LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

SmofKabiven Nutribase

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

SE/H/792/05/DC

This module reflects the scientific discussion for the approval of SmofKabiven Nutribase. The procedure was finalised on 2021-11-24. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for SmofKabiven Nutribase, Emulsion for infusion.

The active substances is sodium glycerophosphate, anhydrous, fish oil, rich in omega-3-acids, glycine, valine, calcium chloride dihydrate, tyrosine, olive oil, refined, tryptophan, zinc sulfate heptahydrate, magnesium sulfate heptahydrate, triglycerides, medium-chain, sodium acetate anhydrous, calcium chloride anhydrous, serine, soya-bean oil, refined, glucose (anhydrous), methionine, proline, magnesium sulfate, anhydrous, isoleucine, potassium chloride, histidine, threonine, taurine, phenylalanine, lysine, glucose monohydrate, leucine, zinc sulfate anhydrous, lysine acetate, alanine, arginine, sodium acetate trihydrate. A comprehensive description of the indication and posology is given in the SmPC.

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

The application is an extension, new strength, of the previously authorised product SmofKabiven, emulsion for infusion, marketed by Fresenius Kabi AB since 2007. Please note that a Public Assessment Report is not available for SmofKabiven.

The application for SmofKabiven Nutribase, emulsion for infusion, is submitted according to Article 10a of Directive 2001/83/EC. The applicant, Fresenius Kabi AB applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, BE, BG, CY, HR, CZ, DK, EE, FI, FR, DE, EL, HU, IE, IS, LU, LV, LT, NL, NO, PL, PT, RO, SI, SK, ES, UK(NI)as concerned member states (CMS).

Potential similarity with orphan medicinal products
According to the application form and a check of the Community Register of orphan medicinal products there is no medicinal product designated as an orphan medicinal product for a condition relating to the indication proposed in this application.

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

Pharmacology, Pharmacokinetics, Toxicology
This is a line extension to already approved Smof Kabiven to reduce the amino acid content and caloric density of the mixed ready-to-use solution.

The maximum doses of the components are well within the limits of the already registered products containing the individual components. No further non-clinical studies are required to support this new strength.

Environmental Risk Assessment (ERA)
A justification for not performing ERA studies was submitted.

The active substances are natural substances, the use of which will not alter the concentration or distribution of the substance in the environment. Therefore, SmofKabiven Nutribase is not expected to pose a risk to the environment.

IV. CLINICAL ASPECTS

Pharmacokinetics
N/A.

Pharmacodynamics
The data presented on PD are based mainly on reports in the literature. The clinical pharmacology of the individual components and combinations within a range covering the current Application is well known.

Clinical efficacy

The efficacy claim for SmofKabiven Nutribase is based on the evidence available for the nutritional efficacy of its individual components. The extensive experience of clinical use in parenteral nutrition with the individual compounds (lipids, amino acids, glucose, and electrolytes) and their combination is considered sufficiently documented by the Applicant. In general, the effects of all components of SmofKabiven Nutribase and their combination are considered well known and generally established for clinical use.

The proposed dose and infusion rate for SmofKabiven Nutribase are primarily based on the data from clinical studies and post marketing data for SmofKabiven as well as the evidence relating to the components of SmofKabiven taking into account the similarities and differences in the composition between SmofKabiven Nutribase and its parent products in the SmofKabiven product range.

The clinical studies presented in the clinical overview have already been assessed in the previous procedures for SMOF range of the products. No new information has been provided regarding efficacy, and previous conclusions remain unchanged.

Taking into consideration that SmofKabiven Nutribase is a line extension of the SmofKabiven, the efficacy claim for SmofKabiven Nutribase is based on the evidence available for the nutritional

efficacy of its individual components. The applicant's proposal to use the evidence available for the efficacy of the individual components, in a dose range covered by what has already been approved, to support the efficacy claim for the product is accepted.

The paediatric posology has been adequately supported based on literature and is in line with consensus guideline recommendations. The proposed dosage for adults and children from 2 years age of SmofKabiven Nutribase is considered as adequately justified in relation to nutritional requirements of adult and paediatric patients in the proposed therapeutic indication. The dose should be individualised to the patient's clinical condition, body weight (bw), nutritional and energy requirements, adjusting dosage based upon additional oral/enteral intake, which is adequately reflected in the SmPC section 4.2.

Clinical safety

No additional studies have been conducted for SmofKabiven Nutribase. The application concerns a line extension for a combination of already approved products used in line with current guidelines and previously approved posology. Maximum doses of the single components are within the limits of already registered SmofKabiven product range.

SmofKabiven is registered in 74 countries (status June 2020). The product was first launched in Sweden in June 2007.

The safety and tolerability claims for SmofKabiven Nutribase are made on the basis of the data available for the SmofKabiven product range and the individual components of the product. The safety profile is therefore not expected to differ from already approved products, in line with the study data provided.

Use in children from 2 years of age has been approved for the product range, is in line with guideline recommendations, and has been sufficiently justified by the supportive data provided.

Risk Management Plan

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 SmofKabiven Nutribase.

Safety specification

Table SVIII.1: Summary of safety concerns

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

Pharmacovigilance Plan
Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The submitted Risk Management Plan, version 2.1 signed 29-Apr-2021 is acceptable.

V. USER CONSULTATION

Content
The applicant has proposed a bridging to a user test carried out on the product SmofKabiven, asp no 2005-0733. The user test of the SmofKabiven leaflet was assessed and accepted in 111:2005/45817.

Layout
The applicant has proposed a bridging to a user test carried out on the product SmofKabiven, asp no 2005-0733.The user test of the SmofKabiven leaflet was assessed and accepted in 111:2005/45817.

A comparison between the parent PL and the daughter PL (including lay-out) together with a critical discussion hereof has been provided. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

SmofKabiven Nutribase is composed of well-known components which are well-established in clinical use for parenteral nutrition. 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 marketed by the MAH, according to which the medicinal product can be considered to be safe and effective. There is no reason to believe that the safety profile of the applied product should be different as compared to other marketed solutions of the class. From a clinical perspective the Application is approvable.
From a quality perspective the Application is approvable.

There are no objections to approval of SmofKabiven Nutribase from a non-clinical point of view.

The overall benefit-risk relation is favourable.

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

N/A

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

N/A

VII. APPROVAL

The decentralised procedure for SmofKabiven Nutribase, emulsion for infusion was positively finalised on 2021-11-24.

LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se