Patient perspectives of temporary change to eligibility for NHS funded onasemnogene abeparvovec (Zolgensma®) in England.

14th February 2023

As SMA Patient Advocacy Organisations we welcome the opportunity to make this submission to MHRA, sharing a range of patient questions and concerns and reflections that we have seen via our networks, to be considered as part of the broader evidence. It is our understanding that the pause and the review of treatment is a direct result from a number of yellow cards submitted to MHRA by clinicians.

With regards to families' views about the benefits and risks of Zolgensma, all the SMA patient groups provided submissions to NICE throughout the appraisal process and responded to their consultation when it was initially not recommended. We believe that our initial message, highlighted in our NICE submissions, remains effectively unchanged.

Patient perspective

As well as themes picked up from social media groups since the approval of Zolgensma in the UK, SMA UK heard from 9 families in more depth about their experience of the treatment process from beginning to end. The ages of the children treated ranged from 6 months to seven and a half years.

Preparation for Treatment

7 out of the 9 of the families were satisfied with the level of information they were given before the infusion. All families understood the sense of urgency, and the fact that this meant they did not have a lot of time to consider their choices. Consequently, honest, detailed consultation with experienced clinicians is very much appreciated:

'*I think doctors try to give you worst case scenarios but thankfully everything went smoothly and there were no side effects'*

'We were brought in the day before and told the process on the day, days following and any risks. We had also been given numerous forms and leaflets and numbers to ring in case of emergency. We also were told most of this prior- when we got the first visit off the neuromuscular team after being diagnosed.'

'We were told about what Zolgensma could do for him but also told that there were no guarantees on what could bring back. We were told about steroids and isolation periods and well informed on this…'

' (Infusion centre name) were brilliant and went through everything and made sure that we knew everything before it happened'

There were at least two experiences where parents did not feel as well prepared as they should have been, including one family who were not given a copy of the Zolgensma patient information leaflet.

'…. There wasn't a lot of information given about the risks other than the liver and heart but we were handed something to sign in preparation and I feel this could have been explained better'

'Preparation tests were described accurately. However, in my opinion these are not enough. Additional processes investigating liver, gallbladder, check for hepatitis like viruses, kidney function etc should be done.'

Communication and understanding between clinical centres.

The greater concern amongst the community seems to be the apparent lack of knowledge and understanding of SMA and treatments in local hospitals. Parents' experiences indicated that the period of post-infusion monitoring, as an inpatient at the infusion centre, varied greatly (from 'a couple of hours' to two weeks) and although individual differences will be a factor in this, many felt that their local hospitals were not equipped to manage the important monitoring phase and there was a lack of efficient and systematic communication strategies between centres.

'They (local hospital) were confident enough with the actual tests but nobody knew what SMA was or the treatment. Felt like we had constantly had to repeat this to numerous doctors. The communication was not good, we would sometimes wait days for a call for the blood results. However in (specialist centre) when we had them done a couple days apart we had a call the same or next day.'

'We were informed that a course of steroids would be used to control liver related side effects. If things a bit more challenging a larger dose of steroids would be needed. But there was no real plan in place for more complex follow up. Which was required in our case.'

'Weekly bloods having to travel to (specialist)rather than our local was stressful and expensive'

'Local hospital was very good, but they were definitely out of their depth. They did everything (specialist centre) requested, but they were too concerned that they could not offer the level of treatment required and wanted patient to be transferred to (specialist centre)'.

'A lot of the local team do not have much knowledge in the treatment or condition so I do find we are the advocate and have to find out the answers to our questions from (specialist centre) a lot more at times. Our local hospital took advice from (specialists) every time.'

'(specialist hospital) was great…Our local just maybe needed some more information on how important it is to get the results a bit sooner to parents or communicate with parents as the experience is a worry and when you're waiting for the blood results you're in panic mode until you know your child is okay. (specialist hospital) were usually given the results off our local and then they would ring us with results. It was good communication but just maybe if our local were aware of the scary process they may have been a bit more eager to ring and give us our results.'

Side Effects

In the majority of experiences shared, across all ages and all weights, there has been some sort of adverse effect from the Zolgensma infusion. Parents indicated that most of these were appropriately dealt with in a timely manner. Some experienced side effects that were not listed on the label, so not expected. In these situations, parents have turned to their community through social media groups to ask if anyone else had experienced the same or similar symptoms; for example, mood swings. To get an overall impression, as a focussed question, we asked the 9 families to rate (0-10) how confident they were that any side effects were being managed in the best possible way. The range of scores collected was 0 (not confident)-10 (very confident) and the average score was 4.

'(Name) experienced a lot of dark hair growth and has got a lot more cranky and mood swings even now when weaning her steroids I think has been the worst.'

‘(Name) was quite unwell in terms of sickness but seemed okay on the whole. Now, 9 months past though, liver enzymes had doubled so he was put back on steroids, this is still an ongoing situation which is being looked in to.’

‘As liver injury is the most common side effect, the appropriate clinicians must be fully educated and prepared to deal with immuno-mediated liver inflammation including use of immune suppressants or steroid sparing drugs as a standard (as long term steroid use can also cause issues).’

In-depth personal experience and reflections from the father of treated child

A child, 20kg was infused with Zolgensma at Bristol Hospital.

Prior to the infusion, the consultations about side effects and post infusion steps were undertaken and it sounded quite straight forward: “Yes, we expect liver enzymes to go up, but we have protocols for dealing with those – steroids etc; if the initial dose of steroids does not work, these can be doubled and then we can use IV steroids to arrest side effects. A few days in the hospital and discharged home. If things go wrong, local hospital is point of contact and they will be able to help.”

In reality, steroids did not actually help, and a serious liver injury resulted – clotting was significantly decreased and human blood product required to control it; Albumin production was affected resulting in oedemas in the body and albumin infusion was required. The child spent several weeks hospitalised in three different hospitals and had to have a liver biopsy resulting in very severe complications. The local hospital was very much out of its depth and a lack of beds in specialised hospitals meant that the child could not be assessed by the specialist team in real time. All decisions were made remotely. This resulted in mistakes and possibly complicated the situation. Once the child was moved to the specialist hospital the situation was resolved, however the damage has been already done. The child is still recovering from the liver injury after 4 months.

There are patients who are younger with much higher LFTs numbers who respond much less effectively to steroid treatments than older children. Therefore, I believe that a deeper/more detailed screening process into individual biological differences must be done before infusion can proceed. I think that liver, biliary track and gallbladder should be looked at in more detail, as well as kidneys and heart in order to rule out any underlying conditions that may flare up. However, I also understand that screening individual patient’s for all sort of conditions (kidney/heart and liver) might not be feasible as, still now, we do not know what to exactly screen for (we don’t know what makes some patients more vulnerable than others). Perhaps make a liver ultrasound mandatory even for patients with normal liver enzymes at baseline could be proposed.

Questions and considerations

As representatives of SMA families, embedded in the community, we have seen how Zolgensma has given children living with SMA life, and a far less medicalised life, bringing new opportunities for the whole family. We have heard experiences where the aftercare has been effectively managed, communication between centres has been efficient and the outcomes have been positive.

Looking at the experiences of families within our networks, it seems unjustifiable to have a cut of at 12 months as side effects (in particularly liver injury/inflammation) do not have a particular pattern based on age or weight. We do not want to see children who could benefit greatly from this one off treatment being excluded, instead maybe the underlying biological causes of these isolated cases should be investigated, access should be maintained on a case by case basis.

For example, within our community, we have seen two children, both treated at around seven years, one had very serious complications after treatment and the other had none.

There is a possibility that during this pause period a child could be diagnosed late (as many in the community have so painfully experienced) and though they would be of a lower weight, their treatment options will be limited.

We are keen explore how SMA community advocacy groups can further support families through the treatment process as well as the ongoing research.

- **How can cases of good practice be effectively shared and learnt from?**
- **We expect additional clinical data to emerge in upcoming months that will provide additional information on the efficacy vs side effects which will need to be carefully considered.**
- **Systematic and comprehensive national data collection is essential for safety and to develop understanding of adverse effects verses efficacy. How can real world evidence and ongoing data collection be best utilised to optimise management of adverse effects? How will it be disseminated to all stakeholders to ensure the best standard of care across the country?**
- **What are the protocols for individualised monitoring and post-infusion after-care? How can they be improved to ensure more efficient and effective communication between different centres, whilst ensuring the family remain well informed?**
- **How can capacity be made for local hospitals with children living with SMA in their care, to be fully trained in the condition, and its treatment and management pathways, including of any side effects following treatment?**
- **Parents want to be fully educated about the whole process, acutely aware of how side-effects can manifest. How can this be achieved equitably across the UK?**

Patient Groups understand the need to consider patient safety at all times. We respect the very difficult decision-making process for NHS England and the NMDT and trust the concerns, questions and reflections shared by the community will be duly considered as part of the process. We urge that the review of all information is given highest priority and a definite timeline.

spinal muscular atrophy uk
Help for today, hope for tomorrow

Portia Thorman

Advocacy Lead

TreatSMA
Treat Spinal Muscular Atrophy

Dr Gennadiy Ilyashenko

Trustee

Muscular Dystrophy UK
Fighting muscle-wasting conditions

Dr Kate Adcock

Director of Research and Innovation