LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

SmofKabiven extra Nitrogen
Active substances:

Alanine, arginine, glycine, histidine, isoleucine, leucine, lysine acetate, methionine, phenylalanine, proline, serine, taurine, threonine, tryptophan, tyrosine, valine, calcium chloride, sodium glycerophosphate, magnesium sulphate, potassium chloride, sodium acetate and zinc sulphate, glucose monohydrate, soya-bean oil (refined), medium-chain triglycerides, olive oil and fish oil (rich in omega-3-acids)

SmofKabiven extra Nitrogen Electrolyte free
Active substances:

Alanine, arginine, glycine, histidine, isoleucine, leucine, lysine acetate, methionine, phenylalanine, proline, serine, taurine, threonine, tryptophan, tyrosine, valine, glucose monohydrate, soya-bean oil (refined), medium-chain triglycerides, olive oil and fish oil (rich in omega-3-acids)

SE/H/792/03-04/DC

This module reflects the scientific discussion for the approval of SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free. The procedure was finalised on 2017-05-03. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Fresenius Kabi AB has applied for a marketing authorisation for SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free, emulsion for infusion. The active substances, see above, are the same as in SmofKabiven and SmofKabiven Elektrolytfri, emulsion for infusion (SE/H/792/01-02) marketed by Fresenius Kabi AB since 2007. No PAR exists for the previously authorised products, SmofKabiven and SmofKabiven Elektrolytfri.

For approved indications, see the Summary of Product Characteristics.

The marketing authorisation has been granted pursuant to Article 10a of Directive 2001/83/EC.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83 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

III.1 Introduction

The present application concerns extension applications of the previously authorised products SmofKabiven and SmofKabiven Elektrolytfri emulsion for infusion (SE/H/792/01-02). From a non-clinical perspective there are no changes to the products that would warrant new or additional data, and no such data of value for the assessment has been submitted.

III.2 Ecotoxicity/environmental risk assessment

The applicant has not performed an ERA. The product is composed of amino acids, glucose and lipids, with or without electrolytes. In addition, the levels of the constituents are in the same range as in the previously authorised products SmofKabiven and SmofKabiven Elektrolytfri emulsion for infusion (SE/H/792/01-02). Thus, no increased exposure to the environment is expected.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

N/A

IV.2 Pharmacodynamics

No data on pharmacodynamic properties of SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free is available. PD data on the individual components, i.e. SMOFlipid 20%, Aminoven 10% with or without electrolytes, and Glucose 42% described by the applicant is considered acceptable provided that the new formulation of the products are line extensions to the existing approved SmofKabiven product range and the active substances of the products have been in well-established medicinal use.

IV.3 Clinical efficacy

In general, all compartments of SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free and their combination can be considered well known and generally established for medicinal use. The efficacy of similar products is well established. The extensive experience of clinical use in PN with the individual compounds (amino acids, glucose and lipids, with or without electrolytes) and their combination is considered adequately documented in the clinical overview presented by the Applicant.

The proposed dosage for adults of SmofKabiven extra Nitrogen and SmofKabiven Extra nitrogen Electrolyte free is considered as adequate to cover the daily nutritional requirements of adult patients according to the proposed therapeutic indication.

The applicant has submitted a justification to support the inclusion of paediatric indications in children aged 2 years and above for SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free. As taking the recent approved paediatric indication for children aged 2 years and above for SmofKabiven, SmofKabiven Elektrolytfri (SE/H/792/01-02/II/76) and

SmofKabiven Perifer (SE/H/861/01/II/73) into consideration, the applicant's proposal is accepted.

IV.4 Clinical safety

SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free are composed of well-known components which are well-established in clinical use for PN. Accordingly, there is extensive experience concerning safety of the individual components and their combination. Furthermore, the applicant refers to post marketing experience available from other SmofKabiven products as marketed by the MAH, according to which the medicinal product is considered to be safe and effective with a positive benefit-risk ratio.

There is no reason to believe that the safety profile of the applied product should be different as compared with other marketed solutions of the class.

The applicant's response to question related to include hyperglycaemia in Summary of Product Characteristics 4.8 is accepted

IV.5 Risk Management Plans

The MAH has submitted a risk management plan (RMP), 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 SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free.

No additional pharmacovigilance activities beyond routine pharmacovigilance are deemed necessary.
No risk minimisation measures or additional minimisation measures are proposed, which is endorsed.

Safety concerns

Important Identified risk	Metabolic/electrolytes abnormalities
Important Potential risk	Refeeding syndrome
Missing information	Use in pregnant and lactation women Use in children

The RMP is approved

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

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to SmofKabiven and SmofKabiven Elektrolytfri (SE/H/792/01-02/MR). The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

In general, all compartments of SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free and their combination can be considered well known and generally established for medicinal use. The efficacy of similar products is well established. The extensive experience of clinical use in PN with the individual compounds (amino acids, lipids, and glucose, with and without electrolytes) and their combination is considered adequately documented in the clinical overview presented by the Applicant. The applicant refers to post marketing experience available from other SmofKabiven products as marketed by the MAH, according to which the medicinal product is considered to be safe and effective with a positive benefit-risk ratio.

Concerning use of SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free in the adult and children aged 2 years and above according to the indication, the benefit risk ratio is assessed to be positive.

The proposed dosage for use of SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free is considered as adequate to provide the daily nutritional requirements of target populations according to the proposed therapeutic indication.

To conclude, the benefit-risk ratio is considered positive. The product information is acceptable. The applications for SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free are therefore recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 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

The Decentralised procedure for SmofKabiven extra Nitrogen and SmofKabiven extra Nitrogen Electrolyte free, emulsion for infusion was positively finalised on 2017-05-03.

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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
SE/H/xxxx/WS/499 (SmofKabiven extra Nitrogen Electrolyte free, SE/H/792/04)	To add information on dosing in intra-dialytic parenteral nutrition (IDPN) to the SmPC and Package Leaflet.	Yes	2022-03-18	Approval	Posology for intradialytic parenteral nutrition (IDPN) is provided.

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

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