LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Fludeoxyglucose (18F) Akademiska sjukhuset fludeoxyglucose (F-18)

Asp no: 2019-0773

This module reflects the scientific discussion for the approval of Fludeoxyglucose (18F) Akademiska sjukhuset. The procedure was finalised on 2020-08-04. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Uppsala University Hospital has applied for a marketing authorisation for Fludeoxyglucose (18F) Akademiska sjukhuset, 0.9 - 4.5 GBq/ml, solution for injection. The active substance is fludeoxyglucose (F-18) (It is designed for the capture of diagnostic images of some parts of the body. Once a small amount of Fludeoxyglucose (18F) Akademiska sjukhuset has been injected, medical images that are obtained with a special camera (a so-called PET camera) will enable the doctor to capture images and to see where the illness is or how it is progressing).

For approved indications, see the Summary of Product Characteristics.

The marketing authorisation has been granted pursuant to Article10a of Directive 2001/83/EC.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

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

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

The applicant has provided a summary of available literature of the pharmacological and toxicological aspects of FDG (18F). Considering the clinical experience with FDG 18F, and the agreed core SmPC, no further assessment of the literature has been made.

IV. CLINICAL ASPECTS

IV.1 Introduction

The indications are (shortened; refer to SmPC for full statement):
This medicinal product is for diagnostic use only. Fludeoxyglucose (18F) is indicated for use with positron emission tomography (PET) in adults and paediatric population.

- Oncology
- Cardiology
- Neurology
- Infectious and inflammatory diseases

IV.2 Pharmacokinetics

The applicant has provided a brief summary of the pharmacokinetic (PK) information regarding Fludeoxyglucose (18F). Since Fludeoxyglucose (18F) is for diagnostic use only, will be administered in a clinical setting at a limited number of occasions, is dosed individually, based on both patient related factors and factors related to equipment, by trained health care personnel PK becomes secondary and the lack of data is considered acceptable.

The SmPC for Fludeoxyglucose (18F) Akademiska sjukhuset follows the core SmPC published by EMA regarding the pharmacokinetic information.

IV.3 Clinical efficacy and safety

The applicant has provided a clinical summary of use in oncology, cardiology and neurology, mainly in the period 1995-2001, i.e. more than 15 years ago. Notwithstanding that no summary of clinical data on use in infectious diseases is presented, it is noted that marketing authorizations for fludeoxyglucose (18F) were granted for several applicants in 2010, in accordance with article 10a (well-established use). They were found to be in accordance with a core SPC approved by MRFG in March 2005, that is, the oncology, cardiology, and neurology indications were already considered well established 10 years ago. The infectious diseases indication was included in the now superseded Core SmPC from 2010, i.e. data supporting an EU indication in infectious and inflammatory diseases was found to be sufficient nine years ago. Of further note, importantly, the current core SmPC (19 July 2012) explicitly points out that it was prepared on the basis and taking into account the available published scientific literature dated from more than 10 years. This most recent core SmPC includes the current infectious and inflammatory diseases indication, why well-established medicinal use for the claimed therapeutic indication within the Union for at least ten years, with recognised efficacy and an acceptable level of safety, must be considered the case.

IV.4 Risk Management Plans

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Fludeoxyglucose (18F) Akademiska sjukhuset, 0.9 - 4.5 GBq/ml, solution for injection.

Safety specification

	Routine risk minimization activities sufficient	**If yes, provide description of routine activity and justification**
Important identified risk: None identified	N.A.	—

Important potential risks: None identified	Yes	Expedited reporting of individual case safety reports (ICSR) Annual periodic safety update reports (PSUR): Fludeoxyglucose, has been approved since 16 May 2005 and is approved in seven countries. Based on the published literature and experience from marketing of other Fludeoxyglucose for over 2 years, potential safety issues have been considered in this document. No significant safety concern or significant lack of information have been identified.
Important missing information: None identified	Yes	as above

Pharmacovigilance Plan

In the applicant's view, the safety specification for Fludeoxyglucose (18F) Akademiska sjukhuset does not indicate an identified or a potential safety concern or lacking information. Therefore, routine pharmacovigilance activities are considered sufficient.

Risk minimisation measures

The applicant proposes that no risk minimization plan is considered necessary. Since its approval a single spontaneous report with no adverse events have been received.

Summary of the RMP

The applicant has identified and discussed potential safety concerns and missing information by reviewing literature. Hypersensitivity, incorrect diagnosis, exposure during pregnancy to ionizing radiation, risks related to exposure to ionizing radiation from Fludeoxyglucose and computed tomography (e.g., PET-CT) in the paediatric population, incorrect handling of test procedures, long-term safety, concomitant administration of colony-stimulating factors (CSFs), glucose and insulin, and medicinal product that modify blood glucose level, and overdosing.

The applicant was invited to also discuss the relevance of including safety concerns of giving dose to women who are breast feeding, other causes for altered uptake (recent food intake, coffee, excercise), and exposure to relatives (LoQ; refer to the Non-Clinical & Clinical AR).

The MAH has satisfactorily responded to the questions raised and the RMP is in no need for an update.

Issue is resolved.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the MPA;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

IV.5 Discussion on the clinical aspects

The quality of the generic product, Fludeoxyglucose (18F) Akademiska sjukhuset, is found adequate. There are no objections to approval of Fludeoxyglucose (18F) Akademiska sjukhuset, from a non-clinical and clinical point of view. The product information is acceptable.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) for Flucorpus, 0,09 - 2,72 GBq/ml injektionsvätska, lösning, has been performed on the basis of a bridging report making reference to MetaTrace FDG solution for injection 3000 MBq/ml, UK/H/2656/001/MR. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Fludeoxyglucose (18F) Akademiska sjukhuset, is found adequate. There are no objections to approval of Fludeoxyglucose (18F) Akademiska sjukhuset, from a non-clinical and clinical point of view. The product information is acceptable. The application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

Fludeoxyglucose (18F) Akademiska sjukhuset, 0.9 - 4.5 GBq/ml, solution for injection was approved in the national procedure on 2020-08-04.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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