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**EPAR summary for the public**

# Flebogamma DIF[1]

human normal immunoglobulin

This is a summary of the European public assessment report (EPAR) for Flebogamma DIF. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Flebogamma DIF.

## What is Flebogamma DIF?

Flebogamma DIF is a solution for infusion (drip into a vein). It contains the active substance human normal immunoglobulin.

## What is Flebogamma DIF used for?

Flebogamma DIF is used in patients who need more antibodies in their blood to help fight infections and other diseases. It is used to treat the following conditions:

- Primary immunodeficiency syndromes (PID, when people are born with an inability to produce enough antibodies).
- Hypogammaglobulinaemia (low levels of antibodies) in patients:
  - with chronic lymphocytic leukaemia (a cancer of a type of white blood cell) and frequent bacterial infections after preventive treatment with antibiotics has failed;
  - with multiple myeloma (another cancer of a type of white blood cell) and frequent bacterial infections and in whom vaccination against 'pneumococcal' bacteria has failed;
  - who have had haematopoietic (blood) stem cell transplantation (when the patient receives stem cells from a matched donor to help restore the bone marrow).

[1] Previously known as Flebogammadif

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- Acquired immune deficiency syndrome (AIDS) in children who contracted HIV from birth and have frequent infections.

Flebogamma DIF is also used to treat certain immune system disorders:

- Idiopathic thrombocytopenic purpura (ITP), a condition where people do not have enough platelets in the blood;
- Guillain-Barré syndrome, which causes multiple inflammations of the nerves in the body;
- Kawasaki disease, which causes multiple inflammations of several organs in the body.

The medicine can only be obtained with a prescription.

## How is Flebogamma DIF used?

Flebogamma DIF is given by infusion into a vein by a doctor or nurse, but patients (or their carers) may administer it themselves once they have been trained. The dose and frequency of infusion depend on the disease being treated, and may need to be adjusted for patients depending on their response. For full details, see the summary of product characteristics (also part of the EPAR).

## How does Flebogamma DIF work?

The active substance in Flebogamma DIF, human normal immunoglobulin, is a highly purified protein extracted from human plasma (part of the blood). It contains immunoglobulin G (IgG), which is a type of antibody. IgG has been used as a medicine since the 1980s and has a wide range of activity against organisms that can cause infection. Flebogamma DIF works by restoring abnormally low IgG levels to their normal range in the blood. At higher doses, it can help to adjust an abnormal immune system and modulate the immune response.

Flebogamma DIF is made like Flebogamma, another medicine containing human normal immunoglobulin, with some additional steps in the purification of the product from human plasma.

## How has Flebogamma DIF been studied?

As human normal immunoglobulin has been used to treat these diseases for some time, only two small studies were needed to establish the effectiveness and safety of Flebogamma DIF in patients.

In the first study, involving 46 patients with PID, the medicine was infused every 21 to 28 days. The main measure of effectiveness was the number of serious bacterial infections over a year's treatment.

The second study looked at using Flebogamma DIF in 20 patients with ITP. The main measure of effectiveness was the highest blood platelet level that was achieved during the three-month study.

Flebogamma DIF was not compared with any other treatment in either study.

## What benefit has Flebogamma DIF shown during the studies?

In the first study, the patients had an average of 0.021 serious infections per year. Since this is below the predefined threshold of one infection per year, this indicates that the medicine is effective in replacing the patient's antibodies.

In the second study, up to 14 (73%) of the 19 patients who remained in the study had a platelet count above 50 million platelets per millilitre at least once during the study.

## What is the risk associated with Flebogamma DIF?

Side effects such as chills, headache, dizziness, fever, vomiting, allergic reactions, nausea, arthralgia (joint pain), low blood pressure and moderate low back pain may occasionally occur with Flebogamma DIF. Rarely human normal immunoglobulins may cause a sudden fall in blood pressure and, in a few cases, anaphylactic shock (a severe allergic reaction) even when the patient had no previous allergic reaction to the medicine.

Flebogamma DIF must not be used in people who are allergic to normal human immunoglobulin or any of the other ingredients, or in patients who are allergic to other types of immunoglobulin, especially where they have deficiency (very low levels) of immunoglobulin A (IgA) and they have antibodies against IgA. The medicine must not be used in patients who are intolerant to fructose (a type of sugar). In babies and young children, hereditary fructose intolerance may not yet have been diagnosed and may be fatal; this medicine must therefore not be given to babies and children below two years of age.

## Why has Flebogamma DIF been approved?

According to current guidelines, medicines that have been shown to be effective in patients with PID and in patients with ITP can also be approved for use in the treatment of all types of primary immunodeficiency, as well as low antibody levels due to blood cancers and AIDS in children. They can also be approved for the treatment of patients with Guillain-Barré syndrome, patients with Kawasaki disease and patients undergoing haematopoietic stem cell transplantation, without the need for specific studies in these diseases.

Therefore, the CHMP concluded that Flebogamma DIF's benefits are greater than its risks and recommended that it be given marketing authorisation.

## Other information about Flebogamma DIF

The European Commission granted a marketing authorisation valid throughout the European Union for Flebogammadif on 23 August 2007. The name of the medicine was changed to Flebogamma DIF on 2 September 2010.

The full EPAR for Flebogamma DIF can be found on the Agency's website ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Flebogamma DIF, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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