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Public Assessment Report

Name of the Product:

Erlotinib Pharmascience 100 mg film-coated tablets
Erlotinib Pharmascience 150 mg film-coated tablets

(erlotinib hydrochloride)

Procedure number: HU/H/0682/001-002/DC

Marketing authorisation holder: Pharmascience International Limited

Date: 11. 01. 2021.

CONTENT

LAY SUMMARY

After careful assessment of its quality and therapeutic benefit/risk ratio, the member states have granted the marketing authorisation of the Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets. The holder of the marketing authorisation is Pharmascience International Limited.

The active substance is erlotinib hydrochloride.

- Erlotinib Pharmascience 100 mg film-coated tablets: each film-coated tablet contains 100 mg erlotinib (as erlotinib hydrochloride).
- Erlotinib Pharmascience 150 mg film-coated tablets: each film-coated tablet contains 150 mg erlotinib (as erlotinib hydrochloride).
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The other ingredients are:

- tablet core: lactose monohydrate; cellulose, microcrystalline (E460); sodium starch glycolate Type A; magnesium stearate (E470b).
- tablet coat: poly(vinyl alcohol) (E1203); titanium dioxide (E171); macrogol 3350 (E1521); talc (E553b); methacrylic acid – ethyl acrylate copolymer (1:1), Type A; sodium hydrogen carbonate.

The appearance of the tablets is:

– The 100 mg film-coated tablets are white to yellowish, round biconvex, engraved with "100" on one side. The diameter of the tablet is 8.9 mm.
– The 150 mg tablets are white to yellowish, round biconvex, engraved with "150" on one side. The diameter of the tablet is 10.5 mm.

The tablets are available in packs in blisters.

Erlotinib Pharmascience contains the active substance erlotinib hydrochloride. Erlotinib Pharmascience is a medicine used to treat cancer by preventing the activity of a protein called epidermal growth factor receptor (EGFR). This protein is known to be involved in the growth and spread of cancer cells.

Erlotinib Pharmascience is indicated for adults. This medicine can be prescribed to patients if they have non-small cell lung cancer at an advanced stage. It can be prescribed as initial therapy or as therapy if the disease remains largely unchanged after initial chemotherapy, provided the cancer cells have specific EGFR mutations. It can also be prescribed if previous chemotherapy has not helped to stop the disease.

This medicine can also be prescribed to patients in combination with another treatment called gemcitabine if they have cancer of the pancreas at a metastatic stage.

What patients need to know before using Erlotinib Pharmascience

Patients must not take Erlotinib Pharmascience if they
- are allergic to erlotinib or any of the ingredients of this medicine.

Warnings and precautions

- if patients are taking other medicines that may increase or decrease the amount of erlotinib in their blood or influence its effect (for example antifungals like ketoconazole, protease inhibitors, erythromycin, clarithromycin, phenytoin, carbamazepine, barbiturates, rifampicin, ciprofloxacin, omeprazole, ranitidine, St. John's Wort or proteasome inhibitors), they should talk to the doctor. In some cases these medicines may reduce the efficacy or increase the side effects of Erlotinib Pharmascience and the doctor may need to adjust their treatment. The doctor might avoid treating patients with these medicines while they are receiving Erlotinib Pharmascience.
- if patients are taking anticoagulants (a medicine which helps to prevent thrombosis or blood clotting e.g. warfarin), Erlotinib Pharmascience may increase the tendency to bleed. Patients should talk to the doctor, who will need to regularly monitor them with some blood tests.
- if patients are taking statins (medicines to lower their blood cholesterol), Erlotinib Pharmascience may increase the risk of statin related muscle problems, which on rare occasions can lead to serious muscle breakdown (rhabdomyolysis) resulting in kidney damage, the doctor should be contacted.
- if patients use contact lenses and/or have a history of eye problems such as severe dry eyes, inflammation of the front part of the eye (cornea) or ulcers involving the front part of the eye, the doctor should be contacted.

Before taking Erlotinib Pharmascience patients should talk to the doctor if they:
- have sudden difficulty in breathing associated with cough or fever because the doctor may need to treat them with other medicines and interrupt their Erlotinib Pharmascience treatment;
- have diarrhoea because the doctor may need to treat them with anti-diarrhoeal (for example loperamide);
- have severe or persistent diarrhoea, nausea, loss of appetite, or vomiting because the doctor may need to interrupt their Erlotinib Pharmascience treatment and may need to treat them immediately in the hospital;
- have severe pain in the abdomen, severe blistering or peeling of skin. The doctor may need to interrupt or stop their treatment;
- develop acute or worsening redness and pain in the eye, increased eye watering, blurred vision and/or sensitivity to light, patients should tell the doctor or nurse immediately as they may need urgent treatment;
- are also taking a statin and experience unexplained muscle pain, tenderness, weakness or cramps. The doctor may need to interrupt or stop their treatment.

Liver or kidney disease
It is not known whether Erlotinib Pharmascience has a different effect if the liver or kidneys

are not functioning normally. The treatment with this medicine is not recommended if patients have a severe liver disease or severe kidney disease.

Glucuronidation disorder like Gilbert's syndrome
The doctor must treat patients with caution if they have a glucuronidation disorder like Gilbert's syndrome.

Smoking
Patients are advised to stop smoking if they are treated with Erlotinib Pharmascience as smoking could decrease the amount of the medicine in the blood.

Children and adolescents

Erlotinib Pharmascience has not been studied in patients under the age of 18 years. The treatment with this medicine is not recommended for children and adolescents.

Other medicines and Erlotinib Pharmascience

The doctor or pharmacist should be told if patients are taking, have recently taken any other medicines or might take any other medicines.

Erlotinib Pharmascience with food and drink

Erlotinib Pharmascience cannot be taken with food.

Pregnancy and breast-feeding

Patients should avoid pregnancy while being treated with Erlotinib Pharmascience. If patients could become pregnant, they should use adequate contraception during treatment, and for at least 2 weeks after taking the last tablet.
If patients become pregnant while they are being treated with Erlotinib Pharmascience, they should immediately inform their doctor who will decide if the treatment should be continued.
Patients cannot breast-feed if they are being treated with Erlotinib Pharmascience, and for at least 2 weeks after taking the last tablet.

If patients are pregnant or breast-feeding, think they may be pregnant or are planning to have a baby, the doctor or pharmacist should be asked for advice before taking this medicine.

Driving and using machines

Erlotinib Pharmascience has not been studied for its possible effects on the ability to drive and use machines but it is very unlikely that the treatment will affect this ability.

Erlotinib Pharmascience contains a sugar called lactose monohydrate.
If patients have been told by their doctor that they have an intolerance to some sugars, the doctor should be contacted before taking this medicinal product.

How to use Erlotinib Pharmascience

This medicine must always be taken exactly as the doctor or pharmacist has told. If patients are not sure the doctor or pharmacist should be checked with.

The tablet should be taken at least one hour before or two hours after the ingestion of food.

The recommended dose is one tablet of Erlotinib Pharmascience 150 mg each day if patiens have non-small cell lung cancer.

The recommended dose is one tablet of Erlotinib Pharmascience 100 mg each day if patients have metastatic pancreatic cancer. Erlotinib Pharmascience is given in combination with gemcitabine treatment.

The doctor may adjust patients' dose in 50 mg steps.
For the different dose regimens Erlotinib Pharmascience is available in strengths of 100 mg or 150 mg.
Erlotinib Pharmascience is not available in 25 mg and 50 mg strengths. For these dosages, pateints should take other medicinal products available on the market.

For oral use.

What to do if more Erlotinib Pharmascience was taken that it should have been?

The doctor or pharmacist should be contacted immediately.
Patients may have increased side effects and the doctor may interrupt their treatment.

What to do if taking Erlotinib Pharmascience was forgotten?

If one or more doses of Erlotinib Pharmascience are missed, the doctor or pharmacist should be contacted as soon as possible. No double dose to make up for a forgotten dose can be taken.

May patients stop taking Erlotinib Pharmascience?

It is important to keep taking Erlotinib Pharmascience every day, as long as the doctor prescribes it for pateints.

In case of any further questions on the use of this medicine, the doctor or pharmacist should be asked.

Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

In case of suffering from any of the below side effects the doctor should be contacted as soon as possible. In some cases the doctor may need to reduce the dose of Erlotinib Pharmascience or interrupt treatment:

- Diarrhoea and vomiting (very common: may affect more than 1 out of 10 people). Persistent and severe diarrhoea may lead to low blood potassium and impairment of the kidney function, particularly if patients receive other chemotherapy treatments at the same time. If patients experience more severe or persistent diarrhoea, they should contact the doctor immediately as the doctor may need to treat them in the hospital.

- Eye irritation due to conjunctivitis/keratoconjunctivitis (very common: may affect more than 1 out of 10 people) and keratitis (common: may affect up to 1 in 10 people).

- Form of lung irritation called interstitial lung disease (uncommon in European patients; common in Japanese patients: may affect up to 1 in 100 people in Europe and up to 1 in 10 in Japan). This disease can also be linked to the natural progression of the medical condition and can have a fatal outcome in some cases. If patients develop symptoms such as sudden difficulty in breathing associated with cough or fever they should contact the doctor immediately as they could suffer from this disease. The doctor may decide to permanently stop the treatment with Erlotinib Pharmascience.

- Gastrointestinal perforations have been observed (uncommon: may affect up to 1 in 100 people). Patients should tell the doctor if they have severe pain in their abdomen. Also, they should tell the doctor if they had peptic ulcers or diverticular disease in the past, as this may increase this risk.

- In rare cases liver failure was observed (rare: may affect up to 1 in 1,000 people). If patients' blood tests indicate severe changes in their liver function, the doctor may need to interrupt their treatment.

Very common side effects (may affect more than 1 in 10 people):

- rash which may occur or worsen in sun exposed areas. If patients are exposed to sun, protective clothing, and/or use of sun screen (e.g. mineral-containing) may be advisable;
- infection;
- loss of appetite, decreased weight;
- depression;
- headache, altered skin sensation or numbness in the extremities;
- difficulty in breathing, cough;
- nausea;
- mouth irritation;
- stomach pain, indigestion and flatulence;
- abnormal blood tests for the liver function;
- itching, dry skin and loss of hair;
- tiredness, fever, rigors.

Common side effects (may affect up to 1 in 10 people):

- bleeding from the nose;

- bleeding from the stomach or the intestines;
- inflammatory reactions around the fingernail;
- infection of hair follicles;
- acne;
- cracked skin (skin fissures);
- reduced kidney function (when given outside the approved indications in combination with chemotherapy).

Uncommon side effects (may affect up to 1 in 100 people):
- eyelash changes;
- excess body and facial hair of a male distribution pattern;
- eyebrow changes;
- brittle and loose nails;
- mild skin reactions such as hyperpigmentation (discoloration of the skin).

Rare side effects (may affect up to 1 in 1,000 people):
- flushed or painful palms or soles (Palmar plantar erythrodysaesthesia syndrome).

Very rare side effects (may affect up to 1 in 10,000 people):
- cases of perforation or ulceration of the cornea;
- severe blistering or peeling of skin (suggestive of Stevens-Johnson syndrome);
- inflammation of the coloured part of the eye.

How to store Erlotinib Pharmascience

This medicine does not require any special temperature storage conditions. It should be stored in the original package in order to protect from light and kept out of the sight and reach of children.

SCIENTIFIC DISCUSSION

This module reflects the scientific discussion for the approval of Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets. The procedure was finalised at 23 December 2020. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

In accordance to the Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, an application has been submitted to the reference and competent authorities of the Member State concerned.

This Decentralised Procedure application (Reference member state, RMS: Hungary, con-cerned member state, CMS: Malta) concerned the generic versions of erlotinib hydrochloride 100 mg and 150 mg.

The application has been filed pursuant to Article 10(1) of Directive 2001/83/EC (generic application) and there-fore contained no new clinical or preclinical data, other than supporting literature where necessary. The Applicant has adequately demonstrated bioequivalence between the product and reference product.

The reference product is Tarceva 100 mg and 150 mg film-coated tablets by Roche Registration GmbH approved in 19 September 2005 in the European Union.

Based on the review of the quality, safety and efficacy data, the Member States have granted marketing authorisations for Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets from Pharmascience International Limited.

The product is indicated for:

<u>Non-Small Cell Lung Cancer (NSCLC)</u>
Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets are indicated for the first-line treatment of patients with locally advanced or metastatic nonsmall cell lung cancer (NSCLC) with egfr activating mutations.

Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets are also indicated as monotherapy for maintenance treatment in patients with locally advanced or metastatic nsclc with stable disease after 4 cycles of standard platinum-based first-line chemotherapy.

Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets are also indicated for the treatment of patients with locally advanced or metastatic nsclc after failure of at least one prior chemotherapy regimen.

When prescribing Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets, factors associated with prolonged survival should be taken into account.

No survival benefit or other clinically relevant effects of the treatment have been demonstrated in patients with Epidermal Growth Factor Rceptor (EGFR)-IHC negative tumours.

Pancreatic cancer:
Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets in combination with gemcitabine is indicated for the treatment of patients with metastatic pancreatic cancer.

When prescribing Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets factors associated with prolonged survival should be taken into account. No survival advantage could be shown for patients with locally advanced disease.

Similarity assessment in view of the orphan drug legislation
The MAH provided a similarity assessment versus the authorized orphan medicinal product Onivyde in the context of similarity. Onivyde has orphan market exclusivity for "Treatment of pancreatic cancer" (based on designation EU/3/11/933) started on 18/10/2016. The MAH stated that erlotinib is considered not to be similar to Onivyde. The member states agree that Erlotinib Pharmascience is not similar based on principal molecular structure, mechanism of action and indication. Therefore the orphan status and its juridical and procedural aspects are in this case not an issue.

A comprehensive description of the indications and posology is given in the Summary of Product Characteristics.

II. QUALITY ASPECTS

II.1 Introduction

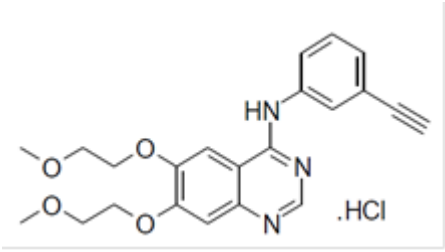
The chemical-pharmaceutical assessment report concerns the application of Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets via a decentralized procedure according to Article 10.1 of Directive 2001/83/EC (i.e a generic application). The products have been developed by Alvogen IPCo S.àr.l.

Reference product is Tarceva 150 mg film-coated tablets (containing 150 mg erlotinib hydrochloride as active ingredient) which is the original products of Roche Registration Limited.

II.2 Drug substance

Data on the quality and manufacture of the active substance were provided in the applicant's submission using the Active Substance Master File (ASMF) procedure with additional data in the marketing authorization dossier. The Quality Overall Summary is adequate.

International non proprietary name (INN): Erlotinib hydrochloride
Chemical name:
N-(3-Ethynylphenyl)-[6,7-bis(2-methoxyethoxy)quinazolin-4-yl]amine hydrochloride
Structure:



The active substance is white to off-white crystalline powder; slightly soluble in methanol, practically insoluble in acetonitrile, acetone, ethyl acetate, isopropanol, n-hexane and water. The molecule does not contain any asymmetric carbon atom. It shows polymorphism, the manufacturer consistently produces the same polymorphic form.

The ASMF holder presented complete details of the manufacturing process. Description of the manufacturing process of the active pharmaceutical ingredient (API) is adequate.

Evidence of the structure has been confirmed by spectroscopy (FT-IR, UV, 1H-NMR, 13C-NMR), mass spectrometry (MS) and elemental analysis. The discussion of the impurity profile of the API contains detailed information about genotoxic impurities, residual solvents and catalysts.

Erlotinib hydrochloride is not official in the Ph.Eur. Therefore, an in-house specification has been set for the active substance, which includes the following tests: appearance, identification, chloride content, water content, sulphated ash, , related substances, residual solvents and assay. The presented specification is in accordance with the Ph.Eur. general monograph on Substances for Pharmaceutical Use and the ICH Q6A guideline. The specifications reflect all relevant quality attributes of the active substance and were found to be adequate to control the quality of the drug substance. The limits set are properly justified.

Testing methods not described in details in the Pharmacopoeia are adequately drawn up and satisfactorily validated. Reference materials used by the active substance manufacturer and the drug product manufacturer for the control of the substance are adequately characterised.
The substance complies with the requirements of the EMA guideline on genotoxic impurities.

Batch analysis data justify the limits, indicate the good performance of testing methods and demonstrate the batch to batch consistency of the production.

Stability studies have been performed with the drug substance. According to the presented stability data the proposed re-test period is acceptable with no special storage condition.

Good Manufacturing Practice (GMP) compliance of the API manufacture is demonstrated by the applicant.

II.3 Medicinal product

The aim was to develop tablets containing erlotinib hydrochloride as drug substance in 100 mg and 150 mg doses bioequivalent and pharmaceutically equivalent to the reference medicinal product Tarceva 150 mg film-coated tablets, the branded original products of Roche Registration Limited.

A satisfactory package of data on development pharmaceutics has been presented. Brief discussion on reasons for inclusion and quantity of excipients has been provided.
The compositions and the pharmaceutical tests evaluated during development of the final formulation are included in the documentation. As a result of development studies product with the following appearance, composition and packaging was obtained.

100 mg: White to yellowish, round biconvex, film-coated tablet, engraved with “100” on one side. The diameter of the tablet is 8.9 mm ± 5 %.
150 mg: White to yellowish, round biconvex, film-coated tablet, engraved with “150” on one side. The diameter of the tablet is 10.5 mm ± 5 %.

As regards dissolution and impurity profile the product is shown to be similar to the reference product.

The excipients used in the finished product are magnesium stearate, microcrystalline cellulose, lactose monohydrate and sodium starch glycolate Type A and coating mixture (sodium hydrogen carbonate, methacrylic acid – ethyl acrylate copolymer (1:1), type A, macrogol 3350, talc, titanium dioxide E171, poly(vinyl alcohol)). All excipients used comply with their respective European Pharmacopoeia monograph. Compliance of the product with the general monograph of the European Pharmacopoeia on the Products with the risk of TSE has been demonstrated by the applicant.

A description and flow chart of the manufacturing method has been provided. Appropriate in-process controls are included in the manufacturing process. Satisfactory batch formulae were also presented. GMP compliance of the manufacturing site has been demonstrated.

The finished product specification is satisfactory. Acceptance criteria have been justified with respect to conventional pharmaceutical requirements as prescribed in the relevant dosage form monograph of the Ph.Eur. and the ICH Q6A guideline. Appropriate control strategy was selected. The test methods have been described and validated, as appropriate. Batch data have been provided and complied with the specification. Certificates of analysis for the batches involved in the bioequivalence study are presented.

The container closure system of the product is OPA/Al/PVC//Al blister and box. Specifications and quality certificates for all packaging components are enclosed.

Finished product stability studies have been conducted in accordance with the current guidelines. Based on the results, a shelf-life of 4 years with no special storage conditions is approved. The Summary of Product Characteristics, patient Information Leaflet and label texts are pharmaceutically acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The product has been shown to meet the current regulatory requirements with regards to its quality and content of the active substance as well as dosage-form characteristics until the end of the approved shelf-life consistently. The manufacture and the quality standards applied adequately support the safe use and efficacy of the product.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Erlotinib Pharmascience is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.2 Discussion onthe non-clinical aspects

This product is a generic formulation of Tarceva, which is available on the European market. Reference is made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Erlotinib is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The overview justifies why there is no need to generate additional clinical data. Therefore, the member states agreed that no further clinical studies are required. For this generic application, the MAH has submitted a bioequivalence study, which is discussed below.

IV.2 Pharmacokinetics

Biowaiver

The Applicant claimed for biowaiver for the dose strength of 100 mg on the basis of general biowaiver requirements (CPMP/EWP/QWP/1401/98 Rev 1/Corr**). Qualitative compositions of the two strengths in the present application (100 and 150 mg) are the same. Quantitative compositions of the two strengths (100 and 150 mg) are proportionally similar. Biowaiver claim for dose strength of Erlotinib film-coated tablets was acceptable.

Bioequivalence studies

To support the application, the Applicant has submitted as report one pilot (coded 13-141) and one pivotal bioequivalence study (Study number: 14-064) with the strength of 150 mg film-coated tablets conducted in healthy volunteers in fasted conditions.

By the Sponsor’s statement the study was conducted in compliance with the requirements of

guideline on Good Clinical Practice ICH Topic E6 (R1) (CPMP/ICH/135/95), Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**, January 2010) and ethical principles stated in the last revision of Declaration of Helsinki.

Study No 14-064 was a randomized, open label, two-period, two-sequence cross-over study under fasting condition, which included 50 adult, male subjects with 14 days washout period. The study was a bioequivalence study of Erlotinib 150 mg film-coated tablets (PharOS Generics Ltd., Cyprus) versus the reference drug Tarceva® 150 mg film-coated tablets (Reference: Roche Registration Limited, U.K.).

Criteria for Bioequivalence:
Test product can be considered bioequivalent to the Reference product, when the ln-transformed Test/Reference LS (least-squares) mean ratios and their 90% confidence intervals of the primary pharmacokinetic parameters fall entirely within the acceptance range of 80.00 - 125.00% for erlotinib.

Based on the submitted bioequivalence study coded 14-064 Erlotinib 150 mg film-coated tablets and Tarceva® 150 mg film-coated tablets (erlotinib) are bioequivalent in healthy adult subjects under fasting conditions.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range)

Treatment	**AUC_{0-t}** ng/ml/h	**$AUC_{0-\infty}$** ng/ml/h	**C_{max}** ng/ml	**t_{max}** h
Test	22625.63 ± 8966.97	24216.63 ± 10145.18	1280.38 ± 432.96	2.50 (0.50 – 5.50)
Reference	22413.34 ± 7629.67	23343.09 ± 8192.74	1214.03 ± 381.10	2.50 (0.50 – 5.50)
***Ratio (90% CI)**	97.36 % (87.97 – 107.75%)		102.97 % (92.91 – 114.11%)	

AUC_{0-t} Area under the plasma concentration curve from administration to last observed concentration at time t.
$AUC_{0-\infty}$ Area under the plasma concentration curve extrapolated to infinite time.
$AUC_{0-\infty}$ does not need to be reported when AUC_{0-72h} is reported instead of AUC_{0-t}
C_{max} Maximum plasma concentration
t_{max} Time until Cmax is reached

*ln-transformed values

The results of No 14-064 with strength of 150 mg film-coated tablets formulation can be extrapolated to other strength 100 mg according to conditions in Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr*, section 4.1.6.

IV.3 Pharmacovigilance

IV.3.1 Summary of the Pharmacovigilance System

The Applicant has submitted a signed Summary of the Applicant's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation 520/2012 and as detailed in the relevant GVP module, the Summary is considered acceptable.

IV.3.2 Risk Management Plan

Summary of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

As the active substance has been used for decades and its safety concerns are well-known so there were no safety concerns applicable for this EU RMP based on the requirement to present only the important identified or potential risks and missing information linked to further pharmacovigilance activities or additional risk minimization measures in the EU.

Pharmacovigilance Plan

Routine pharmacovigilance activities are considered sufficient to manage all of the safety concerns connected to Pharmascience International Limited’s products containing erlotinib hydrochloride.

No additional activities are proposed.

Risk Minimisation Measures

Routine risk minimisation measures (i.e. wording in SmPC, PL and classification as a prescription only medicine) are considered sufficient to manage all of the safety concerns connected to Pharmascience International Limited’s products containing erlotinib hydrochloride.

No additional activities are proposed. For any further information on risk minimisation, please refer to the product information.

IV.3.3 Periodic Safety Update Reports

The requirements for submission of periodic safety update reports for these medicinal products are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Tarceva. No new clinical studies were conducted. The MAH demonstrated through a bioequivalence study that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

The application contains an adequate review of published clinical data.

The application concerns a generic product.

The products is indicated for:

5 mg tablets

Hypertension:
Treatment of hypertension in adults.

Heart failure:
Treatment of symptomatic heart failure in adults.

Stable coronary artery disease:
Reduction of risk of cardiac events in adult patients with a history of myocardial infarction and/or revascularisation.

10 mg tablets:

Hypertension:
Treatment of hypertension in adults.

Stable coronary artery disease:
Reduction of risk of cardiac events in adult patients with a history of myocardial infarction and/or revascularisation.

There is no objection against granting the marketing authorization from a clinical point of view.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

V.1 Summary

The present application concerns Erlotinib Pharmascience 100 mg, 150 mg film-coated tablets. The applicant and the future holder of authorisation is Pharmascience International Limited.

The application was submitted according to Article 10(1) of Directive 2001/83/EC (generic application). The originator product was Tarceva 100 mg and 150 mg film-coated tablets by Roche Registration GmbH approved in 19 September 2005 in the European Union.

The products is indicated for:

Non-Small Cell Lung Cancer (NSCLC)
Erlotinib Pharmascience 100 mg, 150 mg film-coated tablets are indicated for the first-line treatment of patients with locally advanced or metastatic nonsmall cell lung cancer (NSCLC) with egfr activating mutations.

Erlotinib Pharmascience 100 mg, 150 mg film-coated tablets are also indicated as monotherapy for maintenance treatment in patients with locally advanced or metastatic nsclc with stable disease after 4 cycles of standard platinum-based first-line chemotherapy.

Erlotinib Pharmascience 100 mg, 150 mg film-coated tablets are also indicated for the treatment of patients with locally advanced or metastatic nsclc after failure of at least one prior chemotherapy regimen.

When prescribing Erlotinib Pharmascience 100 mg, 150 mg film-coated tablets, factors associated with prolonged survival should be taken into account.

No survival benefit or other clinically relevant effects of the treatment have been demonstrated in patients with Epidermal Growth Factor Rceptor (EGFR)-IHC negative tumours.

Pancreatic cancer:
Erlotinib Pharmascience 100 mg, 150 mg film-coated tablets in combination with gemcitabine is indicated for the treatment of patients with metastatic pancreatic cancer.

When prescribing Erlotinib Pharmascience 100 mg, 150 mg film-coated tablets factors associated with prolonged survival should be taken into account. No survival advantage could be shown for patients with locally advanced disease.

The submitted documentation is administratively adequate and scientifically sound. The quality of the product is satisfactory. There were no non-clinical or clinical concerns raised. The therapeutic benefit/risk assessment is therefore positive.

Based on the review of the quality, safety and efficacy data, the Member States have granted marketing authorisation for Erlotinib Pharmascience 100 mg and 150 mg film-coated tablets from Pharmascience International Limited.

V.2 Classification

Prescription only

V.3 Package Leaflet and user consultation

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the patient information leaflet was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. UPGRADE: STEPS TAKEN AFTER THE INITIAL PROCEDURE WITH AN INFLUENCE ON THE PUBLIC ASSESSMENT REPORT

This module reflects the procedural steps and scientific information after the finalisation of the initial procedure.

Scope	Procedure number	Product information affected	Date of start of the procedure	Date of end of procedure	Approval or non approval	Assessment report attached