may affect action of some medicines as warfarin (given to prevent blood clots). Patients taking warfarin may need to do blood tests often.

Table 13: Missing Information

Risk(s)	What is known
Use in pregnant and breast-feeding women (Use in pregnancy and lactation)	Gefitinib could harm a baby; hence it is recommended to avoid becoming pregnant while on treatment with gefitinib. Also gefitinib is not to be consumed while breast feeding for the safety of the baby
Exposure to children below 18 years of age (Paediatric exposure)	Enough information in children and adolescents aged less than 18 years have not been established with gefitinib. There is no relevant use of gefitinib in this population for NSCLC.
Use in patients with severe kidney problems (use in patients with severe renal impairment)	Limited data is available for use of gefitinib in patients who suffer from severe kidney problems. Hence caution is advised for use of gefitinib in these patients.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics 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

Not applicable.

VI.2.7 Summary of changes to the Risk Management Plan over time

Changes to the Risk Management Plan over time is provided in the table below.

Version	Date	Safety Concerns	Comments
1.0	22-June-2017	**Important identified risks:** 1. Cutaneous toxicity 2. Interstitial Lung Disease (ILD) 3. Liver injury 4. Gastrointestinal perforation 5. Ocular toxicity 6. Drug drug interactions 7. Lactose intolerance **Important potential risks:** None **Missing information:** 1. Exposure during pregnancy and lactation 2. Paediatric exposure 3. Use in patients with severe renal impairment	First version of the RMP.
V1.1	16-Feb-2018	Change in the list of safety concerns to align with risks per innovator RMP. List of risks updated to: **Important identified risks:** 1. Interstitial lung disease (ILD) 2. Hepatitis 3. Gastrointestinal perforation 4. Drug-drug interactions: interactions with inducers and inhibitors of CYP3A4 isoenzyme; interactions mediated by CYP2D6 isoenzyme; interactions with medicines that cause significant sustained elevations of gastric pH. **Important potential risks** 1. Haemorrhage events (including gastrointestinal haemorrhage and tumour haemorrhage) 2. Cerebrovascular events 3. Drug-drug interactions: interactions with oral anticoagulants **Missing information**	List of safety concerns updated as per Day 70 comments from RMS (NL) to align with the latest RMP of the innovator (RMP version 10). Relevant sections also updated to reflect the correct list of safety concerns.

Version	Date	Safety Concerns	Comments
		1. Use in pregnant or lactating women 2. Use in patients with severe renal impairment	