SULFLUX® KP-05 PLASMA SEPARATOR

Prior to use, carefully review the "LIPOSORBER® LA-15 System Operator's Manual" in its entirety and follow all directions, procedures, and instructions therein. Use only under the direction of a licensed physician with appropriate training.

SULFLUX®

PLASMA SEPARATOR KP-05

Instructions for use in Familial Hypercholesterolemia (FH)

FH

Caution: Federal law restricts this device to sale by or on the order of a physician.

Distributed by
Kaneka Medical America LLC
623 Fifth Avenue, New York, NY 10022

Manufactured by
ASAHI KASEI MEDICAL MT CORP.
2111-2 Oaza Sato, Oita-shi, Oita 870-0396, Japan

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I. Introduction

The SULFLUX® KP-05 Plasma Separator is one of three disposable device components of the LIPOSORBER® LA-15 System.

The technical characteristics of the SULFLUX® KP-05 Plasma Separator are explained in Section III of this instructions for use.

Before using the SULFLUX® KP-05 Plasma Separator, carefully review this instruction for use and the "LIPOSORBER® LA-15 System Operator's Manual."

II. Indication

The LIPOSORBER® LA-15 System is indicated for use in performing low density lipoprotein cholesterol (LDL-C) apheresis to acutely remove LDL-C from the plasma of the following high risk patient populations for whom diet has been ineffective and maximum drug therapy has been either ineffective or not tolerated:

Group A. Clinically diagnosed Familial Hypercholesterolemic Homozygotes with LDL-C > 500 mg/dL;

Group B. Clinically diagnosed Familial Hypercholesterolemic Heterozygotes with LDL-C ≥ 300 mg/dL;

Group C. Clinically diagnosed Familial Hypercholesterolemic Heterozygotes with LDL-C ≥ 100 mg/dL and either documented coronary artery disease or documented peripheral artery disease; and

Group D. Clinically diagnosed Familial Hypercholesterolemic Heterozygotes with LDL-C ≥ 100 mg/dL, lipoprotein(a) [Lp(a)] ≥ 60 mg/dL and either documented coronary artery disease or documented peripheral artery disease.

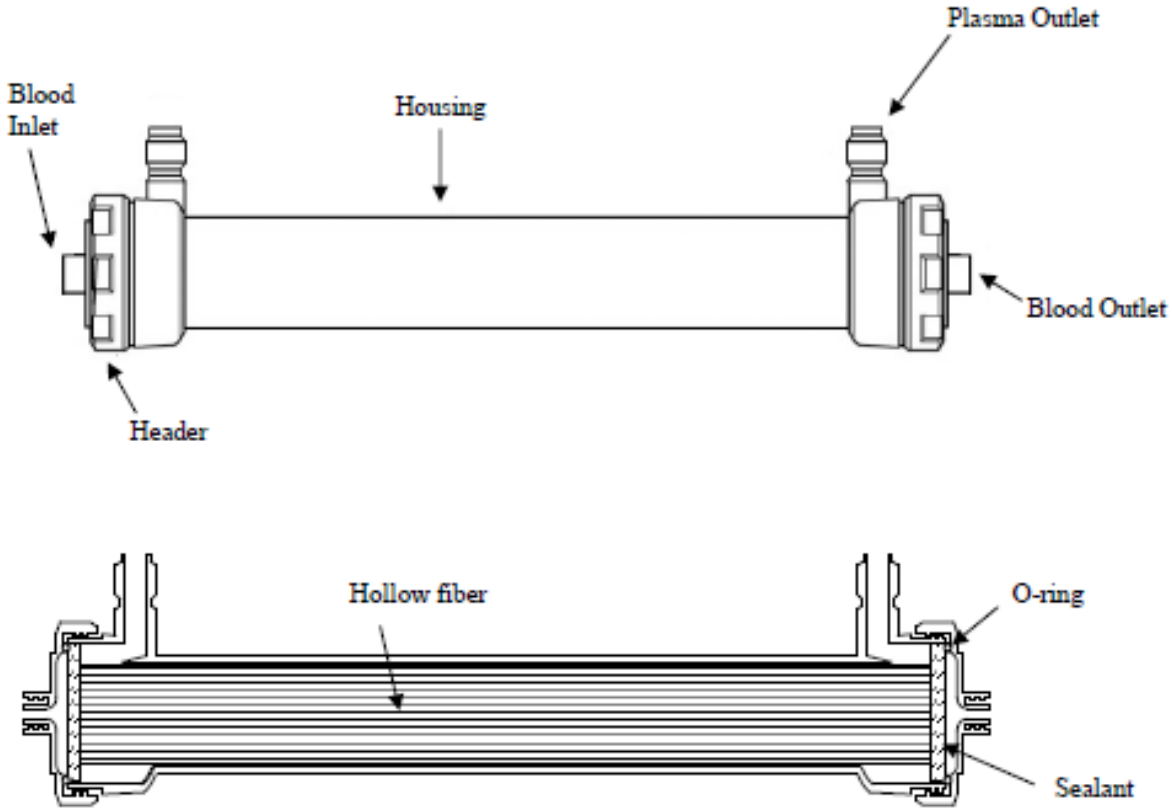
The LDL-C levels for the indicated patient populations are baseline LDL-C levels obtained after the patient has had a trial of diet and maximum tolerated combination drug therapy to reduce LDL-C according to the current professional guidelines on the management of blood cholesterol.

Documented coronary artery disease (CAD) includes CAD diagnosed by invasive or computed tomography (CT) coronary angiography, or by electron beam (ultrafast) CT (EBCT), or documented by a history of myocardial infarction (MI), percutaneous coronary intervention (PCI), or coronary artery bypass graft (CABG) surgery.

Documented peripheral artery disease (PAD) includes PAD diagnosed by symptoms and/or physical exam (e.g., using the Rutherford classification), ankle-brachial index (ABI), ultrasound exam, pulse volume recording (PVR), or peripheral vascular angiography, or documented by a history of peripheral vascular intervention, peripheral vascular bypass surgery, or minor or major amputation.

Baseline lipid levels are to be determined after stabilization on diet and drug therapy by making two measurements during a 2- to 4-week period. (Note: The two values should be within 10% of each other, indicating a stable condition.)

III. Technical Characteristics



Hollow Fiber	material inside diameter membrane thickness effective surface area pore size	polyethylene (coated with ethylene vinyl alcohol copolymer) 330 μm 50 μm 0.5 m^2 0.3 μm
Housing	material size	polycarbonate 34 mmΦ x 290 mm
Sealant	material	polyurethane
Priming Volume	blood side plasma side	55 mL 75 mL
Filling Liquid	composition	Saline solution
Sterilization Method	methodology	γ-ray irradiation (25 kGy)

IV. Performance Characteristics

Sieving Coefficients of Plasma Components were obtained *In vivo* from a clinical investigation (N=63).

Plasma Component	Sieving Coefficient	
	Mean	S.D.
Total Protein	1.00	0.02
Albumin	1.02	0.04
IgA	1.00	0.06
IgG	1.00	0.05
IgM	1.01	0.09
Total Cholesterol	1.03	0.14
Triglycerides	1.04	0.12

V. Operations

Carefully review and follow the "LIPOSORBER® LA-15 System Operator's Manual" and use only under a licensed physician's direction. **Do not reuse**.

VI. Contraindications

The LIPOSORBER® LA-15 System must not be used in:

1. patients who are being treated with angiotensin-converting enzyme (ACE) inhibitors;

   Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. Temporal ceasing of ACE inhibitor intake to remove its bioactivity from the patient's blood may not always be sufficient to avoid such adverse reactions. The ACE inhibitors should be switched to another antihypertensive medication (for example, angiotensin II receptor blockers (ARBs)) at the medical discretion of the treating physician.

2. patients for whom adequate anticoagulation cannot be achieved, such as those with severe hemophilia, severe hemorrhage diathesis, severe gastrointestinal ulcers, or who are receiving vitamin K antagonist medications after surgery;

3. patients for whom extracorporeal circulation therapy with LIPOSORBER® LA-15 System cannot be tolerated such as those with severe cardiac insufficiency, acute myocardial infarction, severe cardiac arrhythmia, acute apoplexy, or severe uncontrollable hypertension or hypotension; and

4. patients with hypersensitivity to dextran sulfate cellulose, heparin or ethylene oxide.

VII. Warnings

1. **Before using the LIPOSORBER® LA-15 System, including the SULFLUX® KP-05 Plasma Separator, carefully review the instructions for use provided for each of the disposables and the "LIPOSORBER® LA-15 System Operator's Manual." Persons performing the procedures must be qualified to perform extracorporeal procedures, and have completed the required training program.** Users should follow all operating or maintenance procedures published by Kaneka Medical America LLC and use only the disposable device components recommended by Kaneka Medical America LLC. Failure to do so may result in serious injury or loss of life.

2. **The storage and use of this disposable device other than in accordance with the instructions published by Kaneka Medical America LLC or the use of disposable device components not recommended by Kaneka Medical America LLC may result in serious patient injury or loss of life**. The manufacturer and distributor(s) of this device will not be responsible for patient safety if the procedures to operate and maintain the LIPOSORBER® LA-15 System are other than those specified in this instructions for use and the Operator's Manual.

3. The LIPOSORBER® LA-15 System may be used only as prescribed by a licensed and appropriately trained physician. While connected to the extracorporeal system, the patient must be attended to at all times by a physician or qualified health-care professional adequately trained in all aspects of the procedure.

4. **Prior to use of the SULFLUX® KP-05 Plasma Separator, the Plasma Separator must be rinsed with 1000mL of 0.9% Sodium Chloride Injection (USP) and subsequently primed with 500mL of heparinized Lactated Ringer's Injection (USP) pursuant to the automated rinsing and priming process conducted by the LA-15 System**. This procedure must be completed for **every** Plasma Separator prior to use. Because air bubbles in the Plasma Separator may lead to complications such as coagulation of blood and impairment of performance, the operator must ensure that there is no air bubble migration into the Plasma Separator during rinsing and priming.

5. SULFLUX® KP-05 Plasma Separator is capable of efficient separation of plasma from the blood flow from 70 to 130 mL/min when the plasma filtrate ratio (plasma flow rate / blood flow rate) is not more than 30%.

6. While operating, **the transmembrane pressure (TMP) of the SULFLUX® KP-05 Plasma Separator must be under 60 mmHg**. If the TMP rises above 45 mmHg, the plasma pump will decelerate until the TMP falls below 45 mmHg. If the TMP reaches or exceeds 65 mmHg for a duration of three seconds or more, the plasma pump will cease operation.

7. **Citrate preparation (ACD) should never be used as an anticoagulant in the system**. **The LIPOSORBER® LA-15 System is designed solely for treatment using heparin as an anticoagulant.** Anticoagulation is required to prevent thrombus formation from occurring within the extracorporeal circuit. Anticoagulation with too much heparin is associated with an increased risk of bleeding for the patient, especially after the procedure. In order to reduce the risk of bleeding, the puncture sites should be sufficiently compressed so that bleeding is stopped (See Operator's Manual at Section **1.6 Adverse Events**). **In some patients the potential for development of a coagulopathy extending several days post-therapy may exist.** In addition to adjusting heparin dosage based on clinical observation during and after the apheresis procedure, Activated Clotting Time and/or partial thromboplastin time (PTT) values may be used. (See Operator's Manual at Section **1.8.3 Instructions for Use regarding "Determining Heparin Dosage"**)

8. No chemicals or solvents are to be used either inside or outside of this disposable device.

9. The SULFLUX® KP-05 Plasma Separator is disposable and is **intended for use in a single procedure only**. **Never reuse**. Discard this disposable after each use.

VIII. Precautions

1. Physicians and operators should follow the OSHA and the CDC/ACIP Adult Immunization Guidelines for Hemodialysis Patients. It is recommended that patients be screened for Hepatitis B and other infectious diseases, however, due to possible exposure to hepatitis virus, human immunodeficiency virus, and other infectious agents when handling extracorporeal blood circuits, blood or blood products, universal precautions should be taken at all times to prevent the exposure to and transmission of such agents.

2. When disposing of the disposable device components and wastes, comply with all local requirements and the policies of the facility regarding precautions for and prevention of infection and environmental pollution.

3. All connections of the extracorporeal circuit should be checked carefully prior to initiating and during the procedure. Avoid unnecessary kinking of the tubing lines and the patient's vascular access devices at all times.

4. Drip chambers in the extracorporeal circuit should be kept at least 2/3 to 3/4 full and monitored at all times in order to decrease the risk of air embolism.

5. The fluid circuit of this system is intended to be sterile and nonpyrogenic. Aseptic handling techniques are necessary to maintain these conditions. Prior to use, carefully examine the packaging of the Plasma Separator to ensure that it is intact and undamaged. Do not use the Plasma Separator if the package, sterile bag, protective cap or the product itself is not intact or is damaged. Do not open the bag containing the Plasma Separator until immediately prior to use.

6. In transporting and storing the Plasma Separator, handle with care. Store the Plasma Separator in a clean and secure area at room temperature (0-30°C), avoiding exposure to direct sunlight, high humidity or excessive vibration. **Handle the SULFLUX® KP-05 Plasma Separator with care to avoid dropping or other sudden impacts and never allow it to freeze**. **Do not use a Plasma Separator that may have been dropped, damaged or frozen**.

7. The expiration date of the SULFLUX® KP-05 is 3 years from the sterilization date. The Plasma Separator must never be used after the expiration date.

SULFLUX® KP-05 PLASMA SEPARATOR

Prior to use, carefully review the "LIPOSORBER® LA-15 System Operator's Manual for use in the treatment of adult and pediatric patients with primary focal segmental glomerulosclerosis (FSGS)" in its entirety and follow all directions, procedures, and instructions therein. Use only under the direction of a licensed physician with appropriate training.

SULFLUX®

PLASMA SEPARATOR KP-05

Instructions for use in adult and pediatric focal segmental glomerulosclerosis (FSGS)

FSGS

Humanitarian Use Device

Authorized by Federal (USA) law for use in the treatment of adult and pediatric patients with nephrotic syndrome associated with primary focal segmental glomerulosclerosis (FSGS) when:

- Standard treatment options, including corticosteroid and/or calcineurin inhibitors, are unsuccessful or not well tolerated and the patient's glomerular filtration rate (GFR) ≥ 60 mL/min/1.73 m^2 or
- The patient is post renal transplantation.

The effectiveness of this device for this use has not been demonstrated.

Caution: Federal law restricts this device to sale by or on the order of a physician.

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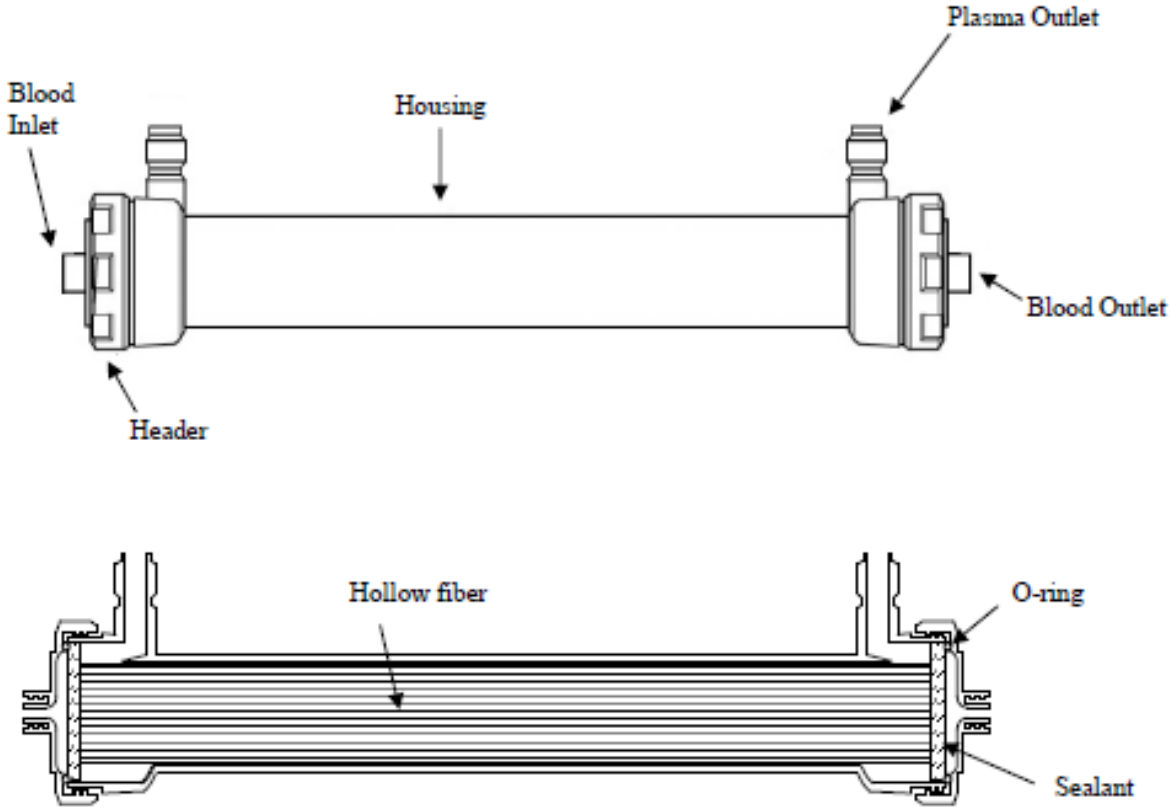
II. Indication

The LIPOSORBER® LA-15 System is indicated for use in the treatment of adult and pediatric patients with nephrotic syndrome associated with primary FSGS when:

- standard treatment options, including corticosteroids and/or calcineurin inhibitor, treatments are unsuccessful or not well tolerated and the patient's glomerular filtration rate (GFR) ≥ 60 mL/min/1.73 m^2 or
- The patient is post renal transplantation.

III. Technical Characteristics



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IgM	1.01	0.09
Total Cholesterol	1.03	0.14
Triglycerides	1.04	0.12

V. Operations

Carefully review and follow the “Operator’s Manual for FSGS” and use only under a licensed physician’s direction. **Do not reuse**.

VI. Contraindications

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