COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Erlotinib Vivanta 25 mg, 100 mg and 150 mg film-coated tablets
(erlotinib hydrochloride)

NL/H/4919/001-003/DC

Date: 14 September 2021

This module reflects the scientific discussion for the non-approval of Erlotinib Vivanta 25 mg, 100 mg and 150 mg film-coated tablets. The procedure was finalised at 17 March 2021.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have refused granting a marketing authorisation for Erlotinib Vivanta 25 mg, 100 mg and 150 mg film-coated tablets, from Vivanta Generics s.r.o.

The indications applied for are:

Non-Small Cell Lung Cancer

- The first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) activating mutations.
- Switch maintenance treatment in patients with locally advanced or metastatic NSCLC with EGFR activating mutations and stable disease after first-line chemotherapy.
- The treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen. In patients with tumours without EGFR activating mutations, Erlotinib Vivanta is indicated when other treatment options are not considered suitable.

When prescribing Erlotinib Vivanta, 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 receptor - immunohistochemistry (EGFR-IHC) negative.

Pancreatic cancer

- Erlotinib Vivanta in combination with gemcitabine is indicated for the treatment of patients with metastatic pancreatic cancer.

When prescribing Erlotinib Vivanta, factors associated with prolonged survival should be taken into account. No survival advantage could be shown for patients with locally advanced disease.

The reference products for the Dutch market are Tarceva 25 / 100 / 150 mg film-coated tablets (first registered in centralized procedure EU/1/05/311/003 since 2005-09-19 (150 mg strength)) marketed by Roche Registration Limited. The applicant used the 150 mg strength tablets for bioequivalence studies.

The marketing authorisation was applied pursuant to Article 10(1) of Directive 2001/83/EC.

The concerned member states (CMS) involved in this procedure were Germany, Denmark, Spain, Finland, Ireland, Norway and Sweden.

II. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The marketing authorisation could not be granted as bioequivalence between Erlotinib MSN 150 mg and the reference product Tarceva 150 mg was not shown. As the bioequivalence study for the higher strength was not considered approvable, the lower strengths (25 mg and 100 mg) are not approvable either.

Clinical

According to the guideline on Investigation of Bioequivalence, exclusion of a subject with lack of any measurable concentrations or very low plasma concentrations can be accepted in exceptional cases for the reference medicinal product only and may question the validity of the trial. One subject had a lack of any measurable concentrations or very low plasma concentrations after administration of the test product, and therefore exclusion of data from this subject is not acceptable. Importantly, a root cause for the observed concentrations has not been identified by the applicant. Instead, the applicant has re-dosed the subject in question with the test product and included this data in the statistical analysis and considers bioequivalence has been shown. However, re-dosing of the subject is not considered an acceptable approach as this is data driven re-analysis. Further, it can be argued that ethical issues may arise in case subjects are called back to the study site in order to repeat the testing procedure in case the outcome of the initial testing procedure is unsatisfactory.

In conclusion, due to the absence of measurable erlotinib concentrations in one subject for the test product which cannot be explained, and the resulting impossibility to assess bioequivalence, Erlotinib Vivanta 150 mg is not considered bioequivalent with Tarceva 150 mg. As discussed before, the lower strengths (25 mg and 100 mg) are also not acceptable.

Therefore, the Board concluded that the marketing authorisation for Erlotinib Vivanta 25 mg, 100 mg and 150 mg film-coated tablets cannot be granted. Agreement on this conclusion was reached with the CMS. The decentralised procedure was finalised with a negative outcome on 17 March 2021.