kaneka

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LIPOSORBER®

LIPOSORBER® Provides Hope...
When Drug Therapy Fails™

NEW LIPOSORBER® INDICATION

GETTING YOUR FH PATIENTS TO
RECOMMENDED THERAPEUTIC TARGETS
IS POSSIBLE WITH LIPOSORBER®

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HOPE WITH LIPOSORBER®

There is hope with LIPOSORBER® for your familial hypercholesterolemia patients with established Coronary Artery Disease (CAD) or Peripheral Artery Disease (PAD) when diet and maximum drug therapies have failed to achieve the recommended therapeutic targets.

LIPOSORBER® is shown to acutely reduce Atherogenic lipoproteins (LDL–C) and Lipoprotein(a) [Lp(a)].

EXPANDED INDICATION

NEW LIPOSORBER® INDICATION

LIPOSORBER® is indicated for use in clinically diagnosed Familial Hypercholesterolemic patients with either documented Coronary Artery Disease (CAD)* or Peripheral Artery Disease (PAD)†, if:

- **LDL-C ≥100 mg/dl**

OR

- NEW **Lp(a)≥60 mg/dl and LDL-C≥100 mg/dl**

And diet and maximum tolerable combination lipid-lowering drug therapies have failed to achieve the established therapeutic targets per professional guidelines.

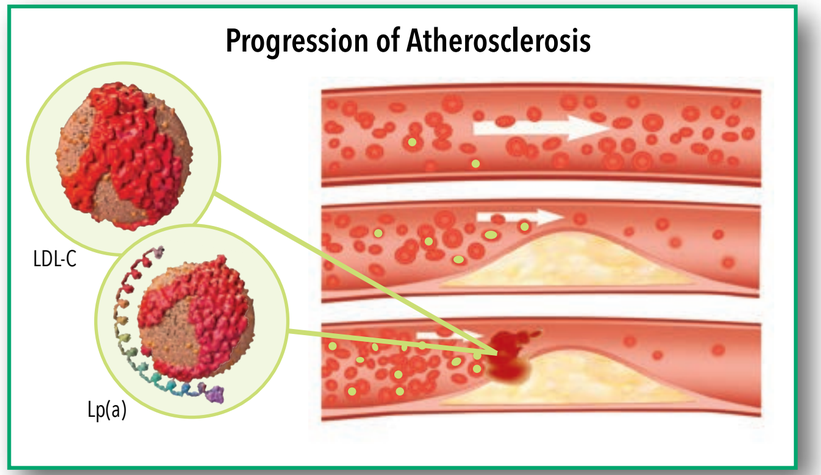
***Documented CAD**: Diagnosed by: - Invasive OR CT Coronary Angiography; Electron Beam CT (EBCT); History of: Myocardial Infarction, Percutaneous Coronary Intervention, Coronary Artery Bypass Grafting

† Documented PAD: Diagnosed by: - Symptoms and/or Physician exam; Ankle-Brachial Index (ABI); Ultrasound Exam; Pulse Volume Recording (PVR); Peripheral Vascular Angiography; History of: Peripheral Vascular Intervention/Peripheral Vascular bypass surgery/minor or major amputation. (Reference: FDA Approval/IFU 4.21.2020)

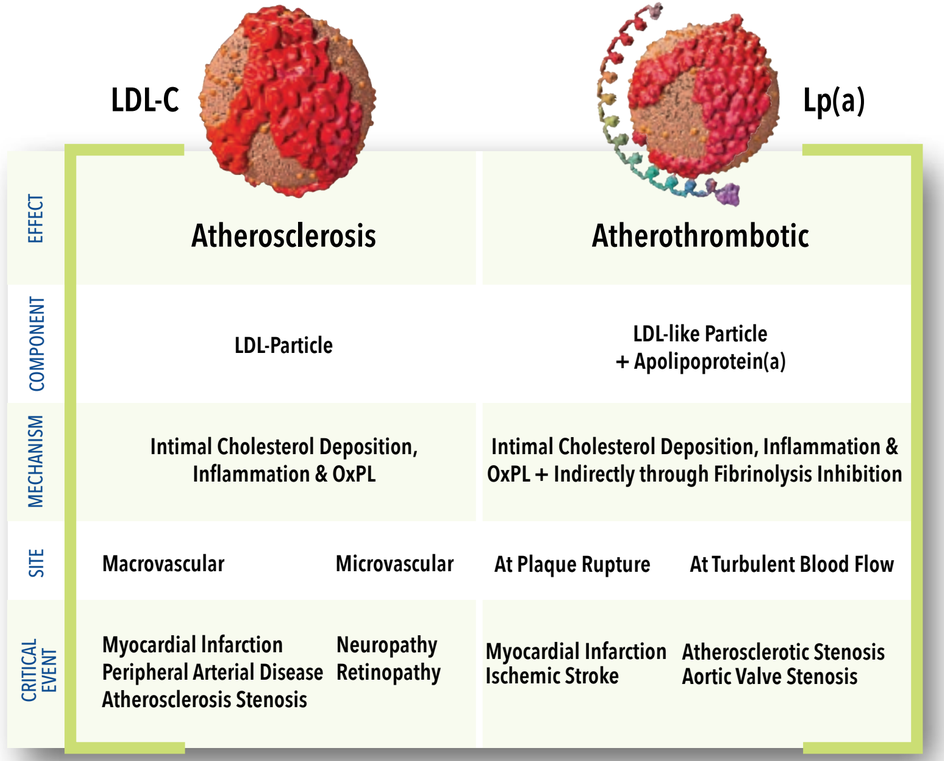
THE DISEASE BURDEN
Facts and Statistics

Atherosclerosis and Artery Stenosis are driven by high LDL-C and/or Lp(a). They are major underlying causes of Coronary Artery Disease (CAD).

Coronary artery disease is characterized by chronic progressive changes in the blood vessel walls. These changes are influenced by various independent risk factors for atherosclerosis development, including increased Lp(a) and LDL-C.



LDL-C and Lipoprotein(a)
A Dual Threat



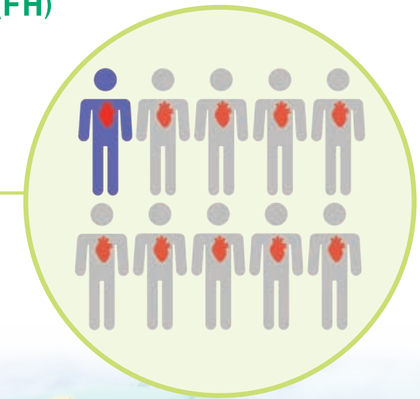
Reference: Wilson DP, Jacobson TA, et al. Use of Lipoprotein(a) in clinical practice: A biomarker whose time has come. A scientific statement from the National Lipid Association. J Clin Lipidol. 2019;13(3):374-392. p.4. doi:10.1016/j.jacl.2019.04.010

FAMILIAL HYPERCHOLESTEROLEMIA (FH)

Challenges and Unmet Needs

An estimated **1 in 250** Americans have FH; however,

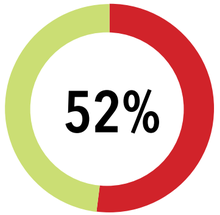
90% have not been accurately diagnosed.*



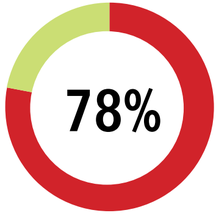
FH PATIENTS need to be on a THERAPEUTIC TRACK.

Reference: FH Foundation; https://thefhfoundation.org

Untreated FH patients have **20 times** the risk of developing coronary artery disease, compared with the general population.



Did NOT achieve LDL-C <100 mg/dL

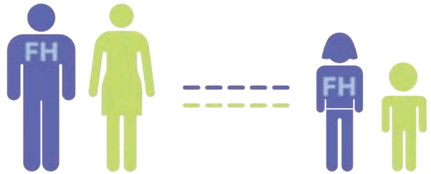


Did NOT achieve LDL-C <70 mg/dL

Unfortunately, the **majority of FH individuals may not be achieving the LDL-C therapeutic targets.**

52% of FH individuals did not achieve LDL-C<100mg/dl. 78% of FH individuals did not achieve LDL-C<70mg/dl despite 2/3 of patients taking two or three lipid-lowering therapies.

Each child of a person with FH has a **50% chance of inheriting** the disorder.



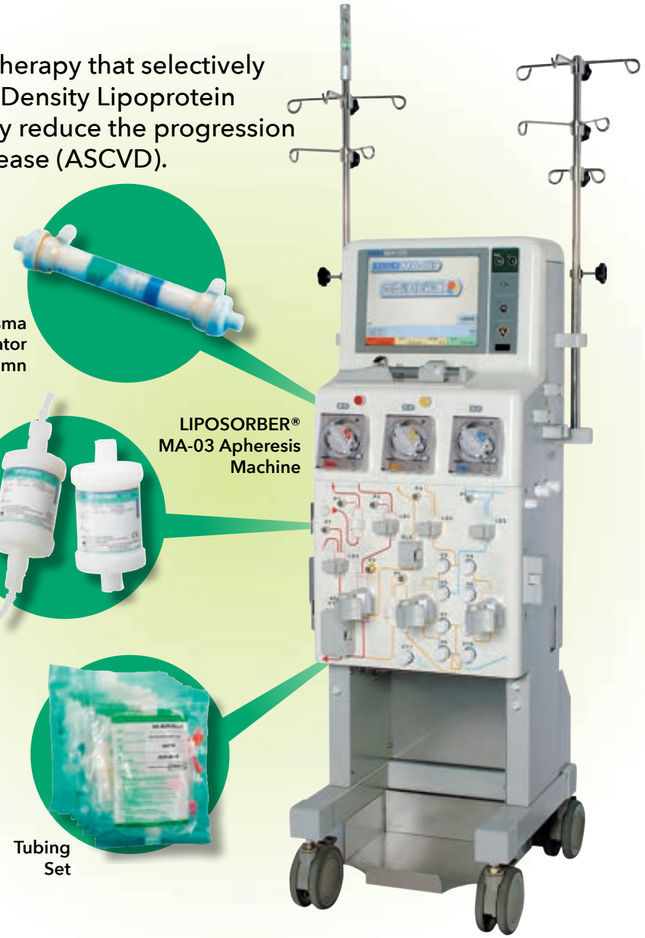
Therefore, it becomes essential to screen parents, siblings and children of a person diagnosed with FH.

Reference: Duell,PB et al. Atherosclerosis, Volume 289, 85-93 2019
Knowles JW, O'Brien EC, Greendale K, et al. Reducing the burden of disease and death from familial hypercholesterolemia: a call to action. Am Heart J. 2014;168(6):807-811. doi:10.1016/j.ahj.2014.09.001

ABOUT LIPOSORBER®

LIPOSORBER® is an extracorporeal therapy that selectively removes LDL-C, Lp(a), and Very Low Density Lipoprotein (VLDL) from the blood to significantly reduce the progression of atherosclerotic cardiovascular disease (ASCVD).

The LIPOSORBER® System

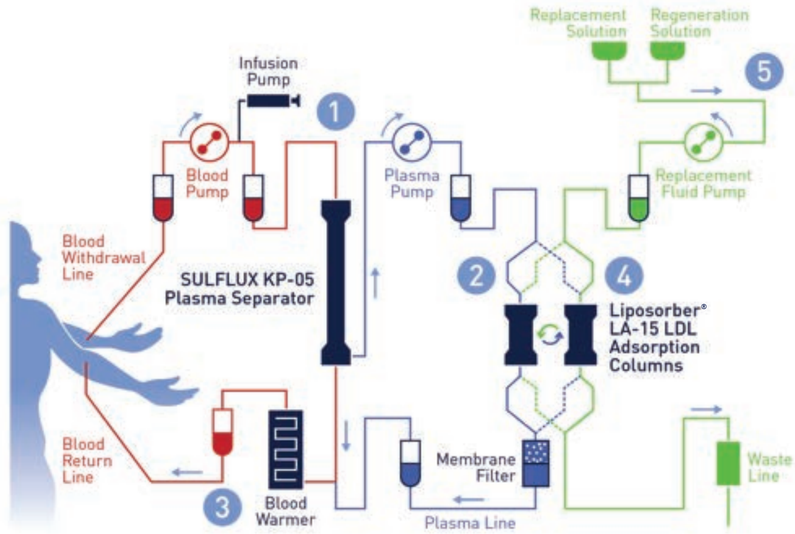


TREATMENT FREQUENCY

Patient LDL-C Level	Regimen
≥300mg/dL	1 Session Every Week
100-200 mg/dL	1 Session Every 2 Weeks
Lp(a)≥60mg/dL & LDL-C≥100mg/dL	1 Session Every 2 Weeks

HOW LIPOSORBER® WORKS

Each treatment lasts 2-4 hours on average.



Blood Line:
Takes blood out, puts blood back in

Plasma Line:
Moves separated plasma and removes LDL, Lp(a) and VLDL using Liposorber® LDL Adsorption Columns

Regeneration Line:
Prepares primary and secondary adsorption columns for the next cycle and eliminates waste to allow for continuous treatment

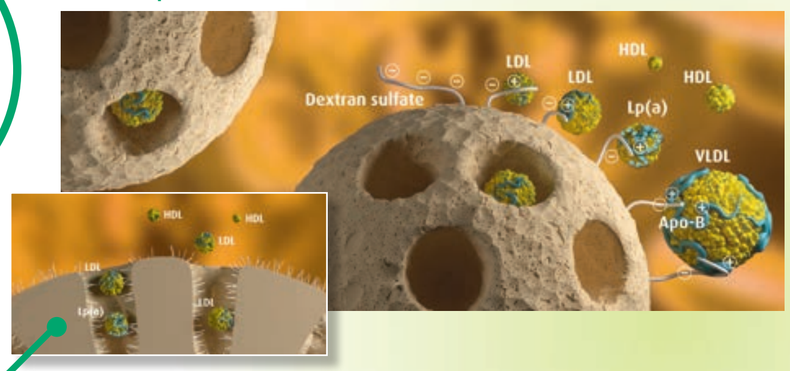
1. Blood is withdrawn and goes through the plasma separator.
2. Plasma passes through the LIPOSORBER® Adsorption Column, selectively removing LDL, Lp(a) and VLDL.
3. Plasma is recombined with blood cells and returns to the blood warmer, then is returned to the patient.
4. When the primary LIPOSORBER® Adsorption Column processes certain amounts of blood, the computer-regulated machine automatically switches the plasma flow to the secondary column.
5. The primary column is regenerated, eluting waste and re-primed to be ready for the next adsorption cycle.

Reference: LA-15 SYSTEM Operator's Manual No.870en-R7

SELECTIVITY FEATURE

LIPOSORBER® selectively removes LDL-C, Lp(a), and VLDL

The Principle of the LIPOSORBER® LA-15



The adsorbent columns are made of dextran sulfate cellulose beads, which provides specific binding to Apo-B containing lipoproteins such as **LDL-C, Lp(a), and VLDL.**

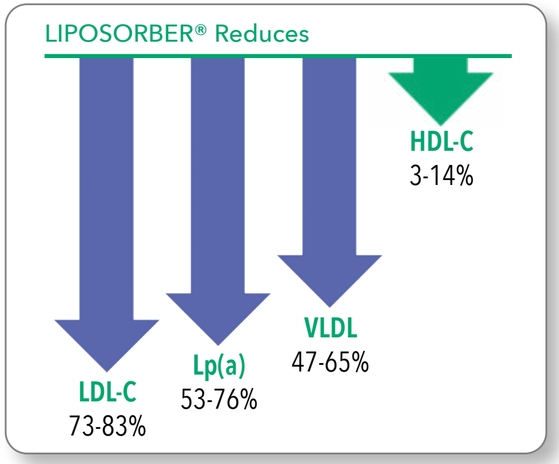
These three are **selectively removed** by the electro-static interaction between the negatively charged dextran sulfate and the positively charged moiety of Apo-B. Unlike therapeutic plasma exchange (TPE), LIPOSORBER® minimally affects other blood components.

Reference: Palcoux et al., 2008, Therapeutic Apher Dial; 12(3):195-201; Hudgins et al., 2008, American Journal of Cardiology; 102(9):1199-1204; Koga 1999, Therapeutic Apheresis; 3(2): 155-160; Gordon et al., 1998, American Journal of Cardiology; 81(4): 407-411; Parker, 1994, Chem Phys Lipids; 67-68, 331-338
Yokoyama S. et al. Arteriosclerosis. 1985 Nov-Dec;5(6):613-22.
Rubba S et al. Circulation. 1990 Feb;81(2):610-6.

LIPOSORBER® EFFICACY PROFILE

LIPOSORBER® Acutely Reduces Atherogenic Lipoproteins

The system effectively removes harmful atherogenic lipoproteins such as Apo-B containing lipoprotein (Lp(a), LDL-C, and VLDL) associated with serious cardio-vascular disease and vascular complications in familial hypercholesterolemia patients.

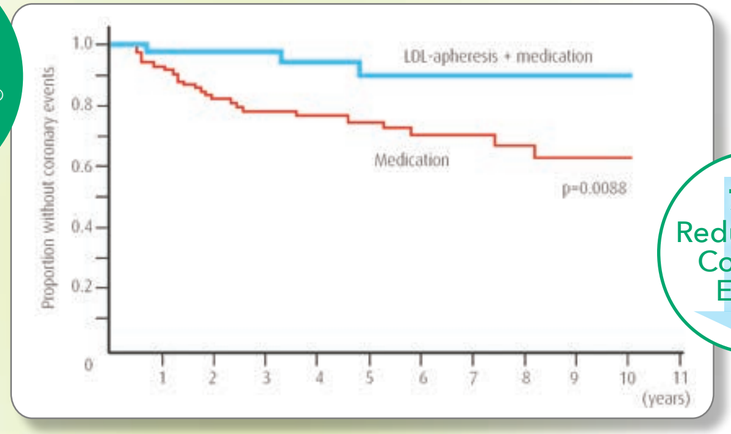


Reference: Gorden et al,;1998, American Journal of Cardiology; 81(4):407-411
Kaneka. (2021) LIPOSORBER® LA-15 System: Operator's Manual. New York, NY: Kaneka Medical America, LLC.

LIPOSORBER® CLINICAL OUTCOMES

Long-term efficacy of low-density lipoprotein-apheresis (LA) on coronary heart disease in familial hypercholesterolemia (FH) was studied. Investigators examined long-term efficacy and safety of LA in heterozygotes familial hypercholesterolemia (HeFH) patients with history of CHD. LA was shown to be an effective & well tolerated treatment for HeFH: 58% acute reduction in LDL-C levels and 72% reduction in total coronary events.

Long Term Efficacy of **LIPOSORBER®**



72% Reduction in Coronary Events

Referece: Mabuchi et al., 1998, American Journal Of Cardiology; 82(12):1489-1495

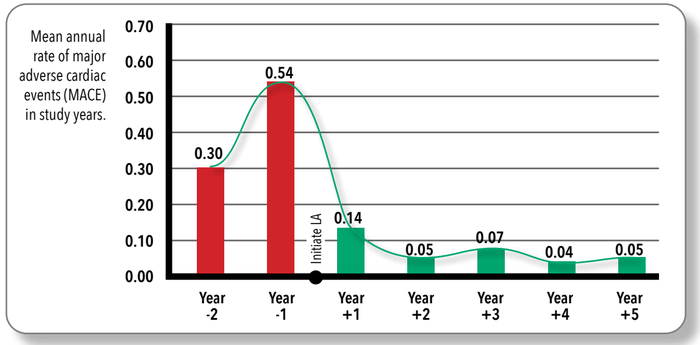
Pro(a)–LIFE STUDY

LIPOPROTEIN-APHERESIS & Lp(a) Patients

The aim of Pro(a)-Life was to assess the efficacy of lipid-apheresis in high-risk patients with elevated Lp(a) >60 mg/dl and progressive cardiovascular disease. The study evaluated the event rates for major adverse coronary events (MACE) and adverse cardiac or vascular events (ACVE) with prospective five years of follow-up, and demonstrated:

- **After 2 years Lp(a) significantly reduced by 68.8± 9.5% & LDL-C by 67.2±10.2% (p<0.0001).**
- **MACE was reduced annually by 78% (p<0.0001) NNT=3 after 2 years & reduced 81% annually after 5 years from initiating LA.**

Clinical Course of Patients with Lipoprotein(a)-Hyperlipoproteinemia and Progressive Cardiovascular Disease



LA is an effective & well tolerated therapeutic tool that significantly reduces cardiovascular events in FH patients who have progressive cardiovascular diseases with elevated Lp(a) ≥60mg/dl.

LIPOSORBER® is indicated in FH patients with cardiovascular disease and Lp(a) ≥60 mg/dl and LDL-C >100 mg/dl.

Reference: - E.Roseler et. al, 2016, Arteriosclerosis Thromb Vasc. Biol.; 36:2019-2027
J.Leepman et al., 2013, Circulation;128: 2567-2576)

LIPOSORBER®: CLINICAL BENEFITS ASSOCIATED WITH LIPID LOWERING

LACMART Study:

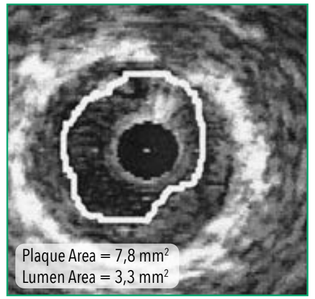
The Low Density **L**ipoprotein-**A**pheresis **C**oronary **M**orphology **A**nd **R**eserve **T**rial

Aggressive lipid lowering therapy by using LIPOSORBER® with maximum tolerable drug therapies **stops progression of coronary atherosclerosis in FH patients.**

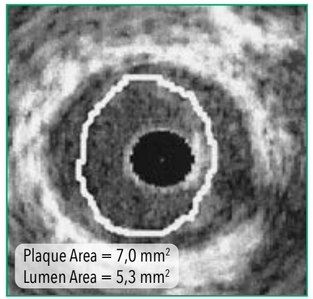
Achieve the recommended **THERAPEUTIC TARGET**

IVUS Imaging

Baseline LAD #8



Follow-Up LAD #8



Matzusaki et al. (LACMART) and Tatami et al demonstrated that an aggressive lipid-lowering therapy by applying lipoprotein-apheresis in combination with lipid-lowering drugs induced (coronary) atherosclerotic plaque regression in FH patients.*

Change in Parameters from Coronary Angiogram and IVUS

	LDL-A Group			Medication Group			
	Baseline	Follow-Up	Net Change	Baseline	Follow-Up	Net Change	p Value*
MLD (mm)	1.99 ± 0.73	2.11 ± 0.81	0.12	2.24 ± 0.89	2.16 ± 0.84	−0.08	0.008
Plaque area (mm^2)	8.45 ± 4.22	7.76 ± 4.34	−0.69	7.19 ± 2.88	8.08 ± 3.14	0.88	0.017
Lumen area (mm^2)	9.84 ± 5.43	9.87 ± 5.55	0.03	9.13 ± 4.33	8.63 ± 3.18	−0.51	0.52
Vessel area (mm^2)	18.29 ± 8.84	17.63 ± 9.05	−0.66	16.4 ± 5.63	19.0 ± 4.36	0.3	0.26

Data presented are mean value SD. *Data obtained from two-way repeated-measures analysis of variance.
IVUS intravascular ultrasound; LDL-A low density lipoprotein-apheresis; MLD minimal lumen diameter.

Reference: M. Matsuzaki et al, 2002, Journal of American College of Cardiology; 40(2):220-7.

SAFETY PROFILE

LIPOSORBER® LA-15 received FDA approval in 1996. It has been in worldwide use since 1986 with more than 600,000 LIPOSORBER® treatments performed on over 6,000 patients. Typically, the adverse events associated with LIPOSORBER® treatment are those observed in any procedure involving the circulation of blood outside the body.

FDA Approved since 1996.

Performed on over 6,000 patients.

ADVERSE EVENTS

The most common adverse events are hypotension (0.8%), nausea/vomiting (0.5%), and flushing/blotching (0.4%). Other adverse reactions include angina/chest pain, fainting, light-headedness and anemia.

*Please see **www.liposorber.com** for a full list of adverse events.

CONTRAINDICATION

Angiotensin converting enzyme [ACEI(s)] inhibitors are contraindicated with LIPOSORBER® due to possible bradykinin reaction. ACE Is should be replaced with angiotensin II receptor blockers (ARBs) or any other antihypertensive agent – as determined by the prescribing physician.

For additional contraindications and complete safety information please visit https://bit.ly/31UDfnC

References: Palcoux et al., 2008, Therapeutic Apher Dial; 12(3):195-201
Hudgins et al., 2008, American Journal of Cardiology; 102(9):1199-1204
Koga 1999, Therapeutic Apheresis; 3(2): 155-160

References: Elico et al., 1997, Artificial Organs; 21(4): 334-5
Sinzinger et al., 2000, Thromb Res; 100(1):43-6
Kojima et al., 1997, Hypertension Res; 24(5): 595-98

HOW LIPOSORBER® CAN BENEFIT YOUR PRACTICE

Use LIPOSORBER® to attain the recommend therapeutic target for your familial hypercholesterolemia patients with elevated Lp(a).

Offer a comprehensive lipid-lowering treatment line to your practice.

Practice benefits include:

- Comprehensive lipid lowering service
- Insurance coverage by Medicare and most commercial insurers
- User-friendly automated continuous-flow system
- Usable in hospital outpatient or physician office-based setting

Our services for starting a program:

- Clinical staff training
- Nurse hotline support
- Technical support
- Educational awareness initiatives, seminars, and grand rounds.

If you're interested in **starting a lipoprotein-apheresis program** in your area or need help referring a patient for treatment, please contact us at **800-526-3522** or info@liposorber.com

LIPOSORBER® Provides Hope... When Drug Therapy Fails™

Consider **LIPOSORBER®** for your FH patients with elevated Lp(a) levels when drug therapies (statins, PCSK9is) fail to achieve the recommended therapeutic targets per established clinical guidelines.