NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Contract Variation Agreement No. 1 to Managed Access Agreement for Ataluren (Translarna™) for treating nonsense mutation Duchenne muscular dystrophy

Contract/Variation Reference: On 4 July 2016, NHS England and NHSE Improvement (NHSE&I), PTC Therapeutics International Limited (PTC), NICE together with two other parties (collectively the "Parties" and each a "Party") entered into the "Managed Access Agreement for ataluren relating to the supply of ataluren (Translarna™) for treating nonsense mutation Duchenne muscular dystrophy (the **"MAA"**).

IN WITNESS OF WHICH the Parties have signed this Variation Agreement No.1 on the date(s) shown below

Date of agreement	28 July 2021
NHS England and NHS Improvement	Signed ..... John Stewart National Director, Specialised Commissioning, NHS England and NHS Improvement
PTC Therapeutics International Limited	Signed ..... Adrian Haigh Senior Vice President, Head of International PTC Therapeutics International
Clinical Expert (NorthStar Clinical Network)	Signed ..... Adnan Manzur NorthStar Clinical Leader
Patient Organisation(s)	Signed ..... Catherine Woodhead, CEO MDUK ..... Florence Boulton, National Director, Action Duchenne
NICE	Signed ..... Brad Groves, Associate Director, Managed Access, NICE

Date of this Variation Agreement No.1: Day 28 July 2021

This variation agreement relates to the variation of the MAA as set out below (the "Variation Agreement No.1").

Capitalised words and phrases in this Variation Agreement No.1 have the meanings given to them in the MAA.

In consideration of their respective obligations under the MAA (as varied by this Variation Agreement No.1) the Parties have agreed to the following variation to the MAA:

1. Clause 3.1 shall be deleted and replaced as follows:

    3.1 This MAA shall take effect on the date of publication of the Guidance and will remain in force until the earlier of: (i) publication of the updated NICE HST for ataluren or; (ii) 20 January 2023.The MAH will provide the relevant data required for the update of the guidance in a submission to NICE on the product performance in accordance with the evaluation timelines issued by NICE. The relevant data to be incorporated into the MAH evidence submission is including but not limited to data collected during the MAA term from the sources detailed in this MAA and the analyses detailed in the statistical analysis plan. NICE will issue updated guidance to the NHS in England based on a review of the evidence submitted by the MAH and stakeholders for the guidance update of ataluren within its licenced indication.

2. Clause 9.1 and 9.2 shall be deleted in their entirety.

3. Appendix 1 of the Addendum to Managed Access Agreement July 2019 shall be deleted in its entirety and replaced as set out in Appendix 1 of this Variation Agreement No.1

All other definitions terms and conditions contained in the MAA shall continue to apply in full force and effect.

The variations set out in this Variation Agreement No.1 take effect on Day 28 July 2021.

Appendix 1

Ataluren (Translarna™) for nonsense mutation Duchenne muscular dystrophy (nmDMD)
Managed Access Patient Agreement

NICE have approved reimbursement of ataluren, licensed as Translarna™, subject to a number of measures that will be used to assess the compliance to a Managed Access Agreement (MAA)[1] in England and to ensure that all relevant stakeholders have a common understanding that such measures have the agreement and backing of all involved and will therefore be implemented.

The NICE MAA includes: -

- The clinical criteria for starting and stopping treatment with ataluren.
- Agreement that patient information will be collected and included into the NorthStar database in order to monitor patients' responses to ataluren treatment.
- Agreement between the MAH and NHS England, which is in addition to the patient access scheme, in order to manage financial risk for NHS England.

1. Patient Eligibility

The clinical community and patient organisations feel it is appropriate and right that all patients diagnosed with Duchenne muscular dystrophy (DMD) resulting from a nonsense mutation who are aged 2 years and over and who are ambulatory should have access to ataluren (Translarna™) in England.

Ataluren will be added to existing standard treatment, including use of corticosteroids.

Patients must be made aware of the start and stop criteria for receiving ataluren treatment and are required to attend their clinics 2 times for assessment within a 14-month period.

All patients will sign up to the 'Managed Access Patient Agreement'.

2. Access to treatment and data collection

The start criteria in this MAA have been used because they form the basis upon which the European licence for Translarna™ (ataluren) was granted.

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[1] Variation to the Addendum to Managed Access Agreement: ataluren for treating nonsense mutation Duchenne muscular dystrophy (nmDMD), dated 20 July 2019.

3. Start Criteria

- Patients must have a confirmed diagnosis of Duchenne muscular dystrophy resulting from an in-frame nonsense mutation in the dystrophin gene. The presence of a nonsense mutation in the dystrophin gene should be determined by genetic testing.
- Patients must be aged 2 years and older and able crawl, stand with support or walk.
- Patients should only start once a full set of standard baseline specialist neuromuscular clinical and physiotherapy assessments (including an initial blood test) have been obtained.
- Patients / parents will be expected to attend their clinic 2 times a year for assessment within a 14-month period.

4. Stop Criteria

Patients will become ineligible for further treatment where: -

- The patient is non-compliant with assessments for continued therapy where non-compliance is defined as fulfilling fewer than 2 attendances for assessment within any 14-month period.
- Patients who are taken off treatment will continue to be monitored for disease deterioration and supported with other clinical measures. These patients should continue to be assessed to allow gathering of important information.

The MAA (and therefore agreed funding for ataluren) expires upon publication of the updated NICE guidance for ataluren **OR** on 20 January 2023, whichever occurs earlier.

Accordingly, there are currently no arrangements to enable access to ataluren to be available as part of standard NHS care following the expiry of the MAA. Any continued access to ataluren beyond this point will be subject to NHS England agreeing the terms of such funding with PTC, the manufacturer of ataluren.

Appendix 1

Ataluren (Translarna™) for nonsense mutation Duchenne muscular dystrophy (nmDMD)
Managed Access Patient Agreement

If you feel that you and/or your child will be able to comply with the above, please fill in your details below and sign for reimbursed treatment to begin.

Patient Name: _____

Parent/Carer Name: _____

Parent/Carer Signature: _____

Date: _____

Name of Clinician: _____

Signature of Clinician: _____

Date: _____