Children’s Services

Nusinersen (Spinraza) for Spinal Muscular Atrophy (SMA) type 1, 2 & 3 and presymptomatic patients

Information for patients and families

This leaflet contains information on the drug nusinersen. It will describe the following:

- what nusinersen is
- how it is given
- what the side effects are
- what the Managed Access Agreement (MAA) is
- which children are eligible to receive nusinersen and why some children may not be eligible to receive it

What is nusinersen?

Nusinersen is a highly specialised drug that can increase the production of SMN (Survival Motor Neuron) protein, which is lacking in SMA. It is produced by the pharmaceutical company Biogen under the brand name SPINRAZA™. It is called an antisense oligonucleotide, which works to increase the SMN protein produced by the SMN2 gene.

How is nusinersen given?

Nusinersen is a medicine which is administered intrathecally by injection. This means that nusinersen is delivered injected into the cerebrospinal fluid (CSF) that surrounds the brain and spinal cord.

A specially trained senior doctor will access the CSF using a lumbar puncture; this is where a needle is inserted through the skin between the bones in your lower spine. You lie on your side, with your legs pulled up and your chin tucked in. This allows the needle to be inserted between the bones more easily.
In children, a lumbar puncture may be carried out either with a local anaesthetic topical cream or with a general anaesthetic or sedation. Your doctor will be able to decide what is best and safest for your child. The doctor will draw off a small amount of CSF and then inject the nusinersen medicine slowly, over five minutes.

The first three doses of nusinersen will be given two weeks apart. This is then followed by the fourth dose 35 days later. A maintenance dose is then given after this, once every four months. Sometimes, it may not be possible to get the timings of administration exact, due to hospital capacity or staffing. However, if this is the case, nusinersen will still be given at the earliest opportunity. It is extremely important to keep to the dates which have been allocated to you for your nusinersen dose.

Nusinersen will be administered on a ward, special treatment room or in a theatre, if your child requires a general anaesthetic. Parents/carers will not be allowed to be present during the administration of the medicine. This is a short procedure and as soon as it is complete your child can be brought back to their bed space and you will be able to be with them whilst they recover.

Following the administration of nusinersen, you will be required to remain completely flat for three to four hours post the procedure.

Formal consent for all nusinersen injections is required and will be taken by the doctor as rolling consent. Consent for the injection can be withdrawn at any point by the parent/guardian.

**What are the side effects of nusinersen?**

Nusinersen is a fairly recently developed medicine; therefore there is currently no data available about its long term side effects. It has, however, been used in several clinical trials worldwide, in which the following side effects of the medicine 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 the blood can clot. 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. Further testing of platelet levels before subsequent injections may be required.

### Effect on kidney function

Nusinersen can affect how well the kidneys work, particular how the tiny filtering units in the kidneys can filter waste products from the blood. Doctors will check your child’s kidney function by taking a blood sample before starting nusinersen and then more frequently if they feel it is necessary.
In addition, the following side effects were reported during clinical trials:

- respiratory symptoms, including breathing difficulties and lung collapse
- constipation
- low salt (sodium) levels
- skin rash
- high temperature
- drooling and excess saliva production
- runny nose

As nusinersen is delivered directly into the cerebrospinal fluid using a lumbar puncture, there are a number of side effects that may occur as a result of this procedure, rather than the medicine itself. These may be:

- CSF leakage
- headache
- sickness
- pain and discomfort
- bleeding
- Hydrocephalus (build-up of fluid on the brain)

In addition, there are the risks of general anaesthesia or sedation which may be required to carry out this procedure in some children. Healthy children usually cope well with anaesthesia but there are additional risks in children who have a pre-existing medical conditions, such as SMA type 1.

For instance, as breathing may already be affected in SMA type 1, there is a risk that breathing problems may develop or become worse. Children can also feel and be sick, feel dizzy or seem agitated when coming round from the anaesthetic or sedation. An anaesthetist/medical doctor will monitor your child before, during and after the procedure to minimise these risks.

What is a Managed Access Agreement (MAA)?

An MAA is an agreement between NHS England and NICE which enables patients to receive new treatments while long-term data on them is still being gathered and before final funding decisions are taken (at the end of the five years). Such an MAA is in place for nusinersen.

All patients entering the MAA for nusinersen must fulfil the following entry criteria:

- No permanent ventilation (≥16 hours/day for 21 consecutive days in the absence of acute reversible infection)/ tracheostomy requirement at baseline;
- Intrathecal injection must be technically feasible in the opinion of the treating clinician and not contraindicated;
- Must not have severe contractures which, in the opinion of the treating clinician, prohibit measurement of motor milestones;
If gained independent ambulation prior to initiation of therapy must still be independently ambulant, with the exception paediatric patients who have lost independent ambulation in the previous 12 months. Independent ambulation is defined as per the WHO definition: patient takes at least five steps independently in upright position with the back straight. One leg moves forward while the other supports most of the body weight. There is no contact with a person or object;

- Must not be type IV SMA patient i.e. must not have symptom onset at or after 19 years of age.
- Must not be type 0 SMA patient.

Providing a patient meets the entry criteria as specified above, due to equity considerations there is no upper limit of age on treatment initiation.

However, if the patient is diagnosed with an additional progressive life-limiting condition where treatment with nusinersen would not provide long-term benefit such as terminal cancer or catastrophic brain injury they will not be eligible for nusinersen.

The doctors will assess your child to make sure that they meet all the criteria above and are suitable to take part.

If your child is suitable, you will be asked to read the MAA and sign the consent, giving permission for you (or your child) to take part in collecting data for inclusion in a database.

If the patient/family/carer is unwilling to comply with associated monitoring criteria as defined in the MAA or refuses to sign consent they will not be eligible for nusinersen.

You can change your mind at any time, even after you have signed the form – this will have no effect on your child’s usual treatment at any point, now or in the future. If you want to withdraw your child from the nusinersen MAA, just tell the doctors caring for your child.

Under the MAA, the treatment will currently be funded for a limited period of time and Biogen will continue to collect evidence to demonstrate the treatment’s efficacy. At the end of the MAA term, this evidence will be considered by NHS England and NICE in order to make future decisions around funding approval for use.

**Why might nusinersen need to be stopped?**

Unfortunately, sometimes it may not be in the best interest of your child to continue with the nusinersen injections and the doctors may withdraw your child from the MAA. If your child’s condition has not improved or has worsened despite having had nusinersen or if having repeated lumbar punctures with or without anaesthesia or sedation becomes too risky for your child, then they may be withdrawn. Stopping criteria is set out in the MAA.

The pharmaceutical company Biogen may also withdraw the supply of nusinersen at any point, as can the Medicines and Healthcare Regulatory Authority (MHRA) who license medicines in the UK.

If you do not comply with the MAA and CUH agreement, nusinersen will be stopped.
We are a smoke-free site: smoking will not be allowed anywhere on the hospital site.
For advice and support in quitting, contact your GP or the free NHS stop smoking helpline on 0800 169 0 169.

Other formats:

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Document history
Authors
Katrina Cousins, Paediatric Neuromuscular Clinical Nurse Specialist
Pharmacist
Nigel Gooding, Consultant Pharmacist – Neonates & Paediatrics
Department
Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ www.cuh.org.uk
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