Risdiplam compassionate use programme
For patients with SMA types 1 and 2 who are already on nusinersen but who have had their treatment interrupted because of COVID-19.

Roche have recently extended their compassionate use programme (CUP) to include the possibility of including these patients. Any applications for the CUP must be made by individual clinicians. Roche anticipate that applications will mostly be made for patients who have completed their loading doses and are on maintenance nusinersen, however applications will be considered for patients who have only had one dose administered. Clinicians would need to have made best efforts to continue to administer nusinersen.

The Clinical Panel that advises NHS England on the Nusinersen Managed Access Agreement (MAA) and also advises NHS England generally on the care of patients with SMA, has considered the risks and benefits of this opportunity. It has offered the following advice to the SMA clinical community:

- Patients should, wherever possible, **continue to receive nusinersen treatment**.

- Though it is important to maintain a steady concentration of nusinersen to the cerebrospinal fluid, nusinersen delivery can safely be delayed by 1-2 months, with subsequent doses maintained at 4-monthly intervals. If a dose is missed, nusinersen can be administered at the next 4-monthly interval followed by an additional dose at +/ -14 days.

- Some families are understandably very reluctant to visit hospitals because of the risk of contracting COVID-19. This reluctance is likely to continue until there is confidence that hospitals are COVID-19 free and/or there is an effective vaccine available. This reluctance may be particularly acute where there have been large clusters of COVID-19 positive cases in the patient's usual treating centre or where that centre has been temporarily repurposed to treat acutely ill adult COVID-19 patients.

- Where a treatment provider cannot deliver a service that offers safe intrathecal injection or where families are not prepared to attend hospital for treatment, the clinician will need to weigh up the best option for a patient. This will be particularly important when nusinersen has been seen to be effective and children could lose ground whilst not receiving treatment. Options they will consider – until safe delivery of intrathecal injection can be resumed – would be whether it is better for the patient to:

    - Continue to have nusinersen treatment ***or***

    - Stop nusinersen treatment until they and the clinician agree it is safe to resume treatment and for there to be an application to Roche to use risdiplam under the terms of the CUP in the interim

- When discussing these options with patients / their parents/guardians it is important that they understand that:

    - Nusinersen is a licensed product with a known safety profile whilst **risdiplam is an <u>unlicensed product</u> that does not yet have a full safety profile**.

    - NHS England is not aware of any centres that have stopped providing nusinersen treatment to existing patients.

- If a patient or their parents/guardians sign consent to change treatment it should be clear that they have been given and understood this information.

- Patients / their parents/guardians should also be made aware of the following points if an application to Roche by the clinician is successful:

    - Before beginning treatment, the patient will need **to attend hospital** for consent, clinical and physiotherapy assessments and a baseline safety assessment.

    - Until such time as risdiplam receives final approval from the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency, patients need to continue to be assessed with similar frequency to the safety assessments in the current risdiplam trials. They should be given details of this requirement.

    - Roche have indicated that they may be able to arrange for the product to be delivered by a 'cold-chain' courier rather than the family having to pick it up at the hospital pharmacy. This will ensure the medication is delivered safely.

In summary, the Clinical Panel recommends that continuing treatment with nusinersen is preferable, provided that the service (treatment centre) can offer a safe intrathecal injection.