PNH Patient /Parent information brochure

SOLIRIS®
(eculizumab)

ALEXION™

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GLOSSARY OF TERMS

Anaemia
A condition in which your body does not have enough red blood cells; this may lead to fatigue and other symptoms.

Anticoagulants
Sometimes referred to as blood thinners, anticoagulants are drugs that decrease the clotting ability of blood and help prevent the formation of blood clots.

Blood clots
When many platelets in the blood stick together, they form a blood clot. These clots can block blood flow in the veins and arteries, depending on their size and location (see "Thrombosis").

Chronic haemolysis
The destruction of red blood cells (haemolysis) over a long period of time (chronic).

Complement system (also known as the complement cascade or just complement)
Part of your immune system that destroys bacteria and other foreign cells. In PNH, complement is responsible for the destruction of red blood cells that lack specific protective proteins.

Gonococcal infection
Infection sexually transmitted and caused by the bacterium *Neisseria gonorrhoea*e (also named gonorrhea).
Can disseminate and cause widespread blood infection (sepsis).

Haemoglobin
The brownish-red substance in red blood cells that carries oxygen throughout your body. Responsible for the characteristic dark urine seen in PNH.

Haemoglobinuria
Haemoglobin in the urine. This is technical term for the dark "cola-coloured" urine which is sometimes seen in PNH. When the red blood cells are lysed or destroyed, as they are in PNH, haemoglobin is released from the red blood cells. When it is not all processed by the body's system, it is sent out as waste and colours the urine a characteristic cola-brown colour.

Meningococcal infection
Infection caused by the bacterium *Neisseria meningitidis* (also named meningococcus).
Can cause meningitis or widespread blood infection (sepsis).

Paroxysmal Nocturnal Haemoglobinuria (PNH)
A rare blood disorder in which red blood cells are chronically destroyed or haemolysed by the complement system. This can lead to severe problems including anaemia, fatigue and thrombosis.

Red blood cells (RBCs)
Blood cells that carry oxygen using a protein complex called haemoglobin. PNH red blood cells are continually attacked and destroyed by the complement system because they are missing important protective proteins.

Thrombosis (thrombotic events)
The formation or development of a blood clot that often blocks blood from flowing through a vessel. In PNH, blood clots can occur in common place but can also occur in unusual sites, such as in vessels in the abdomen (see Blood clots).

INTRODUCTION

This guide is for adult and adolescent patients suffering from Paroxysmal Nocturnal Haemoglobinuria (PNH)) and for parents of children and adolescent with PNH. The guide gives you information about SOLIRIS®, how it will be given to you and about important safety information that you must be aware of. There is also another guide specifically for parents of young children, which your doctor will be able to give you.

WHAT IS SOLIRIS®?

SOLIRIS® is a medication that is used to treat patients with PNH. It is a type of humanised monoclonal antibody. Antibodies are substances which in the blood can bind to specific targets. Humanised describes the fact that the antibody has been engineered to make it as similar to human antibodies as possible. Monoclonal means that all of the medication comes from one original antibody i.e. they are all exactly the same.

PNH is a disease where a specific part of the natural immune system, called the complement system, is overactive, usually due to a genetic defect in the normal regulation of the complement system. The complement system is always switched on and when it is overactive it can destroy their red blood cells (haemolysis) which can lead to low blood counts, tiredness, difficulty in functioning, pain, dark urine, shortness of breath and blood clots.

SOLIRIS® is an antibody which binds to one of the parts of the complement system and makes it inactive. Therefore SOLIRIS® reduces the haemolysis (destruction of red blood cells) which is the cause of the signs and symptoms of PNH. As PNH is a chronic disease, SOLIRIS® is intended as long-term treatment.

FAQs

WHAT ARE THE SAFETY CONSIDERATIONS RELATED TO SOLIRIS®?

IMPORTANT SAFETY INFORMATION

As SOLIRIS® blocks a part of your immune system it increases the risk of severe infection and sepsis, especially by a type of bacteria called *Neisseria meningitidis*. This can cause cases of meningococcal infection (severe infection of the linings of the brain or/and blood infection) and other Neisseria infections including disseminated gonorrhea

These infections require urgent and appropriate care as it may become rapidly fatal or life-threatening or lead to major disabilities.

It is important to understand the precautions to take to reduce the risk of these infections and what to do if you are worried you may have an infection (see below).

As a safety precaution:

YOU/YOUR CHILD MUST BE VACCINATED against meningococcal infection at least 2 weeks before starting SOLIRIS®. If you initiate/your child initiates SOLIRIS® treatment less than 2 weeks after receiving a meningococcal vaccine you/your child must receive an antibiotic until 2 weeks after vaccination to reduce the risk of infection with *Neisseria meningitidis*.

If no vaccine is available for your young child or if the vaccine is contra-indicated to you, your child / you will be given an antibiotic throughout the treatment period or until 2 weeks after the vaccine can be given.

Children and adolescents less than 18 years of age need to be vaccinated against *Haemophilus influenza* and pneumococcal infections according to national vaccination guidelines at least 2 weeks prior to initiation of SOLIRIS® therapy and following the national vaccination recommendations for each age group.

WHAT ARE THE SYMPTOMS THAT SHOULD ALERT ME DURING TREATMENT?

Vaccination reduces the risk of developing an infection, but it does not eliminate the risk completely.

You will need to be aware of the signs and symptoms of infection and notify your doctor immediately if ANY of the following symptoms occur:

- Headache with nausea or vomiting
- Headache with a stiff neck or back
- Fever
- Rash
- Confusion
- Severe muscle ache combined with flu-like symptoms
- Sensitivity to light

If you cannot reach your doctor, go to an Accident & Emergency department and show them your Patient Safety Card.

For parents/legal guardians of newborns and infants, **please be aware that the typical symptoms of headache, fever and neck stiffness may be hard to detect**, so other symptoms in babies to be aware of include inactivity, irritability, vomiting, and poor feeding.

ARE THERE STEPS I SHOULD TAKE BEFORE STARTING THERAPY?

Prior to commencing treatment, your doctor will discuss with you the importance of:

- Receiving a vaccine against meningitis and in some cases a specific antibiotic to reduce the risk of infection with a type of bacteria called *Neisseria meningitidis*.
- Understanding the symptoms associated with infections and what to do if you experience those symptoms.
- If your child is being treated, understanding your child should be vaccinated against *Haemophilus influenza* and pneumococcal infections according to national vaccination guidelines at least 2 weeks prior to initiation of SOLIRIS® therapy
- Being carefully monitored by your doctor following any discontinuation of SOLIRIS® treatment.

Your doctor or nurse will make sure you receive/your child receives a vaccine against meningococcal infection at least 2 weeks before your first infusion. If you initiate/your child initiates SOLIRIS® treatment less than 2 weeks after receiving meningococcal vaccine your doctor or nurse will make sure you receive an antibiotic until 2 weeks after vaccination to reduce the risk of infection with *Neisseria meningitidis*.

In addition, you will be closely monitored for meningococcal and other infections during the course of your treatment.

HOW DO I GET STARTED ON SOLIRIS® THERAPY?

SOLIRIS® must be prescribed by a doctor.

You will also be given a starter's kit containing:

- **Patient Safety Card:** it is very important to rapidly identify and treat certain types of infection in patients who receive SOLIRIS®; therefore you will be given a Safety Card which lists specific symptoms for which you should always look out. You should carry this card at all times and show it to any health care professional you see.
- **PNH Patient/Parent information brochure**.
- **PNH Parent guide will be given to parents/legal guardians of young children.**
- Your doctor will offer you/your child to participate in the **PNH Registry**. It is your doctor who can register you/your child in this registry.

HOW IS SOLIRIS® ADMINISTERED?

SOLIRIS® is administered through an **intravenous infusion** (introduction of a solution into a vein). The infusion lasts **25 to 45 minutes**. It must be prepared and administered by a doctor or other suitably qualified healthcare professional.

As with all drugs administered through an intravenous infusion, SOLIRIS® may cause immediate or delayed reaction. Please refer to your doctor if that happens.

Because there is a risk of infusion reaction (including allergic reaction), following each infusion you will be monitored for about one hour. Your doctor's instructions should be carefully observed.

WHAT DOSE OF SOLIRIS® IS USED?

For adults:

Initial Phase	Maintenance Phase
Every week for the first four weeks, your doctor will administer an intravenous infusion of diluted SOLIRIS®. Each infusion will consist of a dose of 600 mg (2 vials of 30 ml) and will take 25-45 minutes.	In the fifth week, your doctor will administer an intravenous infusion of diluted SOLIRIS® at a dose of 900mg (3 vials of 30 ml) over a 25 - 45 minute period. After the fifth week, your doctor will administer 900mg (3 vials of 30 ml) every two weeks as a long term treatment.

For children and adolescents:

Body Weight	Initial Phase	Maintenance Phase
≥ 40 kg	600 mg weekly x 4	900 mg at week 5; then 900 mg every 2 weeks
30 to <40 kg	600 mg weekly x 2	900 mg at week 3; then 900 mg every 2 weeks
20 to <30 kg	600 mg weekly x 2	600 mg at week 3; then 600mg every 2 weeks
10 to <20 kg	600 mg weekly x 1	300 mg at week 2; then 300mg every 2 weeks
5 to <10 kg	300 mg weekly x 1	300 mg at week 2; then 300mg every 3 weeks

Children and adolescents with PNH who are 40kg weight and over are treated with the adult dosing recommendations.

Children and adolescents with PNH who are under 40 kg weight require a smaller dose based on how much they weigh. Your doctor will calculate this.

It is very important to make sure that you **do not miss or postpone any scheduled treatment appointment** in order to continue to control haemolysis and experience the full benefits of SOLIRIS® therapy.

HOW LONG WILL I NEED TO TAKE SOLIRIS®?

Since **PNH is a chronic disease**, SOLIRIS® is intended to be **an ongoing therapy**.

Patients who start SOLIRIS® should continue receiving SOLIRIS®, even if they feel better. Interrupting or ending treatment with SOLIRIS® may cause your PNH symptoms to come back more severely soon after stopping SOLIRIS® treatment.

You must not stop your treatment without medical surveillance

If you plan to stop treatment with SOLIRIS®, you need to discuss beforehand with your doctor the possible side effects and risks, which include an increase in the destruction of your red blood cells (hemolysis) that may cause:

- A significant fall in your red blood cell count (anaemia).
- You to become confused or less alert.
- Chest pain or angina.
- Problems with your kidneys (increase in your serum creatinine level).
- Blood clotting (thrombosis).

ARE THERE OTHER CONSIDERATIONS WHILE I AM ON SOLIRIS®?

Infection risk

Due to its mechanism of action, SOLIRIS® should be administered with caution to patients with active systemic infections.

You may also be at risk of other infection with bacteria called Neisseria including disseminated gonococcal infection. If you are at risk of gonorrhea, ask your doctor or pharmacist for advice before using this medicine.

Allergic reactions

SOLIRIS® contains a protein and proteins can cause allergic reactions in some people. If you experience any signs or symptoms after receiving SOLIRIS®, you should consult your healthcare professional.

Other medication

It is important to understand that some medications you are taking, especially anticoagulants (blood thinners), such as aspirin or warfarin, should not be changed without consulting your doctor. Please make sure your doctor knows all medications you are taking.

Elderly

There are no special precautions for treated patients aged from 65 years and over.

Undesirable Effects

SOLIRIS® is generally well-tolerated. The most commonly reported side effects were headache, low white blood cell count (leukopenia) and the most serious side effect is meningococcal infection. Most headaches were mild and did not persist after the initial administration phase of SOLIRIS®.

REFERENCES

01. SOLIRIS® (eculizumab) locally approved leaflet.
02. Hillmen P, Young NS, Shubert J, et al. The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria. N Engl J Med. 2006; 355: 1233-1243.
03. Rosse WF, Hillmen P, Schreiber AD. Immune-mediated hemolytic anemia. Hematology (Am Soc Hematol Educ Program). January 2004: 48-62.

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Reporting of side effects
Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” that appears on the homepage of the Ministry of Health’s website (www.health.gov.il) which links to an online form for reporting side effects, or by the following link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il
and by emailing the Registration Holder's Patient Safety Unit at:
drugsafety@neopharmgroup.com
Tel: 1-800-250-255

For further information, please refer to the Israeli approved leaflet.

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