LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Oktreotid Campus, 50, 100, 200 and 500 microgram/ml, solution for injection
(Octreotide acetate)

Asp. No. 2008-1187, 2008-1188, 2008-1189 and 2008-1190

This module reflects the scientific discussion for the approval of Oktreotid Campus The procedure was finalised at 2010-10-01 For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Campus Pharma AB has gained marketing authorisations for Oktreotid Campus 50, 100, 200 and 500 microgram/ml solution for injection claiming essential similarity to Sandostatin marketed in Sweden by Novartis Sverige AB. The product contains octreotide acetate as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Sandostatin 50, 100, 200 and 500 microgram/ml solution for injection marketed by Novartis Sverige AB in Sweden.

A bioequivalence study has been performed with Octreotide Campus 500 microgram/ml and Sandostatin 500 microgram/ml

II. QUALITY ASPECTS

II.1 Introduction

Oktreotid Campus is presented in the form of solutions for injection containing octreotide acetate corresponding to 50, 100, 200 or 500 microgram octreotide. The excipients are glycine, hydrochloric acid, mannitol and water and for 200 µg/ml in multi-dose vials also phenol as a preservative.
The solutions are filled in ampoules (50, 100 and 500 µg/ml) and vials (200 µg/ml).

II.2 Drug Substance

Octreotide acetate does not have a monograph in the Ph Eur.

Octreotide acetate is a white to off white, amorphous powder which is freely soluble in water, methanol and acetic acid. The structure of octreotide acetate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on the molecular structure is presented. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The active substance specification includes relevant tests and the limits for impurities/degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Oktreotid Campus solution for injection is formulated using excipients described in the current Ph Eur. No components, reagents or raw material of animal origin are used during manufacturing of the drug product.

The development of the product has been described, the choice of excipients is justified and their functions explained.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored at 2ºC – 8 ºC.

III. NON-CLINICAL ASPECTS

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

A new version of octreotide acetate, developed by GP Pharm, was designed to provide the same therapeutic benefits as Sandostatin®. The only difference between the two formulations is that an excipient used in Sandostatin®, lactic acid, has been replaced by glycine.

A bioequivalence study has been submitted for the 500 µg strength. The absence of studies with the other strengths is considered acceptable from a pharmacokinetic point of view, as the pharmacokinetics of octreotide is independent of dose in the applied dose range.

The test product was compared with Sandostatin® 500 µg/mL ampoules in a single dose two-period cross over study in 24 healthy male volunteers under fasting conditions. The doses were administered by deep sc injection (intrafat) on the top of the right (I study period) and left (II study period) thighs. The two periods were separated by a wash out phase of at least 7 days. Blood sampling was performed up to 12 hours after injection.

Standard pharmacokinetic parameters (C_{max}, AUC_{0-t}, , $AUC_{0-\infty}$ and t_{max}) were calculated. The acceptance criterion for bioequivalence was that the 90% confidence interval of the ratio of the mean Octreotide GP-Pharm to the mean Sandostatin® for C_{max} and AUC_{0-t} must be included within the range 0.80-1.25. T_{max} was analysed by non-parametric Friedman test.

C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ all fell within the predefined 80-125% CI interval. T_{max} for the test product was 0.647 ± 0.216 h, and for the reference product 0.521 ± 0.179 h. The difference between treatments was statistically significant (p=0.004). However, the mean difference in T_{max} between treatments was 8 minutes, which is unlikely to be of clinical relevance.

Based on the submitted bioequivalence study, Oktreotid Campus can be considered equivalent with the reference product, Sandostatin®.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refers to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

User consultation

A user consultation with target patient groups on the package information leaflet (PIL) has not been performed.

The risk/benefit ratio is considered positive and Oktreotid Campus 50, 100, 200 and 500 microgram/ml solution for injection was recommended for approval.

VI. APPROVAL

Oktreotid Campus 50, 100, 200 and 500 microgram/ml, solution for injection were approved in national procedures on 2010-10-01.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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