Kepivance®
Material Safety Data Sheet

biovitrum.

Revision Number: 1 **Date Issued** 22-Dec-2008

1. PRODUCT AND COMPANY IDENTIFICATION

Product Name: Common Name:	Kepivance®
Chemical Name: Synonyms:	palifermin 24-163-keratinocyte growth factor (human) palifermin; keratinocyte growth factor, KGF, rHu-KGF
Manufacturer:	Biovitrum AB, 112 76 Stockholm, Sweden
Emergency Telephone Number:	Toll free In EUROPE +800 386 587 21, in USA and CANADA +866 773 5274 In AUSTRALIA +1-800-086468, in NEW ZEALAND +0800-446286 or direct to Call Center +41 61 564 13 28

2. HAZARDS IDENTIFICATION

Emergency Overview

Pharmaceutical product intended for clinical and commercial manufacturing purposes only. Product contains Kepivance® (recombinant human keratinocyte growth factor), an active pharmaceutical ingredient. Overexposure may cause effects on the skin and tongue if systemically absorbed. There is a potential for effect on the developing fetus and on fertility; the systemic absorption by inhalation is not known. Avoid inhalation, skin contact, eye contact, and accidental ingestion.

Potential Health Effects

Principle Routes of Exposure: Inhalation, Skin and Eye Contact, Accidental Ingestion.

Inhalation:	No data with inhalation exposure available.
Skin:	No data with dermal exposure available. Based on its molecular weight, this product should not be readily absorbed through the skin.
Eyes:	No data with ocular exposure available.
Ingestion:	No data with oral exposure available.

See Section 11 for additional Toxicological information.

Occupational Exposure Limit: No exposure guidelines established by ACGIH, NIOSH or OSHA. Amgen recommends an occupational exposure limit (OEL) of 16 µg/m^3 as an 8-hour time weighted average over a 40 hour work week. The OEL is designed as an acceptable airborne concentration of a substance for which it is believed that workers may be repeatedly exposed day after day without adverse health effects. Kepivance® has been classified per Amgen's Health Hazard Classification System as an Occupational Exposure Band 4 R compound (20 µg/m^3- 100 µg/m^3) based on the potential for reproductive/develomental and/or effects.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredients:	See below
CAS-No:	162394-19-6
Formula:	Proprietary Information

Single dose lyophilized vial containing 6,25 mg of palifermin with:

	CAS-No	Amount
Sucrose	57-50-1	25.0 mg
L-Histidine	71-00-1	1.94 mg
Mannitol	87-78-5	50.0 mg
Polysorbate 20	9005-64-5	0.13 mg

4. FIRST AID MEASURES

Eye Contact: Rinse thoroughly with plenty of water for at least 15 minutes and consult a physician.

Skin Contact: Wash off immediately with plenty of water for at least 15 minutes and consult a physician. Consult a physician

Inhalation: Move to fresh air. If symptoms persist, call a physician.

Ingestion: Immediate medical attention is required.

Notes to Physician: Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Flammable Properties: Not applicable.

Extinguishing Media: Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Hazardous Combustion Products: No information available.

Protective Equipment and Precautions for Firefighters: Wear self-contained breathing apparatus and protective suit.

6. ACCIDENTAL RELEASE MEASURES

Spill Procedures: If material is released or spilled, cordon off spill area. Take proper precautions to minimize exposure by using appropriate personal protective equipment in cleaning up a spill. If in powder form, wet down spilled material to minimize airborne dispersion. Soak up material with absorbent e.g., paper towels, and wash spill area thoroughly with appropriate cleaning materials. Dispose of collected material in accordance with applicable waste disposal regulations.

7. HANDLING AND STORAGE

Handling and Storage: Avoid contact with skin, eyes or clothing. Use adequate ventilation to minimize exposure. Wash hands, face and other potentially exposed areas immediately after handling this material. Clean protective equiment thoroughly after each use. Store in a well ventilated area.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Chemical Stability: Stable

Engineering Controls: When practicable, handle material in enclosed processes or in processes with effective local exhaust ventilation or within a chemical hood.

Conditions to Avoid: None

Incompatible Materials: None

Personal Protective Equipment

Hazardous Decomposition Products: No information available

Eye/face Protection: Wear safety glasses with side shields, chemical splash goggles, or safety glasses with side shields and a full-face shield to prevent contact with eyes. The choice of protection should be based on the job activity and potential for exposure to the eyes and face.

Skin Protection: Use gloves or other appropriate personal protective equipment if skin contact with formulation is possible. Wear lab coat or other protective over garment if splashing is possible. The choice of protection should be based on the job activity and potential for skin contact.

Respiratory Protection: When possible, handle material in enclosed processes or containers. If it is properly handled with effective local exhaust ventilation or containment, respiratory protection may not be needed. For procedures involving larger quantities or dust/aerosol generating procedures such as weighing or a large transfer of liquids, an air-purifying respirator with NIOSH approval for dusts and mists may be needed.

Other: Wash hands, face and other potentially exposed areas after handling material (especially before eating, drinking or smoking). Clean protective equipment thoroughly after each use.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	White
Physical State:	Lyophilized powder
Molecular Weight:	16.3 kD
pH:	6.5 (reconstituted)
Flash Point:	Not applicable
Boiling Point:	Not applicable
Melting Point:	No information available
Explosion Limits	Not applicable
Vapor Pressure:	Not applicable
Vapor Density (air = 1):	Not applicable
Specific Gravity:	No information available
Water Solubility:	No information available
Partition Coefficient (log Kow):	No information available

10. STABILITY AND REACTIVITY

11. TOXICOLOGICAL INFORMATION

Single Dose Studies:	Kepivance® single-dose toxicity studies were conducted in rats and monkeys at doses up to 30 mg/kg (IV or SC), or 50 mg/kg (IV), respectively. Observed effects were related to exaggerated pharmacological activity of Kepivance® notably enlarged thymus gland and thickening of the skin, hyperplasia, or both or epithelial cells in numerous tissues.
LD50 Oral:	No formal LD50 test was conducted.
Eye irritation:	No specific studies were conducted to assess the potential to cause eye irritation.
Skin irritation:	No specific studies were conducted to assess the potential to cause skin irritation.
Sensitization:	No specific studies were conducted to assess the potential to cause eye or skin irritation, or skin sensitization.
Repeated Dose Studies	Repeat-dose toxicity studies with Kepivance® were conducted in rats and monkeys and involved daily or intermittent treatment (IV or SC) for up to 28 days at doses 30 - 1000 µg/kg/day. The same spectrum of observations was seen with both routes of administration, although generally at lower doses with IV administration. In rats, most of the findings reflect the pharmacologic activity of the drug including increase liver weight, enlarged thyroid, hyperplasia of the bladder epithelium and changes in the gastrointestinal tract. All effects, except the thyroid reversed after the cessation of treatment. In monkeys at the higher dose, observations noted were swollen lips, skin scaling, pale oral mucosa, salivation, and/or decrease activity. At doses ≥30 µg/kg/day, thickening of the buccal mucosa, tongue, and/or esophagus; increased serum amylase concentrations, and characteristic skin thickening and hyperkeratosis of the skin were observed. In animals treated with ≥10 µg/kg/day, thymic involution was evident. All effects reversed after the cessation of treatment. In clinical trials, the most common adverse reactions attributed to Kepivance® were skin toxicities (rash, erythema, edema, pruritus), oral toxicities (impairment of sensation, tongue discoloration, tongue thickening, alteration of taste), joint pain, and impairment of sensation.
Reproductive and Developmental Toxicity:	In rats, there were adverse effects on male and female reproductive performance at doses ≥300 µg/kg/day (5-fold higher than the recommended human dose). Kepivance® has been shown to be embryotoxic in rabbits and rats when given in doses that are 2.5 and 8 times the human dose, respectively. Treatment with these doses was also frequently associated with maternal toxicity (clinical signs and body weight effects). No evidence of developmental toxicity was observed in rats at doses up to 300 µg/kg/day. Treatment with these doses was also associated with maternal toxicity (clinical signs and reductions in body weight gain/food consumption). No evidence of developmental toxicity was observed in rabbits at doses up to 60 µg/kg.
Mutagenicity/Genotoxicity Studies:	No evidence of genotoxicity in a battery of in vivo and in vitro studies.
Carcinogenicity Studies:	Per ICH S6, no carcinogenicity tests were performed. Not listed by NTP, IARC, or OSHA as a carcinogen
Target Organ Effects:	Skin, Liver , Urinary Tract, Thyroid, Gastrointestinal tract (GI), Immune System

12. ECOLOGICAL INFORMATION

Ecotoxicityeffects:	No information available
Persistence/Degradability:	No information available
Bioaccumulation/ Accumulation:	No information available
Mobility in Environmental Media:	No information available
Other Adverse Effects:	No information available

13. DISPOSAL CONSIDERATIONS

Waste Disposal Method: Dispose of any waste according to prescribed federal, state and local guidelines..

14. TRANSPORT INFORMATION

DOT:

Hazard Class: Not regulated per U.S. or IATA
UN-No: Not regulated per U.S. or IATA

15. REGULATORY INFORMATION

International Inventories

Components are Exempt from Regulatory Requirements

USA - State Regulations

California Proposition 65: This product does not contain any Proposition 65 chemicals.

16. OTHER INFORMATION

Revision Number: 1

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections, which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it may be biologically active.