



Translarna: treatment for Duchenne muscular dystrophy

Who is it for?

Translarna (also known as ataluren) has been developed to treat children whose Duchenne muscular dystrophy is caused by a '**nonsense**' **mutation**. Translarna is the first drug to address an underlying genetic cause of muscular dystrophy to be recommended for use on the NHS in England.

It is available for children who are:

- ▶ aged five years and over
- ▶ are still able to walk – 10 steps unaided

If you are unsure if your child meets these requirements, please speak to his/her neurologist.

Currently, Translarna is not licenced for younger children or children who have lost the ability to walk. More clinical trials will be needed to assess the efficacy and safety of Translarna in these groups of individuals.

Steroids

It is up to an individual's clinician as to whether they recommend steroid treatment alongside Translarna, there is no requirement to start steroid treatment.

Is Translarna available for girls?

The licence for Translarna states a nonsense mutation of Duchenne is required and it does not exclude girls. For girls who have a nonsense mutation, access to Translarna should be discussed with their neurologist.

What is a nonsense mutation?

A gene is a series of letters which carry the information necessary to produce a protein. Genetic mutations can be thought of as spelling mistakes that change the DNA and alter the information it carries.

Different types of mutation can cause a lack of a protein called dystrophin in the muscles, leading to Duchenne muscular dystrophy. Without dystrophin the muscle fibre membranes become damaged and eventually the muscle fibres die.

The main types of mutation causing Duchenne muscular dystrophy are: deletions (where part of the gene is missing altogether), insertions (where an additional piece of DNA is inserted into the gene), duplications (when part of the gene is repeated) and point mutations (where one letter is replaced by another).



Point mutations occur when a single letter in the DNA code is changed and alters the information needed to produce a protein. The mutation can occur anywhere in the dystrophin gene and can sometimes lead to a “stop signal” being inserted into the middle of a gene. This leads to a truncated protein, which is unstable and degraded by the cell. It is this type of point mutation that is known as a **nonsense mutation**. Nonsense mutations are responsible for 10 to 15 percent of all Duchenne muscular dystrophy cases.

Nonsense mutations are different from deletions, insertions and duplications.

How do I know if my child has a nonsense mutation?

The only way to know for sure which type of mutation your child has is through genetic testing. Genetic testing is usually performed on a small sample of blood. The test aims to identify the mutation causing the condition in an individual. Different tests are used to identify deletions, insertions and point mutations. Alternatively the whole gene can be sequenced reading all the information it contains.

If you do not know what type of mutation you or your child has, we would recommend that you speak to your specialist (neurologist), your GP or a genetic counsellor who will be able to advise you further. Take a look at letters from your clinic as it may be mentioned in them.

How does Translarna work?

Translarna works by enabling the protein-making apparatus in cells to ignore and move past the premature stop signal, allowing the cells to produce a functional dystrophin protein. Translarna is taken orally in a powdered solution that is dissolved into a small amount of water.

What have the research trials shown?

The safety and effectiveness of Translarna has been studied in several clinical trials including a large study carried out called “ACT” in Europe and the US. In this particular study, a total of over 228 individuals over the age of five participated. All boys had a nonsense mutation and were still able to walk. The main measure of effectiveness was the distance the participants could walk in six minutes (known as the six-minute walk test) after 48 weeks of treatment with Translarna. This was compared with the results of those who took a placebo, an inactive substance designed to resemble the drug being tested.

The study showed that at the end of 48 weeks of treatment, on average, the participants taking Translarna were able to walk 15m further in six minutes than those who were taking placebo. However, these results were not statistically significant which means that they could have arisen by chance.

The data was subsequently analysed depending on how far the boys could walk in six minutes at the start of the trial. A total of 99 boys fell into this sub-group, 47 of whom received Translarna and 52 who received the placebo. The results showed that the boys who received Translarna were able to walk 47m further in six minutes than those who were taking the placebo. This difference was statistically significant.



Although the largest benefit was observed in this group it does not mean that younger or older boys will not benefit. It is believed that earlier treatment might result in preventing muscle wasting but the duration of this trial might have been too short.

For more information on the clinical trials, take a look at the research sections of our [website](#) or contact the research team on research@muscular dystrophyuk.org

Are there side-effects associated with Translarna?

The most common side-effects associated with Translarna are nausea (feeling sick), vomiting and headaches.

Translarna and availability on the NHS

Translarna is available on the NHS in England as a result of NICE's formal guidance issued in July 2016.

NICE's decision to recommend Translarna for funding by NHS England is based on a **Managed Access Agreement**. We are pleased that the Managed Access Agreement – which Muscular Dystrophy UK called for and has worked to help develop – has led to the approval of the drug.

In a Managed Access Agreement, a drug is made available for a limited period of time (in this case for five years), often at a discounted price. This allows further evidence in support of the results of the large clinical study to be gathered on the benefit of Translarna while also ensuring that patients receive access to the drug.

Under the terms of the Managed Access Agreement, patients' progress will be monitored using the North Star Ambulatory Assessment. Outcome measures developed by the North Star Network were also crucial in demonstrating in medical trials that Translarna is clinically effective.

The agreement states boys should stop treatment no later than 6 months after becoming fully non-ambulant (defined as no longer able to stand even with support and entirely dependent on wheelchair use for all indoor and outdoor mobility, unless this is because of an accident or an un-related illness).

The North Star Network is a group of clinicians, senior physiotherapists and healthcare professionals specialising in the care of young patients with Duchenne muscular dystrophy.

What about the rest of the UK?

The Managed Access Agreement applies only to England. Translarna is also available in **Wales, Northern Ireland** and the **Isle of Man** as a result of NICE's guidance being implemented.

Translarna is also available in **Scotland** but the process for approval was entirely separate. The Scottish Medicines Consortium recommended Translarna not be approved for funding by the NHS in Scotland, but following pressure on the Scottish Government's First Minister Nicola Sturgeon, Translarna is now available through an individual patient treatment request which must be submitted to the Health Board by a patient's consultant.

For more information on [faster access to emerging treatments](#) across the UK, please contact Jonathan Kingsley on j.kingsley@muscular dystrophyuk.org or call 020 7803 4839.

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Here for you

The friendly staff in the care and support team at the Muscular Dystrophy UK's London office are available on **0800 652 6352** or **info@muscular dystrophyuk.org** from 8.30am to 6pm Monday to Friday to offer free information and emotional support.

They are more than happy to signpost you to specialist services close to you, or to other people who can help if they are not able to support you.

www.muscular dystrophyuk.org