In collaboration with researchers, nusinersen was developed by Ionis Pharmaceuticals and Biogen Idec. On 1st June 2017, the European Commission granted nusinersen marketing authorisation\(^1\) under the trade name Spinraza\(^{TM}\) for treatment of those with ‘5qSMA’. This refers to a mistake in the \(SMN1\) gene on the fifth chromosome in the chromosomal region labelled ‘q’ which affects those with SMA Types 1, 2, 3 and 4. This is the first treatment ever for SMA to reach this stage.

Deciding whether this is a treatment you want to request for your child is very personal. This information sheet aims to give you information which you can consider and discuss with your medical team to support you in making your decision.

Includes

- Which children can access the treatment?
- How nusinersen works and how it is given
- What benefits have been seen in clinical trials?
- Possible side effects of the drug and treatment method
- What other care is needed and what are my options?
- Next steps if you are interested in treatment for your child
- Sources of support
Which children can access the treatment?

Access in Scotland

Since May 2018, the Scottish NHS has funded this treatment for children with ‘symptomatic type 1 SMA (infantile onset)’.

Access in England, Wales and Northern Ireland

Since 1st November 2018 it has not been possible to access nusinersen in these countries. To find out why this is and what’s happening now to try to open up access again, go to: www.smasupportuk.org.uk/the-uk-expanded-access-programme-for-nusinersen-for-children-with-sma-type-1 If, after reading this leaflet you would like to try to access nusinersen treatment for your child, please make sure to talk with your medical team as they should have the latest information about access.

What does nusinersen do? / How does nusinersen work?

SMA affects a set of nerve cells called the lower motor neurons which run from the spinal cord out to our 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 a gene called Survival Motor Neuron 1 (SMN1). We all have two copies of this gene. Children with SMA have mutations / coding errors in both copies of their 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.

Another gene called SMN2 also helps with the production of SMN protein. As well as having the two faulty SMN1 genes, children with SMA Type 1 have fewer copies of the SMN2 gene so also miss out on this ‘back-up’ source of SMN protein.

Nusinersen is a highly-specialised medicine that can increase the production of SMN protein by targeting the process through which it is produced by the SMN2 gene.
What benefits has nusinersen shown in clinical trials?

Biogen’s clinical trial, called ENDEAR, was with 122 children with SMA Type 1 of whom two-thirds were treated with nusinersen and one-third were not treated.

Results for the treated children were:

- 51% improved their motor milestones, compared with 0% not receiving treatment:
  - 22% of infants had head control,
  - 10% could roll over,
  - 8% could sit without support,
  - 1% able to stand, compared with 0% not receiving treatment

- 61% did not require a ventilator and were still alive, compared to 32% not receiving treatment.

A greater effect was seen in infants receiving nusinersen at an earlier age (the example used was less than around 13.1 weeks).

The aim of treatment is to achieve any of these outcomes but it is not possible to say with any certainty that your child will show improvements.

How is nusinersen given?

Nusinersen is delivered directly into the Cerebro Spinal Fluid (CSF). Doctors access the CSF using a lumbar puncture. This is when a needle is inserted through the skin into the space between the vertebrae of the spine (back bones). Doctors may use x-ray to locate the best place for the insertion and they will usually use a local anaesthetic such as ‘numbing cream’, although occasionally a general anaesthetic may be considered necessary. A small amount of CSF is drawn off and then nusinersen is injected over one to three minutes.

Injections are given as follows:

- On the first day of treatment, day 0
- Then around day 14, day 28 and day 63
- Then once every 4 months
What are the possible side effects of nusinersen?

As nusinersen is a recently developed medicine, there is no data available about its long-term effects. It has, however, been used in several clinical trials, in which the side effects have been noted:

- **Effects on blood clotting**

  Platelets are important components of the blood which are necessary for clotting of blood. If the platelet level is low, there is a risk of bruising and bleeding or haemorrhage. Nusinersen (and other similar medicines) can affect the levels of platelets in the blood. Doctors will check your child’s platelet levels before starting nusinersen and then at regular points for as long as they are receiving treatment. If the platelet count is low, it may not be safe to go ahead with the administration of nusinersen.

- **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. This is checked by a blood test and by testing a urine sample before starting nusinersen and then at regular points for as long as they are receiving treatment.

- **Other possibilities**

  The following other possibilities were reported during clinical trials but these may not have been due to the treatment itself; for example, they could have been due to the SMA or an unrelated infection:

  - Respiratory symptoms, including breathing difficulties and lung collapse
  - Constipation
  - Low salt levels
  - Skin rash
  - High temperature
  - Drooling and excess saliva production
  - Runny nose

- **Risk of Hydrocephalus**

  There have been reports of rare cases of communicating hydrocephalus during treatment with nusinersen; most cases developed after 2 to 4 loading doses. From September 2018 healthcare professionals have been advised by the UK Medicines and Healthcare products Regulatory Agency (MHRA) to discuss this risk with parents considering the treatment.
What are the possible side effects of the lumbar puncture procedure?

There are a number of side effects that can happen due to the procedure rather than the medication. The most frequent are:

- Local pain / discomfort in the back at the site of the lumbar puncture. This should settle within a few days.
- Headache, sometimes with vomiting. This usually settles within a day or two but occasionally can continue for a longer period and need hospital treatment

Other much rarer complications include:

- Bleeding – this is unlikely unless your child has a problem such as a low platelet count. If your doctor identifies a disorder that predisposes to bleeding they will advise you whether it is safe to go ahead.

- More persistent headaches. When these symptoms are more persistent, it may be because there is a continuing small leak of the fluid (CSF) and very rarely this can then need treatment to stop the continuing leakage.

You can discuss all these with your medical team before making any decision about going ahead with treatment. You would also have the opportunity to go over them again if you do decide to go ahead.

Mostly the procedure is carried out without sedation or general anaesthesia. If either of these is required, though healthy children usually cope well, there are additional risks in children who have a pre-existing medical condition, 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. Children can also feel and be sick, feel dizzy or seem agitated when coming around from the anaesthetic or sedation. An anaesthetist / medical doctor would monitor your child before, during and after the procedure to minimise these risks. Again, you can talk to your medical team about what your child would need for the lumbar puncture before you make any decision and go over this again if you do decide to go ahead.

Will my child only need nusinersen?

Nusinersen is not a cure for SMA Type 1, it’s a treatment and, at the moment, it’s the only one available.

Because SMA Type 1 is a life-threatening condition and neither the longer-term outcomes of nusinersen treatment is yet known, nor how any individual child will react to treatment, a family would also be offered what is called palliative care. This is an active approach to care, aiming to support the physical, emotional and practical needs of your child and family from the point of diagnosis onwards. It includes the management of symptoms and reducing complications of muscle weakness following international guidelines as set out in the 2017 International Standards of Care for Spinal Muscular Atrophy. Palliative care also takes into
account any cultural and spiritual needs you may have and practical support you need. The overall aim is to achieve the best quality of life for your child.

What alternatives are there to nusinersen?

Nusinersen is the only treatment available at the moment. There are other clinical trials of other drugs in the pipeline. If any are happening in the UK, your doctors will discuss these with you and whether your child would be eligible. You can also register with the UK SMA Patient registry which will let you know about any UK trials. You can keep up-to-date with developments in research via SMA Support UK’s website and monthly e-news. Please see contact information at the end of the information sheet.

There are ‘unknowns’ about both the nusinersen treatment in general and about how your individual child will respond. After talking with your medical team, you may decide this is not the right option for you and your child. This is a very personal decision. Your team will completely respect your wishes and ensure that you and your child receive all the care and support you need from palliative care services.

I’m interested in nusinersen for my child, what happens next?

Scotland
Your Scottish medical team will talk with you about what Centre is able to administer treatment and arrange for your child to be assessed for eligibility.

If your child is eligible, doctors will explain again about the treatment and what it involves. They will then ask you to record that you understand what they have said and give your permission for your child to take part. They will talk to you about the plan for when and how your child’s treatment would take place.

You can change your mind at any time, even after you have signed the form consenting to treatment. If you want to withdraw your child or stop treatment, just discuss this with the doctors caring for your child. They will completely respect your wishes and ensure other appropriate care and support is in place.

Your doctors may want to stop treatment if they don’t feel it’s in your child’s best interests, perhaps because your child’s condition has worsened or having repeated lumbar punctures with anaesthesia or sedation is too risky. Again, if this happens, they will discuss this fully with you and make sure you have other appropriate support and care in place.

England, Wales and Northern Ireland
Patient advocacy charities and SMA clinicians are doing all they can to press NICE, NHS England and Biogen to find a solution for accessing nusinersen. The situation may change; for latest information ask your medical team and also please check: www.smasupportuk.org.uk/what-we-are-doing-to-progress-access-in-the-uk
Sources of Support

Your medical team are the best people to talk to about the treatment and about the hospital and community support available to you.

In a more general way, Spinal Muscular Atrophy Support UK provides free information and support to families in the UK affected by SMA. Multisensory toy packs are also available free of charge for babies in the UK diagnosed with SMA Type 1. Our outreach workers are able to visit you at home. They offer personalised support and information and are available to answer questions. They can discuss with you the support you and your family can access. Please note, we do not give medical advice.

Further Resources

- **SMA Support UK** research-related information:

  You will find more information about nusinersen and what is happening in the UK here: [www.smasupportuk.org.uk/nusinersen](http://www.smasupportuk.org.uk/nusinersen)

  This website section tells you about other research developments: [www.smasupportuk.org.uk/drug-treatments-whats-happening-now](http://www.smasupportuk.org.uk/drug-treatments-whats-happening-now)

  You can keep up to date by signing up for SMA Support UK’s monthly e-news: [www.smasupportuk.org.uk/sign-up-for-mailings](http://www.smasupportuk.org.uk/sign-up-for-mailings)

- **SMA Support UK** condition-related information

  You will find a wide range of other leaflets and resources in this section of the website: [www.smasupportuk.org.uk/information](http://www.smasupportuk.org.uk/information)

  If your child has been recently diagnosed you may find this guide helpful: [www.smasupportuk.org.uk/recently-diagnosed-with-sma](http://www.smasupportuk.org.uk/recently-diagnosed-with-sma)

- **Standards of Care for Spinal Muscular Atrophy (2017)**

  You can read about and download the 2017 internationally agreed Standards of Care from here: [www.smasupportuk.org.uk/international-standards-of-care-for-sma](http://www.smasupportuk.org.uk/international-standards-of-care-for-sma)
If you have any feedback about this information, please do let us know at supportservices@smasupportuk.org.uk

We are grateful to the writers and reviewers who assist us in our information production. A list of who this includes may be viewed here: www.smasupportuk.org.uk/our-writers-and-reviewers-panel

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References


