### Hospital Information

**Physician Name:**

**Hospital/Clinic:**

**Physician contact information:**

### Appointments

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INTRODUCTION

This booklet contains information about atypical Haemolytic Uraemic Syndrome (aHUS). If you or a family member has been diagnosed with aHUS, the medical team at the hospital will have spent time with you in order to explain what exactly aHUS is, how it can affect you and what the treatment options are. This booklet is intended to provide you with general information about the disease. It is not intended to replace the discussions that take place with your doctor and if you have any questions about aHUS please make sure to discuss these with your doctor or the medical team.

Topics that are covered in this booklet are:

1. What is aHUS?
2. What causes aHUS?
3. What effect does aHUS have on the body?
4. What is complement?
6. How do I know if I have aHUS and how is it diagnosed and monitored?
7. How is aHUS treated?
8. What are the options?
9. Glossary of terms

1. WHAT IS aHUS?

Atypical Haemolytic Uraemic Syndrome (aHUS) is a very rare disease affecting the kidneys and other organs and can affect both adults and children in a similar way.

In patients with aHUS, blood clots form in small blood vessels throughout the body in a process known as thrombotic microangiopathy (TMA).

In patients with aHUS, the kidneys and the blood cells can become inflamed due to these clots. aHUS can lead to thrombocytopenia (low levels of platelets - the blood cells that are responsible for clotting), as well as low levels of red blood cells, reduced or lost kidney function, bigger blood clots, tiredness and difficulty in carrying out normal everyday activities.

See Glossary of Terms on page 13 for definitions of words in bold
2. WHAT CAUSES aHUS?

aHUS is not caused by a bacteria or virus. In many cases, aHUS has been identified as a genetic problem due to an irregularity in several genes. It is therefore understood to be an inherited disease. However, the genetic problem cannot always be identified in patients with aHUS.

The genetic disorder results in changes to, or mutations in the genes that produce proteins that help control the complement system, which is part of our body’s natural immune defense system.

If these proteins are missing or are not working properly, your body cannot control the complement system. When the complement system is uncontrolled it can cause damage to the tissue within your body.

It has been demonstrated that many of the genetic cases are the result of a deficiency of a protein called Factor H. As a result, this can cause damage to organs such as your kidneys, brain and heart.

aHUS is still not well understood and research is ongoing to try to understand it better.

3. WHAT EFFECT DOES aHUS HAVE ON THE BODY?

aHUS can cause problems in the kidney blood cells, and the vascular system (the network of veins and arteries that transport the blood).

In aHUS the body tries to attack and destroy its own blood cells. While kidney problems are often one of the first obvious signs (uraemia), aHUS does not start in the kidney. Instead, it starts in either the blood or the vascular system.

Red blood cells are broken down and destroyed because some of the small blood vessels in the body have become blocked by very small clots in areas where they are not needed. These are just the right size to cause blockages in the small blood vessels of the kidneys (thrombosis).

These blood clots are formed as a result of an abnormality with a pathway in the body, known as ‘complement’. The complement pathway is responsible for producing an immune response. In patients with aHUS, the complement pathway becomes uncontrolled and this leads to formation of blood clots and damage to different organs in the body, most importantly the kidney.
4. WHAT IS COMPLEMENT?

The complement pathway forms part of the immune system. The complement pathway needs to be carefully regulated so that it targets only unwanted materials and does not attack the body's healthy cells. In aHUS, the complement system is not working properly because certain complement proteins are missing or are not working correctly. This is because of a genetic problem. This means that the body does not have the ability to control the complement system. The complement system becomes out of control and attacks the cells in the body that it normally protects. This causes damage to organs such as the kidneys.

In aHUS, platelets – a type of blood cell responsible for making blood clots and an important part of the body's natural defence system - are also affected. Normally, platelets help protect the body by forming clots in damaged areas. Platelets work only when they are specifically activated. In aHUS, when the complement system is uncontrolled, platelets become overactive too, and this means that cells along blood vessel walls become damaged and inflamed. This process is known as thrombotic microangiopathy (TMA). This can result in low red blood cell and platelet counts, leading to problems in various organs, such as the kidneys, heart, and brain.

5. WHAT ARE THE MOST COMMON SYMPTOMS OF aHUS?

aHUS can present in different patients in different ways. You may have experienced a number of different signs and symptoms.

You may begin to feel ill, really worn out (fatigue), irritable, and very tired (lethargic).

aHUS frequently starts out with flu-like symptoms that do not go away. Eventually, the lethargic behaviour results in loss of appetite.

As the disease causes damage to small blood vessels, organs such as your kidneys can fail to function or slowly lose their ability to function over time.

One of the most common signs of aHUS is kidney failure, which can help lead doctors to a correct diagnosis. Your doctor may do certain tests to monitor how well your kidneys are functioning.

A simple blood test will show abnormal red blood cells, and low platelet counts.
6. HOW DO I KNOW IF I HAVE aHUS AND HOW IS IT DIAGNOSED AND MONITORED?

Damage to the small blood vessels of the kidneys means that the kidneys can suddenly fail to function or slowly lose their ability to function over time. Kidney failure can help lead doctors to the diagnosis of aHUS. Certain kidney function tests can be performed to monitor how well your kidneys are working. One of these tests involves measuring creatinine levels in the blood. Kidney damage can be indicated not only by high levels of creatinine in the blood, but also by oedema (swelling of the tissues, especially ankles), and high blood pressure.

Certain routine blood tests can help to confirm a diagnosis of aHUS. These blood tests can show damaged or broken red blood cells, a low number of red blood cells and a low number of platelets. Your doctor will perform some blood tests to see how aHUS is affecting you. In particular, he or she can look at red blood cell and platelet counts.

Although aHUS is a genetic disease, some people with aHUS will not have an abnormality in their genetic tests. This type of testing is not necessary for your doctor to diagnose you with aHUS and the absence of an identified genetic defect does not rule out aHUS.

You doctor may wish to monitor you by performing regular blood tests and by following up on any other signs or symptoms you experience. It may be helpful to keep a record of how you have been feeling and to discuss these with your doctor or nurse when you see them. (See the Patient Notes section at the end of this booklet)

In aHUS, other organs apart from the kidney can be also be affected in some patients. Individuals may experience one or more of the following:

- Breathlessness
- Heart problems
- High blood pressure
- Neurological problems (e.g. fits or seizures)
- Stomach upsets (e.g. diarrhoea or vomiting)
7. HOW IS aHUS TREATED?

There is no standard treatment for aHUS, as each case is different. Patients with aHUS often develop various complications, so therapy is tailored for each case.

The aim of treatment is to stop the body’s own cells from being damaged by the overactive complement system. Most patients who develop aHUS for the first time are treated with ‘plasma exchange’ but there are other options available. Your doctor will help you decide how your condition should be managed.

- **Plasma exchange**
  
  This involves removing blood from the body and then separating the blood cells from the liquid part of the blood, known as plasma. The blood cells are then added to replacement plasma and returned to the body. The reason for doing this is that the plasma part of the blood can contain immune factors that stimulate conditions like aHUS to occur. By replacing the plasma with new plasma, the activity of these potentially destructive immune factors can be reduced. In aHUS plasma exchange may be undertaken daily. Some, but not all, patients respond to this treatment. Those who do not respond might develop kidney failure and need long-term dialysis. Even those who respond may need to undergo plasma exchange every so often to prevent the disease coming back.

- **Dialysis**
  
  Patients who develop kidney failure as a result of aHUS may require dialysis. This is a way of filtering the blood when the body is unable to perform this function. The blood is collected into a machine which then removes waste products and cleans the blood in the same way that the kidneys do normally. The blood is then returned to the body.

- **Kidney transplantation**
  
  Kidney transplantation has been successful in some patients, but it is not as successful as in other conditions that cause kidney failure. This is because aHUS can recur in the new, transplanted kidney, and when it does there is a high-risk the transplant might fail. Because some of the abnormal complement proteins are produced by the liver, a small number of patients worldwide have undergone a combined liver-kidney transplant. The results of this have been variable but those that have been undertaken in the UK have so far all been successful.

- **Other treatments**
  
  Some drug treatments are being developed for use in diseases with faulty complement proteins. Monoclonal antibodies can be used in the treatment of aHUS. They aim to address the underlying cause of the signs and symptoms of the disease and help regulate the complement system.
8. WHAT ARE THE OPTIONS?

aHUS episode and patients should be monitored very closely. Your doctor will discuss all of the treatment options available with you and will be able to advise you.

Taking care of yourself

There is one important thing that you can do once you have been diagnosed with aHUS: help yourself!

Keep monitoring your body. If you notice anything wrong, go to the hospital and get advice or help.

9. GLOSSARY OF TERMS

Atypical: something that is irregular or unusual.

atypical Haemolytic Uraemic Syndrome (aHUS): a rare genetic disease of the blood in which the complement system becomes overactive and can attack healthy body cells. This can cause low red blood cell and platelet counts, kidney failure, and damage to other vital organs, such as the heart and brain.

Complement system: a network of proteins and enzymes that interact with each other to protect the body against foreign substances, like bacteria and other invading organisms.

Creatinine: a chemical excreted by the kidneys. The amount (level) of creatinine shows whether the kidneys are functioning properly.

Dialysis: a treatment for kidney failure. Normally, the kidneys work to filter the blood and remove waste, excess salt, and water. Kidney failure, also called ‘end-stage renal disease’, occurs when the kidneys stop working completely. During haemodialysis, a machine takes over the job of the kidney by filtering the blood outside of the body removing wastes or toxins from the blood, and then returning the filtered blood back to the body.

Immune system: a complex group of cells, proteins, and other molecules that work together to identify foreign organisms and substances, such as bacteria; the main role of the system is to protect the body against these foreign organisms.
Monoclonal antibodies: special proteins designed to target other very specific cells or proteins in the body.

Oedema: swelling of certain parts of the body due to the presence of abnormally large amounts of fluid.

Plasma: the pale yellow liquid part of whole blood, containing red and white blood cells and various other blood elements.

Plasma exchange: a process of removing, treating, and returning plasma to the body.

Thrombotic: producing blood clots.

Thrombotic microangiopathy (TMA): a description of the process in aHUS of a 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 aHUS.

Thrombosis: the formation of a blood clot that can stop blood flowing through a blood vessel.

Thrombocytopenia: decreased numbers of platelets.

Uraemia: signs and symptoms of kidney failure; signs and symptoms of uraemia can include nausea, vomiting, metallic taste in the mouth, muscle pain and swelling.

Patient Notes
Use these pages to note down how you are feeling on a daily basis, and any questions that you would like to ask your doctor.