Nusinersen treatment

for spinal muscular atrophy (SMA) type 1

This leaflet explains more about the use of nusinersen (also called Spinraza®) as a treatment for SMA, including the benefits, risks and any alternatives. It also provides some information on what you can expect when your child comes in to hospital for treatment. If you have any further questions, please speak to a doctor or nurse caring for your child.

What is nusinersen?

Nusinersen or Spinraza® is a treatment for SMA that has been tested in clinical trials and was approved for use throughout the NHS by its brand name Spinraza® in July 2019. It is provided through a managed access agreement, which means that it can only be prescribed for a patient if particular criteria are met. You will only be offered this treatment for your child if he / she meets the eligibility criteria.

What does nusinersen do and how does it work?

SMA affects a group of nerve cells called the lower motor neurons which run from the spinal cord to the muscles. The lower motor neurons carry messages that make it possible for us to move the muscles we use to crawl and walk, to move our arms, hands, head, and neck, and to breathe and swallow.

For our lower motor neurons to be healthy, we need to produce an important protein called the Survival Motor Neuron (SMN) protein. Our ability to do this is controlled by gene called Survival Motor Neuron 1 (SMN1). We all have two copies of this gene, one inherited from our mother and the other from our father. People with SMA have coding errors (mutations) in both copies of the SMN1 gene.

Having two faulty SMN1 genes means that a child is only able to produce very low amounts of the SMN protein. This causes their lower motor neurons in their spinal cord to deteriorate. Messages from their spinal cord do not efficiently get through to their muscles, which makes movement difficult. Their muscles waste due to lack of use and this is known as muscular atrophy.

The type of SMA is known by how bad it affects the muscles. Babies with SMA type 1 are not able to roll or sit and have weakness of muscles important for feeding and breathing. Infants / children with SMA type 2 are able to sit without support but not able to stand. Children with SMA type 3 are able to stand and walk, although may lose this ability over time.

Another gene called SMN2 also helps with the production of the SMN protein, but usually only small amounts are produced by this gene. Nusinersen is a highly specialised medicine that can increase the production of SMN protein by working on the SMN2 gene.

What are the possible benefits of nusinersen to my child?

Clinical trials have been conducted in patients who had or were likely to develop SMA type 1. These trials have shown that some patients treated with nusinersen showed improvements, including:

- The achievement of physical milestones which, if untreated, they would have been unable to reach.
- Surviving longer than expected considering the typical course of the condition.

It is not possible to be sure that your child will show improvements with the treatment but the aim of treatment is to achieve the outcomes above**.**

How is nusinersen given?

Nusinersen is delivered directly into the cerebrospinal fluid (CSF). This is the fluid which bathes the brain and spinal cord. Doctors access the CSF by lumbar puncture. This is when a needle is inserted through the skin into the space between the vertebrae of the spine (back bones). This will be done either with local anaesthetic, sedation or general anaesthetic. Your doctor will discuss these with you in the clinic and explain which of these is likely to be needed.

If local anaesthetic is used, your child will be awake but will have either cream to numb the area or an injection of local anaesthetic to numb the area.

A small amount of CSF is drawn off and then nusinersen is injected over one to three minutes. At the start of treatment four injections are given in the first two months. After this, injections are needed every four months.

What are the risks/side-effects?

As nusinersen is a recently developed medicine, there is no data available about possible longer term side-effects. In clinical trials the following side effects have been noted.

Effects on blood clotting

Nusinersen (and other similar medicines) can affect the levels of platelets in the blood, which affects how well blood clots. Low levels of platelets may lead to wounds bleeding more severely and for longer than usual. Doctors will check your child's platelet levels before starting nusinersen and then at regular points for as long as your child is receiving treatment.

Effect on kidney function

Nusinersen can affect how well the kidneys work, particularly how the tiny filtering units called glomeruli can filter waste products from the blood. Doctors will check your child's kidney function by testing a urine / blood sample before starting nusinersen and then at regular points for as long as your child is receiving treatment.

Hydrocephalus

A small number of children treated with nusinersen have developed hydrocephalus. This is a serious condition that is due to accumulation of fluid and build-up of pressure in the brain. This may require drainage of fluid to relieve the pressure Hydrocephalus can be life-threatening, especially if it is not recognised at an early stage and can lead to irreversible problems including loss of sight.

Children with hydrocephalus often present with problems with a combination of drowsiness, headache (particularly on waking), vomiting and visual disturbance. If these symptoms occur in

the absence of a clear alternative explanation (eg a tummy bug causing vomiting) you should seek urgent medical advice from your GP/emergency department (A&E).

Other possible side effects/effects of the procedure
Other possible side effects reported during clinical trials may have been related to the diagnosis of SMA rather than to the treatment. These included breathing difficulties, constipation, fever, drooling and runny nose.

As nusinersen is delivered directly into the CSF using lumbar puncture, there are a number of side effects that may occur because of the procedure, rather than the medicine itself. These include:

- CSF leakage which may cause troublesome headaches when sitting or standing.
- Headache after the procedure which may persist for a few days (sometimes for longer) and be worse on sitting.
- Nausea or vomiting.
- Back pain/discomfort at the site of the lumbar puncture.
- Infection – this is a rare complication but if infection is introduced this could result in meningitis.
- Bleeding, if this occurs into the CSF space then this can be serious. The risk of this is very small and your doctor will check a blood test before the procedure to make sure that your child is not at higher risk of this complication.
- Nerve injury. The risk of this is very small but if this occurs it could result in pain and / or weakness.

In addition, there are the risks of general anaesthesia or sedation which may be needed to carry out a lumbar puncture in children. Healthy children usually cope well with anaesthesia but there are additional risks in children who have a pre-existing medical condition, such as SMA. For instance, the breathing muscles in babies/children with SMA type 1 are usually weak so that there is a risk that breathing problems may develop following a general anaesthetic. Children can also feel and be sick, feel dizzy or seem agitated when coming around from an anaesthetic or sedation. If a general anaesthetic is planned some investigations, including breathing tests, will be arranged to assess whether or not it is safe to go ahead with the procedure. An anaesthetist will monitor your child throughout the procedure and your child is likely to be admitted to a ward overnight to ensure that they have fully recovered before discharging them home. You may find our leaflet **Your childs' anaesthetic** useful, please ask staff for a copy.

What are the alternatives?

Nusinersen is currently the only licensed treatment for SMA. It is important to understand that with or without nusinersen treatment, there are a range of options aimed at managing symptoms, reducing complications of muscle weakness and maintaining the best quality of life for as long as possible for your child. In particular physiotherapy advice can be very important. Your doctors will make sure you know about these options.

Giving my consent (permission)

Doctors will assess your child to make sure that they meet all the eligibility criteria for the managed access agreement and are eligible to take part. If your child is eligible, doctors will explain about the nusinersen managed access agreement and what it involves. They will then ask you to sign indicating your agreement to enter the managed access agreement. They will talk to you about the plan for when and how your child's treatment will take place.

You can change your mind about the treatment at any time, even after you have signed the form – this will have no effect on other aspects of your child's treatment. If you want to withdraw your child from the nusinersen managed access agreement, just tell the doctors caring for your child.

Your doctors will recommend stopping the nusinersen treatment if they do not feel it is in your child's best interests, perhaps because their condition has worsened, having repeated lumbar punctures is too risky or they are experiencing side-effects. The managed access agreement does give some guidance on specific circumstances under which discontinuation of treatment should be considered.

What happens after the treatment?

Your doctor will decide whether or not the procedure can be done as a day case or whether it requires an overnight admission. If your child has had a general anaesthetic or sedation they may need to remain in hospital for 24 hours after the injection to make sure that they have fully recovered before going home.

What does my child need to do after they go home?

If your child complains of any pain or discomfort at the injection site or if they have headaches, they can be given pain killers such as paracetamol (calpol) or ibuprofen. They should not need to take painkillers for more than two or three days after the procedure. If headaches are persisting, are severe or associated with vomiting and/or fever, your child needs to be seen by a doctor. This would usually be either your GP or a doctor in your local emergency department (A&E).

Will my child have a follow-up appointment?

Your child will be seen in the outpatient clinic by the doctor and physiotherapist for an assessment, this will usually take place two or three times every year.

Contact us

For urgent advice please call 111/ GP / attend local Emergency Department (A&E).

For non-urgent queries you can contact the neuromuscular team:
Clinical nurse specialists **t:** 0207 188 5944
Physiotherapists **t:** 0207 188 4639
Consultants **t:** 0207 188 3998 / 0207 188 4006 / 0207 188 4648

For more information leaflets on conditions, procedures, treatments and services offered at our hospitals, please visit **w:** www.evelinalondon.nhs.uk/leaflets

Evelina London Medicines Helpline
If you have any questions or concerns about your child's medicines, please speak to the staff caring for them or contact our helpline.
t: 020 7188 3003, Monday to Friday, 10am-5pm **e:** letstalkmedicines@gstt.nhs.uk

Your comments and concerns
For advice, support or to raise a concern, contact our Patient Advice and Liaison Service (PALS). To make a complaint, contact the complaints department.
t: 020 7188 8801 (PALS) **e:** pals@gstt.nhs.uk
t: 020 7188 3514 (complaints) **e:** complaints2@gstt.nhs.uk

Language and accessible support services
If you need an interpreter or information about your care in a different language or format, please get in touch. **t:** 020 7188 8815 **e:** languagesupport@gstt.nhs.uk

NHS 111
Offers medical help and advice from fully trained advisers supported by experienced nurses and paramedics. Available over the phone 24 hours a day. **t:** 111 **w:** www.111.nhs.uk

NHS website
Online information and guidance on all aspects of health and healthcare, to help you take control of your health and wellbeing. **w:** www.nhs.uk

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t: 0800 731 0319 **e:** members@gstt.nhs.uk **w:** www.guysandstthomas.nhs.uk/membership

Was this leaflet useful?
We want to make sure the information you receive is helpful to you. If you have any comments about this leaflet, we would be happy to hear from you, fill in our simple online form, **w:** www.guysandstthomas.nhs.uk/leaflets, or **e:** patientinformationteam@gstt.nhs.uk

Leaflet number: 4873/VER1
Date published: December 2019
Review date: December 2022
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