SPINRAZA (NUSINERSEN) MANAGED ACCESS AGREEMENT (MAA)

1. What is a MAA?

The National Institute for Health and Care Excellence (NICE) makes recommendations on new medicines by reviewing clinical and cost effectiveness evidence. When a medicine shows promising potential but there are gaps in the clinical evidence, it may be recommended for time limited NHS access in England as part of a MAA. This is a way that doctors and the NHS can assess the long-term benefits of a new medicine by collecting agreed test results over a given period of time in patients who have certain symptoms of a condition. At the end of the MAA period, NICE will review the new evidence to make a final recommendation as to whether the medicine will be available to access via the NHS in the long term.

The purpose of a MAA is:

- To enable patients in England access to promising treatments for a specified length of time.

- To collect new information on patients receiving a treatment that will help to address any clinical uncertainties that were identified when the drug was originally evaluated by NICE. This may be long term follow up on patients already receiving the treatment or information on new patients starting the treatment.

- To help the NICE appraisal committee at the end of the agreement to make a better-informed decision on whether a treatment is appropriate for patients and whether it is a good use of NHS money.

For a MAA to achieve its purpose, it is very important that patients attend follow up appointments and all the necessary data is collected (see Data Collection Section) as this will be used to make an evidence case for whether or not there will be future access to a treatment once the MAA has ended.

2. Who has agreed to the nusinersen MAA?

This MAA has been agreed between:

- NICE
- NHS England and NHS Improvement
- Biogen (the drug company that makes Spinraza^{TM})

The following groups / individuals have signed up to the agreement:

- Muscular Dystrophy UK (Patient Group)
- SMA UK (Patient Group)
- TreatSMA (Patient Group)
- Professor Francesco Muntoni, FRCPCH, FMedSci: Dubowitz Neuromuscular Centre and MRC Centre for Neuromuscular Diseases (a lead clinician who represents the healthcare professionals at treatment centres and the SMA REACH UK registry)

3. How long will this MAA last?

This MAA will last for five years, from 24th July 2019 to 23rd July 2024.

The MAA data collection period will last for a minimum of three years and automatically cease at the end of the fifth year (July 2024), unless NICE guidance is published sooner.

4. Who can access nusinersen treatment via this MAA?

There are three sets of criteria that have to be met:

- the broad **eligibility criteria**
- the **starting criteria**
- the **exclusion criteria.**

4.1 Eligibility Criteria:

It is important to know that the definition of '**walking unaided'** (referred to within the MAA starting criteria) is the World Health Organisation (WHO) criteria as follows:

> 'Is able to take at least five steps independently in the 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'.

The MAA eligibility criteria include those who have had a clinical diagnosis of 5q SMA of:

- Type 1. This includes any affected adults who were given this diagnosis before the age of 18 years and who have not been able to walk unaided
- Type 2, including any affected adults, who were diagnosed before the age of 18 years and who have not been able to walk unaided
- Type 3, including any affected adults, who were diagnosed before the age of 18 years, and who are still able to walk unaided
- Type 3 aged under 19 years who, if they were previously able to walk unaided, have *either* lost this ability in the 12 months before their assessment for nusinersen *or* lost their ability to walk in the 12 months before the publication of the NICE guidance on 24 July 2019

Pre-symptomatic infants / children who are potentially eligible for treatment are those who have:

- Had a genetic confirmation of SMA (*either* a homozygous gene deletion *or* a homozygous mutation, *or* a compound heterozygous mutation of the *SMN1* gene) ***and***
    - have two *SMN2* copies or fewer ***or***
    - have three *SMN2* copies and a sibling diagnosed with SMA type 1 or 2

Pre-symptomatic infants / children who will be monitored and would potentially be eligible if they start to show symptoms of SMA are those who have

- Had a genetic confirmation of SMA (as above) ***and***
    - have three *SMN*2 copies and no sibling diagnosed with SMA type 1 or type 2 ***or***
    - have four *SMN*2 copies

Now that the MAA has been agreed, the Expanded Access Programme for those with SMA Type 1 has closed and it is no longer possible to access treatment with the drug via this route.

Patients who were receiving nusinersen treatment in England before the MAA started on 24th July 2019, who meet the entry / starting criteria of the MAA (see below) and want to continue treatment will be asked to enrol onto the MAA by signing the MAA informed assent form.

Patients who were receiving nusinersen in England before the MAA started (before 24th July 2019) and who **do not meet** the treatment starting criteria of the MAA will continue to have their treatment funded by Biogen (the drug company who make Spinraza™).

4.2 Not eligible

This includes those who have had a clinical diagnosis of 5q SMA with:

- Type 0 symptomatic infants
- Type 4 - where the onset of symptoms has been at aged 19 or older
- Type 3 – who are unable to walk, except for the group described as eligible above

4.3 Starting/entry criteria

If you / your child meet the eligibility criteria, you also need to meet these starting / entry criteria. These criteria were agreed following detailed discussion involving NHS England and NHS Improvement, NICE, SMA clinicians, patient groups and the manufacturer of Spinraza™ (Biogen).

The child / young person / adult must:

- Not be on permanent ventilation. This is:
    - when they need to use a non-invasive ventilator (NIV such as BiPaP) for more than 16 hours/day for 21 consecutive days and this is not because of an acute reversible chest infection *or*
    - when they have a tracheostomy
- In the opinion of the treating clinician be someone for whom it is technically feasible and safe to give an intrathecal injection
- Not have had spinal fusion surgery following a diagnosis of scoliosis which, in the opinion of the treating clinician, means safe administration of nusinersen is not possible
- Not have severe contractures which, in the opinion of the treating clinician, make it impossible to measure motor milestones;

4.4 Exclusion criteria

These describe any conditions that may prevent a patient from receiving treatment within the MAA. These include if a child, young person or adult 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.

Other exclusions are if the patient/family/carer:

- is unwilling to comply with required monitoring criteria that is explained to them
- refuses to sign consent to treatment

- is unwilling to cooperate with the treatment centre so that they/their child receive the appropriate standard of care management for their condition and circumstances, especially for nutrition and respiratory care and vaccinations, such as influenza and respiratory syncytial virus **(**RSV).

5. Stopping criteria

Nusinersen is likely to be stopped if a patient is not or is no longer benefiting from the treatment. In making a decision to stop or continue treatment, the treating clinician will take the following criteria into consideration:

- worsening of motor function;
- requirement for permanent ventilation;
- an inability to administer the drug safely.
- being unable to regain ambulation within 12 months of treatment (applicable to paediatric patients who have lost ambulation in the 12 months prior to initiation of treatment)

Anyone considering starting treatment will have the opportunity to discuss these stopping criteria with their clinical team.

6. What happens at the end of the MAA?

Towards the end of the MAA period (approximately year four) the company that produces Spinraza™ (Biogen) will make an evidence submission to NICE. This will include the data that has been collected from patients throughout the MAA (see Data Collection). Patient groups and clinicians can also contribute to this process and make submissions.

The NICE appraisal committee will then evaluate the evidence submissions. They will consider both the clinical and cost effectiveness of the drug and make a final decision on whether nusinersen should continue to be funded on the NHS after the MAA has expired.

If NICE reviews the evidence that has been collected within the MAA and no longer recommends Spinraza™ for NHS funding, then all NHS England funding will stop. NHS England will agree with the company if and how treatment for existing patients will continue.

This means that if NICE no longer recommends Spinraza™ for NHS funding or makes no recommendation, treatment with Spinraza™ may stop regardless of whether a patient is doing well on treatment or not. No new patients would be able to start treatment. In this scenario all patients would have a discussion with their clinical team regarding the most appropriate NHS standard of care treatment.

If NICE recommends Spinraza™ for further NHS funding, then Spinraza™ will continue to be funded in England according to the arrangements between NICE and NHS England at that time.

7. What is the role of the MAA Clinical Panel?

The role of the Clinical Panel is to ensure that decision making is consistent and equitable. It is there to:

- Provide advice to clinicians at treating centres on interpretation of the MAA criteria, including: starting and stopping criteria, and diagnosis

- Give advice to clinicians at treatment centres on the feasibility of safe intrathecal administration of the drug, particularly in light of spinal surgery and taking into account spinal instrumentation.
- Advise NHS England on any patients who appear to meet stopping criteria but who remain on treatment.

Membership comprises:

- Representatives from NHS England (who chair and run the Panel)
- Pharmaceutical adviser
- Two neuromuscular physicians who are expert in the treatment of children with SMA
- Two neuromuscular physicians who are expert in the treatment of adults with SMA
- Two physiotherapists who are expert in the treatment of patients with SMA

It is likely that the Panel will meet monthly, although this will be on a virtual basis to allow rapid responses to queries.

Queries to the Clinical Panel will be submitted via healthcare professionals at treatment centres.

8. What is the role of the Managed Access Oversight Committee (MAOC)?

The MAOC is responsible for monitoring the implementation of the MAA and recommending actions to support its operation. This may include:

- Monitoring the progress of data collection and analyses as described in the MAA and data specification
- Reviewing enrolment to and continuation in the MAA, including the number of patients who have discontinued treatment
- Agreeing communications (including for patients, clinicians, service providers).
- Considering proposed amendments to the MAA (which would be subject to renegotiation by NHS England and the Company)
- Receiving updates from the NHS England Clinical Panel on patient referrals and prioritisation relevant to the data collection agreement

Membership comprises:

- NICE Managed Access Associate Director (Chair)
- NICE Technical Advisor or Analyst
- NICE Data Collection Manager (Co-chair)
- A representative from NHS England (who will also provide updates on behalf of the clinical panel)
- Two paediatric clinical experts in the treatment of children with spinal muscular atrophy
- One clinical expert in the treatment of adults with spinal muscular atrophy
- One physiotherapist involved in the treatment of spinal muscular atrophy
- A representative from Spinal Muscular Atrophy UK (patient organisation)
- A representative from TreatSMA (patient organisation)
- A representative from Muscular Dystrophy UK (patient organisation)
- SMA-REACH Academic Lead
- SMA-REACH (Global) Trial Manager
- Two standing representatives from Biogen (company) and 1 substitute representative.

It is anticipated that the committee will meet six-monthly. If patients and their families have questions for the MAOC these can be delivered via the Patient Advisory Groups listed above.