KANEKA MEDICAL AMERICA LLC
623 FIFTH AVENUE, 27th FLOOR
NEW YORK, NY 10022

TEL: (800) 526-3522
TEL: (212) 705-4340

KANEKA MEDICAL AMERICA LLC

Date (February 10, 2022)

URGENT:[1] MEDICAL DEVICE RECALL[2]

<LIPOSORBER® LA-15 SYSTEM Labeling>

(1) Attention to Customer:

Customer Name

Liposorber LA-15 System Labeling

Street Address

Town, State, Zip Code

Dear Device Customer,

(2) Purpose of this letter

The purpose of this letter is to advise you that Kaneka Medical America LLC is voluntarily recalling LIPOSORBER® LA-15 System Labeling for the following indications:

- for use in performing low density lipoprotein cholesterol (LDL-C) apheresis to acutely remove LDL-C from the plasma of the specified high risk patient populations for whom diet has been ineffective and maximum drug therapy has been either ineffective or not tolerated.
- for treatment of adult and pediatric patients with nephrotic syndrome associated with primary focal segmental glomerulosclerosis (FSGS) for specific reasons.

The labeling includes: Instructions for us (IFU-FH & FSGS), operators manuals (FH & FSGS), and patient guide (FSGS).

Note: **Serious injuries have occurred or could occur due to the treatment with the Liposorber LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication treatment associated with this recall. We have reports 2 serious injuries to the FDA.**

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[1] Recommended for Class I and II recalls. "Urgent" should be noted on both the letter and envelope as per 21 CFR 7.49(4)(b).

[2] For radiation-emitting electronic products, a recall action is governed by 21 CFR 1004 – Repurchase, Repairs, or Replacement of Electronic Products – under which manufacturers are required to bring such products into conformity with applicable performance standards or correct any reported device defect at no charge to the user. Medical device recalls are governed by 21 CFR 806 – Reports of Corrections and Removals – which does not contain an equivalent requirement.

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(3) Reason for the Voluntary Recall:

Kaneka submitted a special PMA supplement to address the risk of potential severe anaphylactoid reactions including shock due to treatment with Liposorber LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication treatment. FDA has approved the changes in January 2022, to the Liposorber IFU, guides, and manuals. Kaneka Medical America, determined that there are obsolete Liposorber IFU, guides, and manuals with the old Contraindications, Warnings, and Other Potential Adverse Events for ACE-I.

See Appendix A: FH Table of Modifications, and Appendix B: FSGS Table of Modifications.
.

- **Adverse events** (6 minor injuries and 2 serious injuries) with symptoms including:
  - Chest pain
  - Difficulty breathing
  - Tachycardia
  - Hypertension
  - Hypotension
  - Lightheadedness
  - Fainting
  - Nausea
  - Abdominal pain
  - Flushing

(4) Risk to Health:

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

(5) Actions to be taken by the Customer/User:

Please take the following actions:

1. Locate all Liposorber operator's manuals, patient guides, and IFUs in your facilities control and dispose of these documents.
2. Ensure the updated operator's manuals, patient guides, and IFUs are distributed to the necessary persons within the organization and that they are adhered to when selecting and using the Liposorber.
3. Retain this letter in a prominent position.
4. Acknowledge receipt of this notification and disposal of the documents with Kaneka Medical America via email or regular mail using an electronic or physical copy of the acknowledgement letter found at the bottom of this letter.

(6) Product and Distribution Information:

- See Appendix C: All Affected Product Identification Codes".
- The images below are of the covers for the Liposorber labeling being corrected by this recall:

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FSGS Instruction for use

LIPOSORBER® LA-15

LDL ADSORPTION COLUMNS

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 m² 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.

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)" and use only under the direction of a licensed physician with appropriate training.

kaneka

Distributed by
KANEKA PHARMA AMERICA LLC
546 Fifth Avenue, 21st Floor New York, New York 10036

Manufactured by
KANEKA CORPORATION
2-3-18, Nakanoshima Kita-ku, Osaka 530-8288, Japan

XXXX-X
Printed in Japan, xx / xxxx

FSGS Operator Manual

Manual No. 1002en-Rx

LIPOSORBER® LA-15 SYSTEM

Operator's manual for use in the treatment of pediatric patients with primary focal segmental glomerulosclerosis (FSGS)

Humanitarian Use Device

Authorized by Federal (USA) law for use in the treatment of 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 m² 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.

Important:
Be sure to carefully read this operator's manual before use.
Keep this manual by the machine for immediate reference.

This manual is applicable to the KANEKA MA-03 with the software version 1.2.
The software version is displayed on the KANEKA MA-03's screen.

KANEKA PHARMA AMERICA LLC
NEW YORK, NY

FSGS Patient Guide

A PATIENT GUIDE TO THE LIPOSORBER® LA-15 SYSTEM

Humanitarian Use Device

Authorized by Federal (USA) law for use in the treatment of 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 m² or
- The patient is post renal transplantation.

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

Notes: The Liposorber® LA-15 System is approved for pediatric patients with focal segmental glomerulosclerosis (FSGS). All references to "you" in this booklet refer to "you", if you are legally allowed to give your own consent (i.e., if you are age 18-21 years old). If you are providing consent on behalf of a child under the age of 18 "you" refers to your child.

Table of Contents

KANEKA MEDICAL AMERICA LLC
623 FIFTH AVENUE, 27th FLOOR
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TEL: (800) 526-3522
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FH Instruction for use

LIPOSORBER® LA-15

LDL ADSORPTION COLUMNS

Instructions for use in Functional Hypercholesterolemia (FH)

FH

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

Carefully review the "LIPOSORBER® LA-15 System Operator's Manual" and use only under the direction of a licensed physician with appropriate training.

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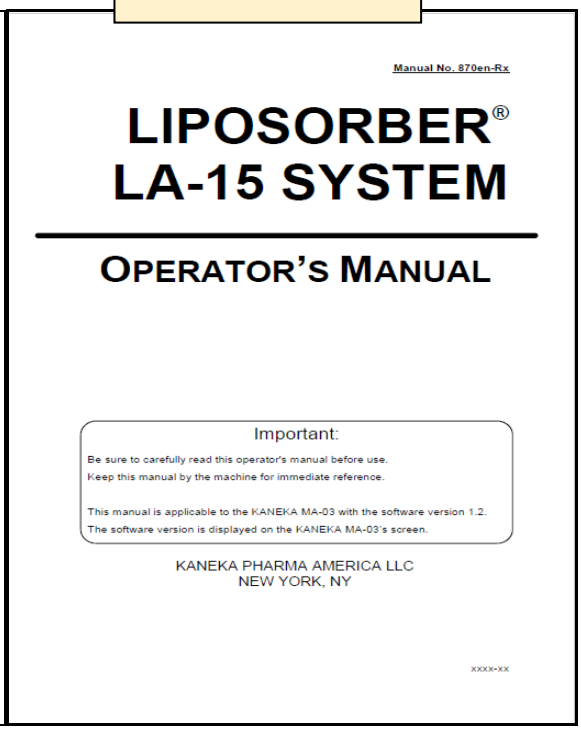
Manufactured by
KANEKA CORPORATION
2-3-18, Nakanoshima Kita-ku, Osaka 530-8288, Japan

S205H-7
Printed in Japan, 04 / 2019

Instructions for use in adult and pediatric Focal Segmental Glomerulosclerosis start from the back cover

FH Operator Manual



Manual No. 870en-Rx

LIPOSORBER®
LA-15 SYSTEM

OPERATOR'S MANUAL

Important:
Be sure to carefully read this operator's manual before use.
Keep this manual by the machine for immediate reference.

This manual is applicable to the KANEKA MA-03 with the software version 1.2.
The software version is displayed on the KANEKA MA-03's screen.

KANEKA PHARMA AMERICA LLC
NEW YORK, NY

xxxx-xx

(7) Type of Action by the Company:

Please find attached the revised operator's manual, patient guides, and IFU in PDF format. Please notify us if you would like us to send to you a paper copy of these documents.

(8) OTHER INFORMATION:

Authorized by:

Ahmad Al-Sattari

Director of Sales and Marketing

- If you have any question or concerns about this recall please contact Kaneka Medical America LLC. Monday through Friday, 8:00 AM to 4:30 PM, Eastern Time, at:
  - Phone: (212) 705-4355
  - Email: Ahmad.Al-Sattari@kaneka.com
- Please reference the following attachments:
  - Acknowledgement and Receipt Form
  - Instruction for use (FH)
  - Instruction for use (FSGS)
  - Operation Manual (FH)
  - Operation Manual (FSGS)
  - Patient Guide (FH)
  - Patient Guide (FSGS)

Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

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MEDICAL DEVICE RECALL RETURN RESPONSE
Acknowledgement and Receipt Form

Response is Required

Customer Information:

Customer Name

Street Address

Town, State, Zip Code

LIPOSORBER® LA-15 SYSTEM Labeling

I have read and understand the recall instructions provided in the <date of> letter. Yes _ No_

Any adverse events associated with recalled product labeling? Yes _ No _

If yes, please explain:

_____
_____
_____
_____

Affected Product Information: Please note in the table below if the described labeling is at your facility, and if you will dispose of it by check the appropriate box.

Document Type	None at your facility	Dispose all copies at this facility
FSGS Operator Manual		
FSGS Instruction for use		
FSGS Patient Guide		
FH Operator Manual		
FH Instruction for use		

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Return Response Box:

Please provide any additional information, if applicable.

☐ Please have Customer Service contact me.

We certify that we will dispose of all affected labeling as identified by the recall notice received on ______.

Signature of Recipient: _____

Name/Title	Recipient
Telephone	
Email address	

PLEASE EMAIL COMPLETED RESPONSE FORM TO:
Yu. Tanaka@Kaneka.com
Subject: Recall

OR MAIL TO:

Kaneka Medical America LLC.
ATTN: Recall
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New York, NY 10022

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Appendix A: FH Table of Modifications

Labeling Name	Page	Original (current)	Modified (proposed)
IFU for LIPOSORBER LA-15 LDL Adsorption Columns FH	FH 4/10	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete.	**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.
	FH 4/10	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs within 24 hours of treatment may cause hypotension in such patients.** When clinically feasible, patients should not receive antihypertensive drugs during the 24 hour period prior to undergoing the LDL-apheresis procedure. Before each treatment, physicians should determine when patients took their last dose of such medication.	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs may cause hypotension in such patients (for ACE inhibitors, see VI. Contraindications).** When clinically feasible, patients should not receive antihypertensive drugs prior to undergoing the LDL-apheresis procedure on the day of receiving the apheresis. Before each treatment, physicians should determine when patients took their last dose of such medication.
	FH 10/10	Patients on antihypertensive drugs, such as diuretics, calcium	Patients on antihypertensive drugs, such as diuretics, calcium

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Labeling Name	Page	~~Original~~ (current)	Modified (proposed)
		antagonists, beta blockers and ACE inhibitors, are at increased risk of hypotensive reactions occurring during therapy. ACE inhibitors have been associated with severe hypotension associated with flushing, dyspnea, and bradycardia. Therefore, **ACE inhibitor should not be administered for 24 hours or longer preceding each apheresis procedure. (See Contraindications.) In order to minimize the potential risks which also may be associated with other anti-hypertensive medications, it is recommended that patients refrain from taking antihypertensive drugs** at least the day before the LDL-apheresis procedure, when clinically feasible. Before each treatment, patients should be requested to advise the attending physician when they last took a dose of such medication. One of the hypotensive events reported in Table 1.1 was attributed to the administration of ACE inhibitors. The administration of ACE inhibitors in conjunction with therapy with the device also has been associated with the occurrence of tachycardia, and three of the reported tachycardia events (two in an emergency use patient) were attributed to the administration of ACE inhibitors.	antagonists, beta blockers and ACE inhibitors, are at increased risk of hypotensive reactions occurring during therapy. ACE inhibitors have been associated with severe hypotension associated with flushing, dyspnea, and bradycardia. Therefore, **patients who are being treated with any ACE inhibitor should not be treated with the LIPOSORBER® LA-15. (See VI. Contraindications). In order to minimize the potential risks which also may be associated with other anti-hypertensive medications, it is recommended that patients refrain from taking antihypertensive drugs** prior to undergoing the LDL-apheresis procedure on the day of receiving the apheresis, when clinically feasible. Before each treatment, patients should be requested to advise the attending physician when they last took a dose of such medication. One of the hypotensive events reported in Table 1.1 was attributed to the administration of ACE inhibitors. The administration of ACE inhibitors in conjunction with therapy with the device also has been associated with the occurrence of tachycardia, and three of the reported tachycardia events (two in an emergency use patient) were attributed to the administration of ACE inhibitors.
IFU for SULFLUX KP-05 PLASMA SE-PARATOR FH	FH - 4 -	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be	**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

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Labeling Name	Page	~~Original~~ (current)	Modified (proposed)
		minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete.	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.
IFU for TUBING SYSTEM FOR PLASMAPHERESIS NK-M3R(UL) FH	FH - 6 -	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete.	**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. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. 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.

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Labeling Name	Page	~~Original~~ (current)	Modified (proposed)
LIPOSORBER LA-15 SYSTEM OPERATOR's MANUAL FH	1-3	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete.	**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.
	1-4	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs within 24 hours of treatment may cause hypotension in such patients.** When clinically feasible, patients should not receive antihypertensive drugs during the 24 hour period prior to undergoing the LDL-apheresis procedure. Before each treatment, physicians should determine when patients took their last dose of such medication.	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs may cause hypotension in such patients (for ACE inhibitors, see 1.3 Contraindications).** When clinically feasible, patients should not receive antihypertensive drugs prior to undergoing the LDL-apheresis procedure on the day of receiving the apheresis. Before each treatment, physicians should determine when patients took their last dose of such medication.
	1-10	Patients on antihypertensive drugs, such as diuretics, calcium antagonists, beta blockers and ACE inhibitors, are at increased risk of hypotensive reactions occurring during therapy. ACE inhibitors have been associated with severe hypotension associated with flushing,	Patients on antihypertensive drugs, such as diuretics, calcium antagonists, beta blockers and ACE inhibitors, are at increased risk of hypotensive reactions occurring during therapy. ACE inhibitors have been associated with severe hypotension associated with

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Labeling Name	Page	~~Original~~ (current)	Modified (proposed)
		dyspnea, and bradycardia. Therefore, **ACE inhibitor should not be administered for 24 hours or longer preceding each apheresis procedure. (See Contraindications.) In order to minimize the potential risks which also may be associated with other anti-hypertensive medications, it is recommended that patients refrain from taking antihypertensive drugs** at least the day before the LDL-apheresis procedure, when clinically feasible. Before each treatment, patients should be requested to advise the attending physician when they last took a dose of such medication. One of the hypotensive events reported in Table 1.1 was attributed to the administration of ACE inhibitors. The administration of ACE inhibitors in conjunction with therapy with the device also has been associated with the occurrence of tachycardia, and three of the reported tachycardia events (two in an emergency use patient) were attributed to the administration of ACE inhibitors.	flushing, dyspnea, and bradycardia. Therefore, **patients who are being treated with any ACE inhibitor should not be treated with the LIPOSORBER® LA-15. (See 1.3 Contraindications). In order to minimize the potential risks which also may be associated with other anti-hypertensive medications, it is recommended that patients refrain from taking antihypertensive drugs** prior to undergoing the LDL-apheresis procedure on the day of receiving the apheresis, when clinically feasible. Before each treatment, patients should be requested to advise the attending physician when they last took a dose of such medication. One of the hypotensive events reported in Table 1.1 was attributed to the administration of ACE inhibitors. The administration of ACE inhibitors in conjunction with therapy with the device also has been associated with the occurrence of tachycardia, and three of the reported tachycardia events (two in an emergency use patient) were attributed to the administration of ACE inhibitors.

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Appendix B: FSGS Table of Modifications

Labeling Name	Page	Original (current)	Modified (proposed)
IFU for LIPOSORBER LA-15 LDL Adsorption Columns FSGS	FSGS 3/19	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete.	**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.
	FSGS 4/19	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs within 24 hours of treatment may cause hypotension in such patients.** When clinically feasible, patients should not receive antihypertensive drugs during the 24 hour period prior to undergoing the LDL-apheresis procedure. Before each treatment, physicians should determine when patients took their last dose of such medication.	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs may cause hypotension in such patients (for ACE inhibitors, see VI. Contraindications).** When clinically feasible, patients should not receive antihypertensive drugs prior to undergoing the LDL-apheresis procedure on the day of receiving the apheresis. Before each treatment, physicians should determine when patients took their last dose of such medication.
	FSGS 18/19	Hypersensitivity (anaphylactoid) reaction: Use of ACE inhibitors	Hypersensitivity (anaphylactoid) reaction: Use of ACE inhibitors

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Labeling Name	Page	~~Original~~ (current)	Modified (proposed)
		within 24 hours of therapy with the device can cause an increase in bradykinin levels, resulting in severe hypotension. ACE inhibitors should not be taken within 24 hours of therapy with the device.	with the device can cause an increase in bradykinin levels, resulting in severe hypotension. **Patients who are being treated with any ACE inhibitor should not be treated with the LIPOSORBER® LA-15 (See V. Contraindications).**
IFU for SULFLUX KP-05 PLASMA SE-PARATOR FSGS	FSGS -4 -	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete	**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.
IFU for TUBING SYSTEM FOR PLASMAPHERESIS NK-M3R(UL) FSGS	FSGS -6 -	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each	**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

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Labeling Name	Page	~~Original~~ (current)	Modified (proposed)
		LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete.	to another antihypertensive medication (for example, angiotensin II receptor blockers (ARBs)) at the medical discretion of the treating physician.
LIPOSORBER LA-15 SYSTEM OPERATOR's MANUAL FSGS	1-2	**patients who have been treated with angiotensin-converting enzyme (ACE) inhibitors within the past 24 hours;** Severe anaphylactoid reactions including shock have been observed in patients treated with the LIPOSORBER® LA-15 LDL Adsorption Column under concomitant ACE inhibitor medication. The risk of an anaphylactoid reaction may be minimized by withholding the administration of ACE inhibitors for approximately 24 hours before each LDL-apheresis procedure. The time period to withhold ACE inhibitors should be prolonged, if determined by the treating physician, considering each individual's renal function and the biological half-life of the ACE inhibitor currently in use. If required, ACE inhibitor administration may be resumed on the day of the apheresis treatment but only after the apheresis treatment is complete..	**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.
	1-5	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs within 24 hours of treatment may cause hypotension in such patients.** When clinically feasible, patients should not receive antihypertensive drugs during the 24 hour period prior to undergoing the LDL-apheresis procedure. Before each treatment, physicians should determine when patients took their last dose of such medication.	**LDL-apheresis treatment of patients who have taken any antihypertensive drugs may cause hypotension in such patients (for ACE inhibitors, see 1.3 Contraindications).** When clinically feasible, patients should not receive antihypertensive drugs prior to undergoing the LDL-apheresis procedure on the day of receiving the apheresis. Before each treatment, physicians should determine when patients took their

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Labeling Name	Page	~~Original~~ (current)	Modified (proposed)
			last dose of such medication.
	1-9	Hypersensitivity (anaphylactoid) reaction: Use of angiotensin-converting enzyme inhibitors (ACEi) within 24 hours of therapy with the device can cause an increase in bradykinin levels, resulting in severe hypotension. ACE inhibitors should not be taken within 24 hours of therapy with the device.	Hypersensitivity (anaphylactoid) reaction: Use of ACE inhibitors with the device can cause an increase in bradykinin levels, resulting in severe hypotension. **Patients who are being treated with any ACE inhibitor should not be treated with the LIPOSORBER® LA-15 (See 1.3 Contraindications).**
A PATIENT GUIDE TO THE LIPOSORBER LA-15 SYSTEM FSGS	Page 5, 6	your doctor is currently treating you with a medication called an angiotensin-converting-enzyme (ACE) inhibitor and believes that this medication cannot be stopped for at least a day before each treatment with the LIPOSORBER®.	your doctor is currently treating you with a medication called an angiotensin-converting-enzyme (ACE) inhibitor and believes that this medication cannot be stopped.

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Appendix C: All Affected Product Identification Codes

Liposorber Disposables

Product Number	Product Description	Lot #	Expiry Date
101785	**LA-15 (AU) LDL Adsorption Column (Luer Lock Type)**	LAP1498	02/28/22
		LAP1505	06/28/22
		LAP1509	07/28/22
		LAP1510	07/28/22
		LAP1523	09/28/22
		LAP1526	10/28/22
		LAP1527	10/28/22
		LAP1533	12/28/22
		LAP1534	12/28/22
		LAP1535	12/28/22
		LAP1536	12/28/22
		LAP1538	02/28/23
		LAP1543	07/31/23
		LAP1544	07/31/23
		LAP1547	09/30/23
		LAP1554	10/31/23
		LAP1555	10/31/23
		LAP1556	10/31/23
		LAP1558	11/30/23
		LAP1561	12/31/23
		LAP1568	02/29/24
		LAP1569	02/29/24
		LAP1578	06/30/24
		LAP1580	06/30/24
		LAP1581	07/31/24
		LAP1582	07/31/24
		LAP1585	07/31/24
		LAP1587	08/31/24
		LAP1588	08/31/24
		LAP1598	10/28/24
		LAP1599	10/28/24
		LAP1607	06/28/25
		LAP1609	09/28/25
		LAP1611	09/28/25

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Product Number	Product Description	Lot #	Expiry Date
101447	KP-05 Sulflux Plasma Separator	TJ3Z3K	03/18/22
		TJ5K5U	05/27/22
		TJ7X7J	07/17/22
		XJXNY1	10/30/22
		XK1X1L	01/19/23
		XK2H2R	02/24/23
		XK4S5E	05/14/23
		XK5K5T	05/27/23
		XK8R92	09/01/23
		XKXAXL	10/20/23
		FKZXZH	12/17/23
		FL1A1K	01/19/24
		FL3N42	03/31/24
		FL3P43	04/01/24
101786	NK-M3R(UL) Tubing (Luer Lock Type)	200210	01/28/23
		200302	02/28/22
		200401	03/28/22
		200502	04/28/22
		200528	04/28/22
		200624	05/31/22
		200720	06/30/22
		200813	07/31/22
		200907	08/31/22
		201005	09/30/22
		201105	10/28/22
		210222	01/28/23
		210301	02/28/23
101788	HDE LA-15(AU) LDL Adsorption Column (Luer Lock Type)	LAP1510	07/28/22
		LAP1526	10/28/22
		LAP1527	10/28/22
		LAP1535	12/28/22
		LAP1544	07/31/23
		LAP1547	09/30/23
		LAP1555	10/31/23
		LAP1558	11/30/23
		LAP1580	06/30/24
		LAP1585	07/31/24
		LAP1598	10/28/24
		LAP1599	10/28/24

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Product Number	Product Description	Lot #	Expiry Date
101473	HDE KP-05 Sulflux Plasma Separator	TJ3Z3K	03/18/22
		TJ7X7J	07/17/22
		XK1X1L	01/19/23
		XK2H2R	02/24/23
		XK5K5T	05/27/23
		XKXAXL	10/20/23
		FL1A1K	01/19/24
101789	HDE NK-M3R(UL) Tubing (Luer Lock Type)	200302	02/28/22
		200624	05/31/22
		200907	08/31/22
		201005	09/30/22
		210222	01/31/23

MA-03 Machines

Product Number	Product Description	SN #	Expiry Date
There 138 systems in distribution in US			
101445	MA-03 Machines	68007-01	NA
		68007-03	
		68007-04	
		68008-01	
		68008-02	
		68008-03	
		68008-04	
		68008-05	
		69005-01	
		69005-02	
		69005-03	
		69005-04	
		69005-05	
		69006-04	
		70013-01	
		70013-04	
		70014-02	
		70014-03	
		70014-04	
		70014-05	
		70015-03	
		70015-04	

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Product Number	Product Description	SN #	Expiry Date
101445	MA-03 Machines	70015-05	NA
		70016-01	
		70016-03	
		70016-04	
		70016-05	
		70017-04	
		70017-05	
		70018-02	
		70018-03	
		70018-05	
		71001-01	
		71001-02	
		71001-03	
		71002-01	
		71002-02	
		71002-05	
		71003-01	
		71003-02	
		71003-03	
		71003-04	
		71004-01	
		71004-02	
		71004-03	
		71004-04	
		71005-03	
		71005-04	
		71005-05	
		71006-01	
		71006-04	
		71006-05	
		71007-01	
		71007-02	
		71007-03	
		71007-04	
		71008-01	
		71008-02	
		71008-03	
		71008-05	
		72001-01	

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Product Number	Product Description	SN #	Expiry Date
101445	MA-03 Machines	72001-02	NA
		72001-03	
		72001-04	
		72001-05	
		72002-01	
		72002-02	
		72002-04	
		72002-05	
		72003-01	
		72003-02	
		72003-03	
		72003-04	
		72003-05	
		72004-02	
		72004-03	
		72004-04	
		72004-05	
		72005-01	
		72005-02	
		72005-03	
		72005-04	
		72005-05	
		72006-01	
		72006-02	
		72006-03	
		72006-04	
		72006-05	
		J1412335	
		J1412337	
		J1412338	
		J1412339	
		J1412615	
		J1412616	
		J1412617	
		J1412618	
		J1412619	
		J1501052	
		J1501053	
		J1501054	

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Product Number	Product Description	SN #	Expiry Date
100445	MA-03 Machines	J1501055	NA
		J1501056	
		J1501359	
		J1501360	
		J1501361	
		J1501362	
		J1501363	
		J1501676	
		J1501677	
		J1501678	
		J1501679	
		J1501680	
		J1501959	
		J1501961	
		J1501962	
		J1501963	
		J1502233	
		J1502236	
		J1502237	
		J1502501	
		J1502502	
		J1502504	
		J1502505	
		J1804799	
		J1804800	
		J1804801	
		J1804802	
		J1804803	
		J1804804	
		J1804805	
		J1804806	
		J1804807	
		J1804808	
		J1914653	
		J1914654	
		J1914655	
		J1914656	
		J1914657	