aHUS Patient/Parent information brochure

SOLIRIS®
(eculizumab)

ALEXION™

This document was last approved in (February 2019) By The Israeli Ministry of Health (MOH)

GLOSSARY OF TERMS

Atypical hemolytic uremic syndrome (aHUS)
A rare disorder caused by chronic and excessive activation of the complement system, a part of your normal immune system. The overactive complement system damages small blood vessels and causes the formation of blood clots throughout the body, a process which is called thrombotic microangiopathy (TMA). TMA can damage many organs including the brain, kidneys and heart.

Blood clots
Blood can form clots to stop bleeding, but in aHUS the blood forms clots very easily causing blockage of blood vessels and damage to organs.

Haemolysis
The abnormal destruction of red blood cells, which can cause varied signs and symptoms in aHUS.

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 normally destroys bacteria and other foreign cells. In aHUS is chronically and excessively actived, which causes damage to your own tissues, by the destruction of small blood vessels and the formation of blood clots which damages the organs including the brain, kidneys, heart, and other organs.

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

Kidney impairment or failure
A condition in which the kidneys stop working and are unable to remove waste products or to be able to regulate the amount of water and essential substances in the body.

Meningococcal infection
An infection caused by the bacteria *Neisseria meningitidis* (also named meningococcus). This can cause meningitis or widespread blood infection (sepsis).

Platelets
Platelets are blood cells that can stick together to form blood clots. In aHUS the platelets very easily form blood clots and as they are used up making clots a blood test may reveal that you have a low number of platelets in the blood.

Red blood cells (RBCs)
Blood cells that carry oxygen using a protein complex called haemoglobin. In aHUS, red blood cells are destroyed as they travel through the blocked and disrupted small blood vessels.

Thrombosis (thrombotic events)
The formation of a blood clot that can stop blood from flowing through a blood vessel. In aHUS, blood clots can occur in small blood vessels, typically within the brain, kidney, heart and other organs.

Thrombotic microangiopathy (TMA)
A description of the process in aHUS of small blood vessel destruction and the formation of blood clots within these damaged vessels. TMA is caused by chronic and excessive activation of the complement system and is what causes the damage and illness in patients with aHUS.

INTRODUCTION

This guide is for adult and adolescent patients suffering from atypical Haemolytic Uremic Syndrome (aHUS) and for parents of children and adolescent with aHUS. 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 aHUS. 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.

aHUS 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 damage the body's own tissues and organs. It does this by causing destruction of small blood vessels and the formation of blood clots which block blood flow to tissues and organs. This process is given the medical name of thrombotic microangiopathy (TMA). TMA in aHUS can cause damage to many organs including the kidney, brain and heart.

SOLIRIS® is an antibody which binds to one of the parts of the complement system and makes it inactive. Therefore SOLIRIS® prevents/reduces small blood vessel destruction and the formation of blood clots and reduces the symptoms and organ damage in aHUS. As the aHUS 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 will need to be vaccinated against *Haemophilus influenza* and pneumococcal infections 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.

If you cannot reach your doctor:
Go to an Accident & Emergency department and show them your/your child Patient Safety Card.

ARE THERE STEPS I SHOULD TAKE BEFORE STARTING THERAPY?

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

- Receiving a vaccination 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.
- **aHUS Patient/Parent information brochure.**
- **aHUS Parent guide will be given to parents/legal guardians of young children.**
- Your doctor will offer you/your child to participate in the **aHUS 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 900 mg (3 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 1200 mg (4 vials of 30 ml) over a 25 - 45 minute period. After the fifth week, your doctor will administer 1200 mg (4 vials of 30 ml) every two weeks as a long term treatment.

For children and adolescents:

Body Weight	Initial Phase	Maintenance Phase
≥40 kg	900 mg weekly x 4	1200 mg at week 5; then 1200mg every 2 weeks
30 to <40 kg	600 mg weekly x 2	900 mg at week 3; then 900mg 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 aHUS who are 40 kg weight and over are treated with the adult dosing.

Children and adolescents with aHUS 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 thrombotic microangiopathy and experience the full benefits of SOLIRIS® therapy.

HOW LONG WILL I NEED TO TAKE SOLIRIS®?

Since **aHUS 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 aHUS symptoms to come back after stopping SOLIRIS® treatment.

Some patients who have stopped SOLIRIS® treatment have experienced return of the signs and symptoms of aHUS. You should not stop SOLIRIS® treatment without discussing this with your healthcare professional and 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 a return of small blood vessel destruction and blood clot formation. This may cause:

- Symptoms you may experience: Decreased urination (problems with your kidneys), Confusion or change in how alert you are.
- Following blood tests results: A significant fall in your level of platelets as they are used up forming blood clots, a significant rise in destruction of your red blood cells, an increase in your serum creatinine level (problems with your kidneys).
- Chest pain or angina, shortness of breath.

ARE THERE OTHER CONSIDERATIONS WHILE I AM ON SOLIRIS®?

Infection risk

Due to the way in which SOLIRIS® works in your body, it should be administered with caution if you have an active systemic infection.

You may also be at risk of other infection with bacteria called Neisseria including disseminated gonococcal infection. If you are at risk of gonorrhea (a sexually transmitted infection), 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 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, and 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.

Provided as a patient educational service by Neopharm.

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.

237-Mar-2019

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