

# Aragam

## PACKAGE LEAFLET: INFORMATION FOR THE USER

### Aragam 50 mg/ml solution for infusion

Human normal immunoglobulin

#### Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

#### In this leaflet:

1. What Aragam is and what it is used for
2. Before you use Aragam
3. How to use Aragam
4. Possible side effects
5. How to store Aragam
6. Further information

### 1. WHAT ARAGAM IS AND WHAT IT IS USED FOR

Aragam is a solution for infusion which contains the human protein immunoglobulin. Immunoglobulins are antibodies and normal constituents of human blood and they protect you from infections. Aragam is used to raise antibody levels in your blood when the antibody level is too low or if you need additional antibodies in certain diseases. The administration of antibodies can also have an effect in case of a disrupted immune system.

#### Aragam is used for:

**Replacement therapy** (treatment of patients who do not have sufficient antibodies) in adults, and children and adolescents (0-18 years) in:

- Primary immunodeficiency syndromes (diseases which are caused by a hereditary disorder of the immune system) with impaired antibody production.
  - Hypogammaglobulinemia (complete or partial lack of the immune response caused by a complete or partial deficit of antibodies) and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (malignant bleeding disorder), in whom prophylactic antibiotics have failed.
  - Hypogammaglobulinemia and recurrent bacterial infections in plateau phase multiple myeloma (malignant bone marrow tumour) patients who have failed to respond to pneumococcal immunisation.
  - Hypogammaglobulinemia in patients after allogeneic haematopoietic stem cell transplantation (HSCT).
  - Congenital AIDS with recurrent bacterial infections.

**Immunomodulation** (influencing a disrupted immune system) in adults, and children and adolescents (0-18 years) in:

- Primary immune thrombocytopenia (ITP, a bleeding disorder caused by a reduced number of platelets), in patients at risk of bleeding or prior to surgery to correct the platelet count.
- Guillain Barré syndrome (this is a syndrome of unknown cause at which muscle paralysis occur).
- Kawasaki disease (a very rare disease in children with defects of the skin, mucous membrane, blood vessels of the brain and coronary arteries).

### 2. BEFORE YOU USE ARAGAM

#### Do not use Aragam

- if you are allergic (hypersensitive) to immunoglobulins or any of the other ingredients of Aragam.
- if you have immunoglobulin A (IgA) deficiency with antibodies against IgA. Aragam contains a small amount of IgA which might cause an allergic reaction.

If an allergic reaction occurs, administration of Aragam should be discontinued immediately.

#### Take special care with Aragam

You will be observed carefully during the infusion period to detect potential adverse reactions (unwanted side effects). Certain adverse reactions may be related to the rate of infusion, therefore your doctor makes sure that the infusion rate is suitable for you. If you experience a reaction during infusion, tell your doctor immediately. The doctor will decide if the infusion will be discontinued.

Certain adverse reactions may occur more frequently:

- in case of high rate of infusion.
- if you have hypo- or agammaglobulinemia (a complete or partial lack of antibodies) with or without IgA deficiency.
- if you receive Aragam for the first time.
- in rare cases, when the human normal immunoglobulin product is replaced by another product or there has been a long interval since the previous infusion.

#### Risk factors during treatment with Aragam

Please tell your doctor if any of the following factors concerns you, since these might be risk factors during the treatment with Aragam. In particular, tell your doctor if you have:

- renal insufficiency (when your kidneys are not working well).
- nephrotoxic (toxic for the kidney) medication.

- diabetes (abnormally high glucose levels in the blood)
- history of vascular (blood vessel) diseases or thrombosis (formation of a clot inside a blood vessel).
- hypertension.
- overweight.
- diseases which increase blood viscosity (thickness of the blood).
- hypovolemia (a decrease in circulating blood volume).
- advanced age (over 65).

#### While using Aragam the following should be taken into account

- adequate hydration before infusion of Aragam.
- follow-up of urine output.
- follow-up of serum creatinine levels (a substance which is an indicator of the activity of the kidneys).
- avoiding concomitant use of certain diuretics (so called loop diuretics).

#### Effects on blood tests

If you will have blood tests taken, please tell your doctor that you are using Aragam, since Aragam contains antibodies and this may result in misleading positive results in antibody tests.

#### Using other medicines

- Do not mix Aragam with other medicinal products.
- Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

#### Vaccination

Tell your doctor if you have planned to take a vaccination. Aragam may impair the efficacy of vaccines such as measles, rubella, mumps and varicella. After using Aragam, an interval of three months should elapse before vaccination with these vaccines. In case of measles, this impairment may persist for up to one year.

#### Using Aragam with food and drink

While using Aragam adequate hydration before infusion should be taken into account.

#### Fertility, pregnancy and breast-feeding

- Clinical experience with immunoglobulins suggests that no harmful effects on fertility are to be expected.
- In pregnant women the safety of this medicine has not been investigated. Therefore caution should be taken with pregnant women and women who are breast-feeding. Clinical experience with immunoglobulins indicate that these are not expected to have a harmful effect on the course of a pregnancy nor on the foetus (unborn child) or the newborn.
  - Immunoglobulins are excreted in breast-milk and can contribute to the transfer of protective antibodies to the newborn.
  - Ask your doctor or pharmacist for advice before taking any medicine.

#### Driving and using machines

The ability to drive and operate machines may be impaired by some adverse reactions associated with Aragam. Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

#### Important information about some of the ingredients of Aragam

Aragam contains glucose 50 mg/ml (5 %). Please note this may increase your blood glucose levels. If you are a diabetic, your doctor will decide if there is a need to monitor your blood glucose levels and a need for insulin, especially if high doses of Aragam are given.

#### Special warnings and special precautions for use

- When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.
  - The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped viruses such as hepatitis A virus and parvovirus B19.
  - Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

#### Batch number control:

It is strongly recommended that every time you receive a dose of Aragam **the name and batch number of the**

**product are recorded** in order to maintain a record of the batches used.

### 3. HOW TO USE ARAGAM

- Aragam is given to you by your doctor or nurse. Aragam may be self administered if it is an approved practice in your country and when you have been trained sufficiently. Always use Aragam exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
- Bring Aragam to room or body temperature before use.

Start the intravenous infusion of Aragam as soon as possible after puncturing the stopper.

- The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits. Discard any unused solution.

#### Dosage and route of administration

Aragam is intended for infusion into a vein. Dosage will vary depending on your condition and weight. If you administer Aragam yourself your doctor will tell you the dose and infusion rate.

#### If you use more Aragam than you should

Overdose may lead to fluid overload and hyperviscosity (an increased thickness of the blood). Tell your doctor immediately.

#### If you forget to use Aragam

Tell your doctor immediately and follow his/her instructions. Do not take a double dose to make up for a forgotten dose.

#### If you stop using Aragam

If you have any further questions on the use of this product, ask your doctor

### 4. POSSIBLE SIDE EFFECTS

Like all medicines, Aragam can cause side effects, although not everybody gets them.

#### Occasional side effects

- chills,
- headache,
- dizziness,
- fever,
- vomiting,
- allergic reactions,
- nausea,
- arthralgia (joint pain),
- low blood pressure,
- moderate low back pain.

#### Rare side effects

- a sudden fall in blood pressure and in isolated cases, anaphylactic shock, even if you have not experienced hypersensitive reactions during previous administrations.
- reversible aseptic meningitis (meningitis without infection).
- reversible haemolytic anemia/haemolysis (disruption of red cells).
- temporary skin reactions.
- increase in serum creatinine level and/or acute renal failure.

#### Very rare side effects

- thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses (obstruction of veins).

### 5. HOW TO STORE ARAGAM

- Keep Aragam out of the reach and sight of children.
- Store Aragam in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.
- Aragam can be stored at or below 25°C up to six months, for example while travelling, without impairing its efficacy. The date when taken to room temperature should be marked on the package. If not used during six months storage at room temperature the product must be discarded.
- Do not use Aragam after the expiry date which is stated on the label and the carton after EXP.

### 6. FURTHER INFORMATION

#### What Aragam contains

- The active substance is human normal immunoglobulin for intravenous administration. One ml contains 50 mg immunoglobulin, of which at least 95% is immunoglobulin G (IgG).
- The other ingredients are glucose and water for injections.

#### What Aragam looks like and contents of the pack

- Aragam is a solution for infusion. The solution is a clear or slightly opalescent, colourless or pale yellow.
- Aragam is supplied in five pack sizes 20 ml, 50 ml, 100 ml, 200 ml and 400 ml, containing 1 g, 2.5 g, 5 g, 10 g and 20 g of immunoglobulin, respectively. Not all sizes may be marketed.

#### Marketing Authorisation Holder

Oxbridge Pharma Ltd, 15 Fitzroy House, Lynwood Drive Worcester Park, Surrey, KT4 7AT, United Kingdom Telephone: +44 208 335 4110

#### Manufacturer

Stichting Sanquin Bloedvoorziening, Plesmanlaan 125 1066 CX Amsterdam, The Netherlands

This leaflet was last approved in September 2012.

The following information is intended for medicinal or healthcare professionals only:

#### Posology and method of administration

- Aragam must only be administered intravenously.
- Start the intravenous infusion of Aragam as soon as possible after puncturing the stopper. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user. The in-use storage times would normally not be longer than 24 hours at 2°C – 8°C, unless puncturing has taken place in controlled and validated aseptic conditions.
- If you need large quantities of Aragam, it is also possible to transfer the contents of several vials to an Ethyl Vinyl Acetate container (Clintec® EVA-parenteral nutrition container, Baxter, CE0123). A maximum amount of 800 ml of Aragam can be transferred to such a container using an aseptic technique. For microbiological reasons, start the infusion as soon as possible after transfer of Aragam into the EVA-container, but not later than three hours after the transfer.
- The dose and dosage depend on the indication. Aragam is given as an intravenous infusion under controlled circumstances at an initial rate of 0.5 ml/kg/hr for 20 minutes. If well tolerated, the rate of administration may gradually be increased to 1.0 ml/kg/hr for 20 minutes and thereafter increased to a maximum of 3.0 ml/kg/hr for the first time user. In adult patients who receive Aragam on a regular basis with good tolerance, the infusion rate may be increased to a maximum of 7.0 ml/kg/hr.
- The dose and dosage regimen is dependent on the indication.
- In replacement therapy the dosage may need to be individualized for each patient dependent on the pharmacokinetic and clinical response. The following dosage regimens are given as a guideline.

The dosage recommendations are summarised in the following table:

Indication	Dose	Frequency of injections
<i>Replacement Therapy</i>		
Primary immunodeficiency syndromes with impaired antibody production	starting dose: 0.4 - 0.8 g/kg  thereafter: 0.2 - 0.8 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed	0.2 - 0.4 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation	0.2 - 0.4 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Hypogammaglobulinaemia in patients after allogenic haematopoietic stem cell transplantation	0.2 - 0.4 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5g/l
Congenital AIDS with recurrent bacterial infections	0.2 - 0.4 g/kg	every 3-4 weeks
<i>Immunomodulation</i>		
Primary Immune thrombocytopenia (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count.	0.8 - 1.0 g/kg  or  0.4 g/kg/d	on day 1, possibly repeated once within 3 days  for 2-5 days
Guillain Barré syndrome	0.4 g/kg/d	for 5 days
Kawasaki disease	1.6 – 2 g/kg  or  2 g/kg	in several doses for 2 – 5 days in association with acetylsalicylic acid  in one dose in association with acetylsalicylic acid

#### Special precautions

It is strongly recommended that every time you receive a dose of Aragam the name and batch number of the product are recorded in order to maintain a record of the batches used.

#### Incompatibilities

Aragam should not be mixed with other medicines.

#### Instructions for handling and disposal

Bring Aragam to room or body temperature before use. The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits. Discard any unused solution.