Lipid Apheresis using Plasma Fractionator Evaflux™

For patients with hyperlipidemia refractory to conventional drug therapy

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**What is Familial Hypercholesterolemia (“FH”)?**

“FH” is an autosomal dominantly-inherited disease due to a congenital absence of low-density lipoprotein receptor (LDL-R), that transports cholesterol-carrying lipoprotein particles into cells. A congenital absence of LDL-R results clinically in elevated concentrations of plasma LDL and cholesterol.

**Common clinical signs of “FH”**

1. Hypercholesterolemia
2. Tendon Xanthoma
3. Coronary Artery Disease

The patients with “FH” develop atherosclerosis at a young age due to the inefficient uptake of LDL by the liver and the denatured LDL which is deposited in blood vessel tissues. In case of the patients with homozygous “FH”, the early diagnosis and the treatment to lower LDL levels and treat other coronary risk factors are very important because they are prone to premature atherosclerosis.

**General treatment for “FH”**

Restriction of calorie, lipid or cholesterol intake etc.

Fibrates, HMG-CoA reductase inhibitor, cholestyramine, probucol, Ezetimibe etc.

Some patients with “FH” do not respond to diet and drug therapy. For them, LDL apheresis becomes a feasible and effective option.

**When should LDL apheresis commence?**

<table>
<thead>
<tr>
<th>Homozygous FH</th>
<th>Heterozygous FH</th>
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<tbody>
<tr>
<td>Pattern of Inheritance</td>
<td>Inheritance of the abnormal gene from both parents</td>
</tr>
<tr>
<td>Serum LDL-Cholesterol Levels</td>
<td>450–1,000 mg/dL</td>
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<tr>
<td>Frequency</td>
<td>Approx. 1 case per 1 million persons</td>
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</tbody>
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**FDA**
- Functional **Homozygotes** with LDL >500 mg/dL
- Functional **Heterozygotes** with no known cardiovascular disease but LDL ≥ 300 mg/dL
- Functional **Heterozygotes** with known cardiovascular disease and LDL ≥ 200 mg/dL

**Germany**
- **FH Homozygotes**
- Patients with severe hypercholesterolemia with whom maximal dietary and drug therapy for >1 year has failed to lower cholesterol sufficiently

**UK**
- For patients who have failed prior treatment plans consisting of diet therapy and maximum drug therapy for at least 6 months
  - **FH Homozygotes** in whom LDL is reduced by <50% and/or >9 mol/L [348 mg/dL] with drug therapy
  - **FH Heterozygotes** or a “bad family history” with objective evidence of coronary disease progression and LDL >5.0 mmol/L [193 mg/dL] or decreases by <40% despite drug therapy
  - Progressive coronary artery disease, severe hypercholesterolemia, and Lp(a) >60 mg/dL in whom LDL remains elevated despite drug therapy

**Spain**
- **FH Homozygotes**
- **Heterozygotes** with symptomatic coronary artery disease in whom LDL is >4.2 mmol/L [162 mg/dL] or decreases by <40% despite maximal medical management

*Journal of Clinical Apheresis: Therapeutic Apheresis—Guidelines 2010*
**Double / Cascade Filtration Plasmapheresis**

Double/ Cascade Filtration plasmapheresis is one of the LDL apheresis methods with the following principle.

*Therapeutic Apheresis 4 (1):29-33, 2000

![Flow Diagram of Double Filtration Plasmapheresis with Evaflux 5A](image1)

![Flow Diagram of Cascade Filtration (CF) with Evaflux 5A](image2)

![Flow Diagram of Thermo DFPP with Evaflux 5A](image3)

Plasma is warmed before being passed through Evaflux. Warming of the plasma would lower the plasma viscosity and sustain permeability of membrane.

![Flow Diagram of Cascade Filtration (CF) with Evaflux 5A](image4)
Performance of DFPP

It is reported that DFPP using Evaflux 5A achieved the high removal rate of LDL, Lp(a) and fibrinogen, which are considered as the risk factors for arteriosclerosis.

Removal rate of risk factors

Total cholesterol, LDL, Lp(a), and fibrinogen were removed by 60-80% after each session of DFPP treatment.

Fig 2: Sieving Coefficient of "Evaflux" (When 1,000 ml of plasma was processed)

- Evaflux 5A can remove LDL while allowing Albumin and HDL to be returned to the patient.
- Removal of high molecular weight proteins would contribute to the improvement of microcirculation.
- As Evaflux 5A returns most Albumin to the patient, it is rarely necessary to substitute Albumin during the procedure.

Fig 3: Removal Rate of Evaflux 5A (When 4,000 ml of plasma was processed)

Each patient was treated with DFPP at 2 weeks intervals for more than 3 years.

DFPP treatment lowers the risk factors and prevents the progression of atherosclerosis.

*Therapeutic Apheresis 2(3):224-227, 1998