Questions and answers on the managed access agreement for risdiplam (January 2022)

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What are the clinical circumstances under which it would be appropriate for an individual to continue to have treatment with risdiplam (or nusinersen) after treatment with onasemnogene abeparvovec or to be initiated on treatment with risdiplam (or nusinersen) after treatment with onasemnogene abeparvovec?

All individuals being considered for treatment with risdiplam (or nusinersen) must meet the Starting criteria and must not meet the Stopping criteria set out in the published Managed Access Agreement (MAA).

In addition, there is specific information on the NICE website if an individual is being considered for treatment with risdiplam (or nusinersen) following treatment with onasemnogene abeparvovec.

If patients have had self-funded treatment with onasemnogene abeparvovec abroad, can they have access to risdiplam (or nusinersen), regardless of their clinical situation?

The above criteria for access to risdiplam (or nusinersen) following treatment with onasemnogene abeparvovec is based on clinical criteria. It will not be relevant who paid for treatment with onasemnogene abeparvovec but rather how the patient responded to that treatment. This is important as it ensures that patients will not be disadvantaged (or advantaged) because of their economic circumstances and how previous treatment was funded, in line with the NHS constitution.

Treatment switching between risdiplam and nusinersen and between nusinersen and risdiplam

What are the clinical circumstances under which it would be possible to switch from treatment with nusinersen to risdiplam or from risdiplam to nusinersen? Under what circumstances would it be possible to switch back to the original treatment?

In order to answer this question, it is important to explain how MAAs work.

Both nusinersen and risdiplam are only available under Managed Access Arrangements (MAAs). An MAA is put in place when a medicine shows promising potential but there is significant uncertainty in the longer-term clinical evidence. MAAs provide a way for patients to receive promising new treatments, while further evidence is collected to assess the long-term benefits of a new medicine.

Based on the evidence available when NICE made its decisions about recommending risdiplam and nusinersen, the long-term benefits for patients were still very uncertain. The MAAs have been designed to allow enough time for additional evidence to be generated for NICE.

At the end of the MAA period, NICE will review the new evidence and review its guidance to indicate whether the medicine should be recommended to use in the NHS – this may result in a difference to what the NHS will pay for the drug for example. While most topics recommended for managed access go on to be recommended for routine use on the NHS, there is no guarantee that it will be recommended when it is reviewed by NICE.

If patients switch between nusinersen and risdiplam, it is likely to be difficult and may not be possible to collect reliable evidence relating to the impact of each individual treatment. As a result, it is possible that the evidence generated under the MAA is insufficient to enable NICE to recommend one or both drugs for use on the NHS.

Patients and families should consider very carefully with their treating clinician whether there is a clinical reason to switch from one treatment (treatment A) to another (treatment B), as switching back to treatment A is only likely to be advisable if:

- treatment B is causing side effects that preclude the administration of treatment B and/or
- there is demonstrable deterioration in motor or respiratory function following the switch to treatment B.

It is recommended that treating clinicians seek advice from the NHS England Clinical Panel in the event that there may be a case for switching back to treatment A.

Given the complex nature of decisions around treatment switching, all discussions must take place face-to-face between the patient/family and their treating clinician.

Where a switch between treatments is necessary, there should be a gap of four months between stopping treatment with nusinersen and starting treatment with risdiplam and a gap of 15 days between stopping treatment with risdiplam and starting treatment with nusinersen (this may be shortened exceptionally). It may be necessary for nusinersen loading doses to be administered again, if a patient switches from nusinersen to risdiplam and then switches back again.

Patients who were eligible for risdiplam on the Early Access to Medicines Scheme but who are not eligible under the NICE guidance/meet the stopping criteria under the nice guidance

There may be some individuals who met the eligibility criteria for risdiplam when it was available under the Early Access to Medicines Scheme but who do not meet the eligibility criteria set out in the NICE managed access agreement. The supply of treatment to these individuals may continue for as long as the patient is receiving clinical benefit from the treatment. The treating clinician should refer these individuals to the NHS England Clinical Panel who will advise if the individual is continuing to receive benefit. It should be noted that the role of the Clinical Panel is advisory only and it is for individual treatment centres to take decisions about individual patients.

Patients who have been on clinical trials

Can patients who have previously had any treatment for spinal muscular atrophy under a clinical trial (whether in the UK or abroad) have access to risdiplam, regardless of their clinical situation?

Patients/families should discuss their individual situation with their treating clinician so that an understanding of the terms of the clinical trial can be determined. This needs to include what information about access to future treatments was given to the patient/family when they enrolled for the trial. Notwithstanding this information, the primary consideration around access to risdiplam will be clinical. These cases should be discussed with the NHS England Clinical Panel.

Can patients who are on risdiplam trials – abroad or in the UK – now cease to be on these trials and receive the treatment on the NHS?

Patients should discuss their individual situation with their treating clinician, including how much longer the clinical trial is expected to last. It is important for patients to continue on ongoing clinical trials where feasible as trials are able to rigorously collect high quality data that can be used to make decisions about whether or not drugs are clinically effective and can be routinely funded by the NHS. Any patient transferring from an ongoing clinical trial will need to meet the eligibility criteria in the NICE guidance.

NICE assessments

Are the baseline and three-month assessments required for patients transitioning from the Early Access to Medicines Scheme (EAMS) to the MAA?

Patients who started treatment under the Early Access to Medicines Scheme are not required to repeat an assessment if a previous assessment captured all the mandated data items in the previous six months, see table 2 in the MAA.

A minimum of one data entry per patient per year is required to be captured after the initial assessment, with any two entries at least four months apart. Any missed clinic appointment for assessments should be rescheduled. If the patient has a worsening in any motor scale score, the patient's next assessments must take place within the next six months. Any patient not complying with the assessment schedule (without good reason) may be deemed as not complying with the terms of the Managed Access Agreement and access to treatment may cease.

What happens if patients who were previously accessing risdiplam via the EAMS are not able to complete the mandated tests set out in the MAA and are therefore unable to demonstrate that they are continuing to meet the starting criteria and are not meeting the stopping criteria?

There may be some individuals who met the eligibility criteria for risdiplam when it was available under the Early Access to Medicines Scheme but who are not able to complete the mandated tests set out in the NICE managed access agreement. The supply of treatment to these individuals may continue for as long as the patient is receiving clinical benefit from the treatment. The treating clinician should refer these individuals to the NHS England Clinical Panel who will advise if the individual is continuing to receive benefit. It should be noted that the role of the Clinical Panel is advisory only and it is for individual treatment centres to take decisions about individual patients. Treating clinicians should endeavour to use a recognised scale where this is feasible (for example, EK or Atend) as this is more likely to permit demonstration of continued benefit to the Clinical Panel.

What is the equivalent measure of deterioration in the RULM scale?

A deterioration of >=2 points.