**Package leaflet: Information for the patient or carer**

**Strimvelis 1-10 million cells/ml dispersion for infusion**

Autologous $CD34^+$ enriched cell fraction that contains $CD34^+$ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you (or your child) are given this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you (or your child) get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.
- Your doctor will give you a Patient Alert Card. Read it carefully and follow the instructions on it.
- Always show the Patient Alert Card to your doctor or nurse when you see them or if you go to hospital.

**What is in this leaflet**



## 1. What Strimvelis is and what it is used for

Strimvelis is a type of medicine called a **gene therapy**.

Strimvelis is used to treat a serious condition called **ADA-SCID** (*Adenosine Deaminase-Severe Combined Immune Deficiency*). With this condition the immune system does not work properly to defend the body against infections. People with ADA-SCID cannot produce enough of an enzyme called *adenosine deaminase (ADA)* because the gene to make it is faulty.

Strimvelis is used to treat ADA-SCID when there is no suitable match from a family member to donate stem cells from their bone marrow for a transplant.

Strimvelis is made specially for each patient, using the patient's own bone marrow cells. It works by putting a new gene into stem cells in the bone marrow so they can make ADA.

Strimvelis is given by a drip *(infusion)* into a vein *(intravenously)*. For more information on what happens before and during treatment, see section 3, *How Strimvelis is given*.

## 2. What you need to know before you (or your child) are given Strimvelis

**Strimvelis is not suitable for some people**

Strimvelis must not be given if you (or to your child):
- are **allergic** to any of the ingredients of this medicine (*listed in section 6*)
- have or have had a type of **cancer** called *leukaemia* or *myelodysplasia*
- have tested positive for **HIV or some other infections** (your doctor will advise you about this)
- have already been treated with **gene therapy**

**Warnings and precautions**

Talk to your doctor or nurse before you (or your child) are given this medicine.

Strimvelis is made specially from the patient's own cells. It must never be given to anyone else.

Inserting a new gene into the DNA could cause leukaemia. In clinical trials of gene therapy for other diseases (not ADA-SCID), some patients developed leukaemia or other cancers of the blood system. This has not been seen in any patient treated with Strimvelis; however, during long-term follow up your doctor has been advised to monitor you (or your child) for any signs of leukaemia.

After you (or your child) have been treated with Strimvelis, you or your child will not be able to donate blood, organs or tissues at any time in future. This is because Strimvelis is a gene therapy product.

**When Strimvelis treatment cannot be completed**
In some cases, it might not be possible to go ahead with the planned treatment with Strimvelis. There are several reasons why this might happen, for example:

- if there was a problem at the time the cells were taken for making the medicine
- if there were not enough of the right type of cells to make the medicine
- if the medicine got contaminated while it was being made
- if there was a delay in the medicine reaching the clinic where treatment is being carried out.

In such cases, the doctor will give you (or your child) replacement stem cells, using the backup sample that was collected and stored before treatment started (*see also section 3, How Strimvelis is given*).

**You may need other treatment**
Strimvelis goes through a range of tests before it is used. Because it is given soon after it is made, the final results of some of these tests will not be ready before the medicine is given. If the tests show anything that might affect you (or your child), the doctor will treat you as appropriate.

**Pregnancy and breast-feeding**
If you are pregnant or breast-feeding, if you think you may be pregnant or are planning to have a baby, tell your doctor before you are given this medicine. Strimvelis should not be given to you if you are pregnant. If it is possible that you could become pregnant, you must use a barrier contraceptive (such as condoms) during treatment and for at least 6 months afterwards.

You should not be given Strimvelis if you are breast-feeding. It is not known whether the ingredients of Strimvelis can pass into breast milk.

**Strimvelis contains sodium**
This medicine contains approximately 3.5 mg sodium per millilitre. This should be taken into consideration by patients on a controlled sodium diet.

## 3. How Strimvelis is given

Strimvelis is given by a drip *(infusion)* into a vein *(intravenously)*. It can only be given in a specialised hospital, and by a doctor who is experienced in treating patients with ADA-SCID and in using this type of medicine.

Strimvelis can only be made if the doctor can collect enough of the right kind of cells from the patient's own bone marrow.

**Before Strimvelis is made**, the doctor will do tests to make sure that you (or your child) are not carrying certain infections (see section 2).

**Two samples are collected**
The doctor will collect two samples of bone marrow stem cells before the planned treatment:

- the **backup sample**, at least 3 weeks before. It will be stored, to be given to the patient as replacement stem cells if Strimvelis cannot be given or does not work *(see 'When Strimvelis treatment cannot be completed' in section 2)*
- the **treatment sample**, 4 to 5 days before. It will be used to make the Strimvelis, by putting a new gene into the cells.

**Before and during Strimvelis treatment**

| **When** | **What is done** | **Why** |
|---|---|---|
| **At least 3 weeks before** treatment | **Backup sample** of stem cells collected | to be stored as a backup *(see above)* |
| **About 4 to 5 days before** treatment | **Treatment sample** of stem cells collected | to make Strimvelis *(see above)* |
| **3 days and 2 days before** treatment | A medicine called **busulfan** is given four times a day for two days (total of 8 doses) | to make the bone marrow ready for Strimvelis |
| **About 15 to 30 minutes before** treatment | An **antihistamine** medicine may be given | to make it less likely that you will react to the infusion |
| **Strimvelis is given…** | by a drip into a vein.<br>This will take about 20 minutes | |

## 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The ones marked * may be related to busulfan.

**Very common side effects**

These may affect **more than 1 in 10 people**:

- runny or blocked nose (*allergic rhinitis*)
- wheezing, difficulty breathing (*asthma)*
- inflamed itchy skin (*atopic dermatitis, eczema*)
- raised temperature (*pyrexia*)
- underactive thyroid gland (*hypothyroidism*)
- high blood pressure (*hypertension*)*

- decreases in the number of red or white blood cells (*anaemia, neutropenia*)*
- increases in liver enzymes*
- blood test results positive for *antinuclear antibody*

If you have any questions about symptoms or side effects, or if any symptoms concern you

→ **Talk to your doctor or nurse.**

C**ommon side effects**

These may affect **up to 1 in 10 people**. They are all caused by the immune system becoming over-active and attacking the body's own tissues.

- red or purple dots on the skin, bleeding under the skin (*immune thrombocytopenic purpura*)
- inflamed thyroid gland (*autoimmune thyroiditis*)
- weakness and pain in the feet and hands (*Guillain-Barré syndrome*)
- inflamed liver (*autoimmune hepatitis*)
- reduced numbers of blood cells (*autoimmune haemolytic anaemia, autoimmune aplastic anaemia*)
- blood test results positive for *antineutrophil cytoplasmic antibody and smooth muscle antibody*

If you have any questions about symptoms or side effects, or if any symptoms concern you

→ **Talk to your doctor or nurse.**

**Reporting of side effects**
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see below). By reporting side effects you can help provide more information on the safety of this medicine.

**United Kingdom**
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

**Ireland**
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; E-mail: medsafety@hpra.ie

## 5. How to store Strimvelis

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date and time (EXP) which is stated on the container label and infusion bag label.

Store at 15-30°C.

Do not throw away any medicines via wastewater. As this medicine will be given by a qualified doctor, they are responsible for correct disposal of the product. These measures will help protect the environment.

## 6. Contents of the pack and other information

**What Strimvelis contains**

- The active substance is autologous (the patient's own) $CD34^+$ enriched cell fraction that contains $CD34^+$ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence. The concentration is 1-10 million $CD34^+$ cells/ml.
- The other ingredient is sodium chloride (*see section 2, Strimvelis contains sodium*).

**What Strimvelis looks like and contents of the pack**

Strimvelis is a cloudy to clear, colourless to pink dispersion of cells for infusion, which is supplied in one or more infusion bags. The infusion bags are provided in a closed container.

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**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

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**The following information is intended for healthcare professionals only:**

Strimvelis is transported directly to the medical facility where the infusion will be administered. The infusion bag is placed inside a closed outer container. The bags must be kept in the outer container until ready to use.

Strimvelis is intended solely for autologous use. The identity of the patient must be matched with the essential unique patient information on the infusion bag(s) and/or outer container prior to infusion.

Gently agitate the infusion bag to re-disperse any cellular aggregates, administer using a transfusion administration set with filter to remove any remaining cellular aggregates.

Following administration, a saline filled 50 ml syringe should be used to flush the bag through.

This medicinal product contains genetically-modified cells. Local biosafety guidelines applicable should be followed.

Strimvelis is not tested for transmissible infectious agents. Healthcare professionals handling Strimvelis should therefore take appropriate precautions to avoid potential transmission of infectious diseases.

Work surfaces and material which have potentially been in contact with Strimvelis must be decontaminated with appropriate disinfectant.

Any unused medicinal product or waste material should be disposed of in accordance with local biosafety requirements.