Erlotinib STADA 25 mg, 100 mg and 150 mg film-coated tablets

17.3.2017, Version V1.2

PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Non-Small Cell Lung Cancer (NSCLC)

Non-small-cell lung cancer (NSCLC) accounts for 80%–85% of all lung cancer cases. The majority of patients present with advanced disease. 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.

Pancreatic Cancer

Pancreatic cancer was the fourth most fatal cancer in men after lung, colorectal, and prostate cancers. Similarly, pancreatic cancer was found to be the fourth most fatal cancer in women after breast, colorectal and lung cancers.

Death due to pancreatic carcinoma is increasing in Europe with the number rising from 75 439 in 2009 to a projected 82 300 deaths in 2014 (+19%). It usually arises in elderly patients with a mean age at onset of 71 years for men and 75 years for women.

Up to 10% of pancreatic cancer patients report a family history of the disease. A family history of pancreatic cancer in first-degree relatives is associated to a 2 to 4-fold excess risk of pancreatic cancer, the risk increasing with the number of relatives affected.

VI.2.2 Summary of treatment benefits

Non-Small Cell Lung Cancer (NSCLC)

For most patients with advanced non-small cell lung cancer, current treatments do not cure the cancer. Surgery may be curative only in early stages. In later stages of the disease chemotherapy or targeted therapies represent available treatment options.

In a study, lung cancer patients treated with erlotinib maintenance following platinum-containing chemotherapy had better outcomes compared to those who received placebo following platinum-containing chemotherapy. Among the patients whose disease was stable, the patients taking erlotinib lived for an average of 12.1 weeks without their disease getting worse, compared with 11.3 weeks in those taking placebo, and survival times were 11.9 months, on average, with erlotinib and 9.6 months with placebo. In another study, in lung cancer patients who had not responded to previous chemotherapy, the patients taking erlotinib survived for an average of 6.7 months, compared with 4.7 months for the patients taking placebo. In another study, in lung cancer patients with EGFR mutations, patients taking erlotinib as initial treatment survived without their disease getting worse for an average of 10.4 months compared with 5.1 months for those receiving chemotherapy medicines.

Pancreatic cancer

Advanced pancreatic cancer still has a dismal prognosis. In the study in metastatic (disease has spread to other parts of the body) pancreatic cancer, the patients taking erlotinib as initial therapy survived without their disease getting worse for an average of 5.9 months, compared

with 5.1 months in those taking placebo. However, there was no advantage for patients whose cancer had not spread beyond the pancreas.

VI.2.3 Unknowns relating to treatment benefits

Erlotinib is not a new, but a well-established drug (more than 10 years in the market). The use is well established with recognised efficacy and acceptable safety. No data is available on erlotinib use in patients with severe hepatic dysfunction and in patients with renal impairment. No data is available on erlotinib use in paediatric population and in pregnant and breast feeding women.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Skin (Cutaneous) Toxicity	Skin toxicity most commonly manifests as mild rash. Rash may develop vey commonly in patients treated with erlotinib (very commonly: may affect more than 1 in 10 people).	Skin toxicity is usually mild and treated with simple topical treatments (topical moisturizers). It might be necessary to change the dose of erlotinib.
Group of disorders characterised by scarring of the lung tissue (Interstitial Lung Disease)	Rare form of lung condition called interstitial lung disease, including cases leading to death, have been reported uncommonly in patients receiving erlotinib for treatment of non-small cell lung cancer (NSCLC), pancreatic cancer or other advanced solid tumors (uncommon: may affect up to 1 in 100 people).	If interstitial lung disease is diagnosed, treatment with erlotinib should be stopped and appropriate treatment should be started as necessary.
Liver (Hepatic) Injury	Rare cases of hepatic failure (including cases leading to death) have been reported during use of erlotinib in postmarketing settings (rare: may affect up to 1 in 1 000 people).	Periodic blood tests to observe changes in liver function should be considered. Dose reduction or interruption of erlotinib dosing should be considered if changes in liver function are severe.
(Gastrointestinal) fluid loss due to vomiting and diarrhoea	Diarrhea and vomiting may occur very commonly in patients treated with erlotinib (very common: may affect	When persistent diarrhea, nausea, anorexia, or vomiting occurs, erlotinib treatment should be

	more than 1 out of 10 people). Persistent and severe diarrhea may lead to low blood potassium and impairment of kidney function, particularly if other chemotherapy treatments are administered at the same time.	interrupted and appropriate management steps should be taken to prevent dehydration. Management steps would include decrease in erlotinib dose and anti-motility medication such as loperamide. In addition, renal function and serum electrolytes including potassium should be monitored in patients at risk of dehydration.
Hole in intestine (Gastrointestinal perforation)	Patients receiving erlotinib are at increased risk of developing gastrointestinal perforation, which was observed uncommonly (including some cases leading to death) (uncommon: may affect up to 1 in 100 people). Patients who have prior history of peptic ulcer or diverticular disease are at increased risk.	Patients are advised to contact treating physician in case of severe abdominal pain. Erlotinib should be permanently discontinued in patients who develop gastrointestinal perforation. Such patients are treated with intravenous infusions, antibiotics, nasogastric aspiration and bowel rest.
Eye problems (Ocular Toxicity)	A wide range of eye problems has been observed. These ranged from mild (e.g. conjunctivitis or pink eye) to significant in severity (e.g., corneal ulceration- ulcers involving the front part of the eye) or corneal perforation (damage of front part of the eye). Eye irritation due to conjunctivitis/keratoconjunctivitis may develop very commonly and keratitis may develop commonly in patients treated with erlotinib (very common: may affect more than 1 out of 1 0 people; common: may affect	Patients who present with acute or worsening redness and pain in the eye, increased eye watering, blurred vision and/or sensitivity to light, should contact their doctor or nurse immediately as they may need urgent treatment.

	up to 1 in 10 people).	
Drug interactions	Some drugs (for example antifungals like ketoconazole, protease inhibitors, erythromycin, clarithromycin, phenytoin, carbamazepine, barbiturates, rifampicin, ciprofloxacin, or St. John's Wort), if taken together with erlotinib, may decrease or increase the amount of erlotinib in blood. As a result, the efficacy of erlotinib may be reduced or the side effects of erlotinib may increase.	Patients receiving medication for other health problems may have to change medication or dose (the concentration of the drug) in order to receive erlotinib as well.
	Some products which change the acidity of the upper digestive tract (for example antacids, omeprazole, or ranitidine), if taken together with erlotinib, may decrease the amount of erlotinib in blood.	If the use of antacids omeprazole, or ranitidine is considered necessary during treatment with erlotinib, they should be taken at least 4 hours before or 2 hours after the daily dose of erlotinib.
	Smoking results in a decrease in the amount of erlotinib in blood.	Patients who smoke should try to stop smoking as early as possible before starting treatment with erlotinib.

Important potential risks

Not applicable.

Missing information

Risk	What is known
Pregnancy/Lactation	Women who can become pregnant must be advised to avoid pregnancy while on erlotinib. It is not known whether erlotinib is excreted in human breast milk. Because of the potential harm to the infant, it is not recommended to breast-feed while receiving erlotinib.
Pediatric population	Erlotinib has not been studied in patients under the age of 18 years. Treatment with erlotinib is not recommended for children and adolescents.
Use in patients with severe hepatic impairment	It is not known whether erlotinib has a different effect in patients whose liver is not functioning normally. Treatment with erlotinib is not recommended for patients with severe liver disease.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) 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 special conditions and restrictions for its safe and effective use (additional risk minimisation measures). How they are implemented in each country however will depend upon agreement between the manufacturer and the national authorities.

These additional risk minimisation measures are for the following risks:

Group of disorders characterised by scarring of the lung tissue (Interstitial lung disease)

Risk minimisation measure(s): Educational material for prescribers to anticipate and manage ILD
Objective and rationale: Additional educational materials for prescribers to anticipate and manage ILD.
Summary description of main additional risk minimisation measures: • Educational material for prescribers to anticipate and manage ILD Full details of educational material can be found in Annex 10.

VI.2.6 Planned post authorisation development plan

No post-authorisation studies have been imposed or are planned. The active substance has been in the clinical practice for more than 10 years.

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

Not applicable, as this is the first risk management plan for Erlotinib Stada.