Soliris® (eculizumab): Atypical haemolytic uraemic syndrome (aHUS) Patient/Parent information brochure
GLOSSARY OF TERMS

Adverse reaction
An adverse reaction is a response to a drug which is noxious (harmful/very unpleasant) and unintended. Adverse reactions – such as infusion reactions and allergic (or anaphylactic) reactions – can occur in some people to the normal doses of an administered drug treatment. The appearance of such reactions may be sudden or may develop over time.

Anaphylactic reaction
An anaphylactic reaction (or anaphylaxis) is a severe and potentially life-threatening reaction to a trigger such as an allergy. Anaphylactic reactions usually develop suddenly and get worse very quickly.

Atypical haemolytic uraemic 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
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”). 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 (RBCs), which can cause varied signs and symptoms in aHUS.

Chronic (continuous) 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 the complement system is chronically (continuously) and excessively activated, which causes damage to your own tissues, by the destruction of small blood vessels and the formation of blood clots which damage organs including the brain, kidneys, heart.

Confusion
Mental confusion or delirium: bewilderment or feelings of disorientation, sometimes accompanied by changes in consciousness or memory loss.

Gonococcal infection / gonorrhea
A sexually-transmitted infection caused by the bacterium Neisseria gonorrhoeae. This infection can disseminate (spread in the body) 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 (known as 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, RBCs 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 living with atypical haemolytic uraemic syndrome (aHUS) and for parents of children and adolescents living with aHUS. The guide gives you information about SOLIRIS®, how it will be given to you, and 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 blocks it. Therefore SOLIRIS® prevents or reduces small blood vessel destruction and the formation of blood clots, and reduces the symptoms and organ damage in aHUS. As aHUS is a chronic (life-long) disease SOLIRIS® is intended as a long-term treatment.
FREQUENTLY ASKED QUESTIONS

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 and/or blood infection and other Neisseria infections including disseminated gonorrhea.

These infections require urgent and appropriate care as they 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 (or your child) 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 start/your child starts 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 (meningitis).

If no suitable vaccine is available for your young child, or if there are medical reasons why you cannot be given the vaccine (i.e. it is contra-indicated in your case), 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 (a type of ‘flu’) and pneumococcal infections (which can cause pneumonia) at least 2 weeks prior to initiation of SOLIRIS® therapy and according to the national vaccination recommendations for their given age group.
What are the symptoms that should alert me during treatment?

Vaccination reduces the risk of developing an infection, but it does not take away 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 (mental confusion, disorientation, or delirium)
- 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/YOUR CHILD’S 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 starting 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 starting SOLIRIS® therapy
- Being carefully monitored by your doctor following any periods of stopping (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 start/your child starts SOLIRIS® treatment less than 2 weeks after receiving meningococcal vaccine your doctor or nurse will make sure you/your child receives 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 be given a Starter’s kit containing:

- **Patient Safety Card**: it is very important to quickly 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/your child should carry this card at all times and show it to any health care professional you see.
- **aHUS Patient/Parent information brochure (this item)**
- **An additional aHUS Parent guide** will be given to parents/legal guardians of young children living with aHUS

How is SOLIRIS® administered?

SOLIRIS® is given (administered) through an **intravenous infusion** (introduction of a solution into a vein). The infusion lasts **25 to 45 minutes** in adolescents (aged 12 years to under 18 years) and adults and between **1–4 hours in children**. It must be prepared and given by a doctor or other suitably qualified healthcare professional.

As with all drugs given through an intravenous infusion, SOLIRIS® may cause immediate or delayed adverse reactions.

Because there is a risk of infusion reaction (including allergic reaction), following each infusion you/your child will be monitored for about one hour. Your doctor’s instructions should be carefully observed. In the event of any delayed reactions, please refer to your doctor.

What dose of SOLIRIS® is used?

*For adults:*

<table>
<thead>
<tr>
<th>Initial Phase</th>
<th>Maintenance Phase</th>
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<tr>
<td>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 adults).</td>
<td>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 (in adults). After the fifth week, your doctor will administer 1200 mg (4 vials of 30 ml) every two weeks as a long-term treatment.</td>
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For children and adolescents:

Children and adolescents with aHUS who weigh 40 kg weight and over are treated with the doses recommended for adults.

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

In children, each SOLIRIS® infusion will take 1–4 hours.

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Initial Phase</th>
<th>Maintence Phase</th>
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<tbody>
<tr>
<td>≥ 40 kg</td>
<td>900 mg weekly x 4</td>
<td>1200 mg at week 5; then 1200mg every 2 weeks</td>
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<tr>
<td>30 to &lt;40 kg</td>
<td>600 mg weekly x 2</td>
<td>900 mg at week 3; then 900 mg every 2 weeks</td>
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<tr>
<td>20 to &lt;30 kg</td>
<td>600 mg weekly x 2</td>
<td>600 mg at week 3; then 600mg every 2 weeks</td>
</tr>
<tr>
<td>10 to &lt;20 kg</td>
<td>600 mg weekly x 1</td>
<td>300 mg at week 2; then 300mg every 2 weeks</td>
</tr>
<tr>
<td>5 to &lt;10 kg</td>
<td>300 mg weekly x 1</td>
<td>300 mg at week 2; then 300mg every 3 weeks</td>
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</tbody>
</table>

It is very important to make sure that you/your child 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 (long-term) disease, SOLIRIS® is intended to be an ongoing therapy (i.e. you/your child may need to take it indefinitely).

Patients who start SOLIRIS® should continue receiving SOLIRIS®, even if they feel better. Interrupting or ending treatment with SOLIRIS® may cause your/your child’s aHUS symptoms to come back after stopping SOLIRIS® treatment.

YOU/YOUR CHILD MUST NOT STOP SOLIRIS® TREATMENT WITHOUT MEDICAL ADVICE AND SURVEILLANCE
If you plan to stop treatment with SOLIRIS®, before doing so you need to discuss 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:

- Problems with the kidneys
- Confusion, seizures, or changes in how mentally alert you are/your child is
- Chest pain or angina, shortness of breath
- A significant fall in the level of platelets in the blood; a significant increase in destruction of red blood cells

Are there other considerations while I am on SOLIRIS®?

Infection risk
Due to the way in which SOLIRIS® works in your/your child’s body, it should be given with caution if you/your child has an active systemic infection. You/your child 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/your child experience any signs or symptoms after receiving SOLIRIS®, consult your healthcare professional.

Other medication
It is important to understand that some medications you/your child are taking should not be changed without consulting your doctor. Please make sure your doctor knows all medications you/your child are taking.

Elderly
There are no special precautions advised for treatment of patients aged 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®.
REPORTING SIDE EFFECTS

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the leaflet.

You can also report side effects directly.

In the UK via the Yellow Card Scheme at yellowcard.mhra.gov.uk

In Ireland via
HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2
Tel: +353 1676 4971
Fax: +353 1676 2517
Website: www.hpra.ie
Email: medssafety@hpia.ie

By reporting side effects you can help provide more information on the safety of this medicine.

You can also report side effects to Alexion, please email: uk.adverseevents@alexion.com or call: UK: 0800 321 3902. Ireland: 1800 936 544

MORE INFORMATION

If you require further information on SOLIRIS®, please call or email Alexion Medical information.
Email: medicalinformation.uk@alexion.com Tel: UK: 0800 689 1592 / Ireland: 1800936 537

Alexion funds a Home Healthcare service, which is available to all patients prescribed with SOLIRIS®.

For more details, please ask your physician about this service and availability.

REFERENCES
