1. **What is nusinersen and how does it work?**

Nusinersen belongs to a group of medicines known as antisense oligonucleotides. It is only used to treat 5q variant spinal muscular atrophy (5q SMA).

People with SMA do not have enough of a protein called ‘survival motor neuron’ (SMN) protein. This protein is essential for the nerve cells, known as motor neurons that help control muscles. Motor neurons are found in the brain and spinal cord and they make contact with muscles.

The SMN protein is made in our cells from two genes, *SMN1* and *SMN2.* People who have SMA lack the *SMN1* gene but have the *SMN2* gene, which mostly produces a short SMN protein that does not work as well as a full-length protein.

Nusinersen is a synthetic antisense oligonucleotide (a small piece of man-made genetic material) that targets the *SMN2* gene and enables it to produce more functional, full-length SMN protein.

Nusinersen is manufactured by the pharmaceutical company Biogen under the trademark SPINRAZA.

For more detailed information see:

EMA Agreed Patient Information Leaflet <https://www.medicines.org.uk/emc/product/2715/pil>

And <https://smauk.org.uk/more-detail-on-how-nusinersen-works-in-sma>

1. **Which cells and tissues in the body does it reach?**

Our nervous system is protected by a border called the ‘blood-brain barrier’. Nusinersen cannot cross this border so it has to be delivered directly into the cerebrospinal fluid (CSF) via an injection into the spinal cord. Upon injection, nusinersen reaches the motor neurons and other cell types in the spinal cord. It may have limited ability to reach other parts of the body. We currently do not know how much SMN protein may be needed in other parts of the body.

You can find more details about nusinersen and how it works in the European Medicines Authority (EMA) agreed Patient Information Leaflet:

<https://www.medicines.org.uk/emc/product/2715/pil>

1. **What have clinical trial results and other evidence shown about the possible outcomes with nusinersen treatment?**

You can read a summary of the evidence from the clinical trial with children with SMA Type 1 in this information sheet:

* [**Nusinersen (also known as SPINRAZATM) treatment for those diagnosed with SMA Type 1**](https://smauk.org.uk/files/files/Publications%20and%20Leaflets/Nusinersen%20Treatment%20for%20those%20diagnosed%20with%20SMA%20Type%201%20V3_1%20November%202019.pdf)

You can read a summary of the evidence from clinical trials with children with SMA Type 2 and longer-term results for children age 2 – 15 years in this information sheet:

* [**Nusinersen (also known as SPINRAZATM) treatment for those diagnosed with SMA Type 2 or 3**](https://smauk.org.uk/files/files/Publications%20and%20Leaflets/Nusinersen%20Treatment%20for%20those%20diagnosed%20with%20SMA%20Type%202%20or%203%20v1_1%20November%202019.pdf)

An in-depth review of clinical data (intended for Health Care Professionals] can be found at:

<https://www.medicines.org.uk/emc/product/2715/smpc>

1. **Has nusinersen shown positive effects in older children and adults?**

Nusinersen reduces the loss of nerve cells and so may improve muscle strength in those with 5q SMA. The clinical trial outcomes for children with SMA Types 1 and 2 and the longer-term studies of children with 5q SMA ages 2 – 15 years can be found in the above information leaflets:

There have been no clinical trials of nusinersen with adults.

Nusinersen has been licensed in the USA and in Europe for the treatment of adults and children. In some countries, adults are receiving treatment. Clinicians and Biogen, are collecting and studying information about the outcomes of this treatment. There are no published studies available at the moment.

Interpreting clinical trial results and other ‘real-world’ data on the outcomes of nusinersen treatment can be complicated. The implications that this information may have for you / your child are best discussed with your clinician in the first instance.