Health technology assessment of the addition of spinal muscular atrophy (SMA) to the National Newborn Bloodspot Screening Programme

Expert Advisory Group meeting (via Zoom) minutes

Friday 18 August 2023

10:00 to 12:00

Expert Advisory Group Attendees:

Name	Initials	Details
Aileen Butler	*AB*	*Principal Clinical Scientist, Clinical Genetics Laboratory Children's Health Ireland at Crumlin*
Abigail Collins	*AC*	*National Clinical Lead, Child Health, Public Health*
David Elliman	*DE*	*Chair, Blood Spot Task Group, United Kingdom*
Mohamed Elsammak	*ME*	*Director and Consultant Chemical Pathologist, National Newborn Bloodspot Screening Laboratory, Children's Health Ireland at Temple Street*
Inese Freimane	*IF*	*Higher Executive Officer, Population Health Screening, Department of Health.*
Claire Gorry	*CG*	*Chief Pharmacist, Medicines Management Programme, HSE*
Paul Marsden	*PM*	*Project Manager for Child Health Screening Programmes, HSE*
Jonathan O'Grady	*JO'G*	*Director, SMA Ireland*
Loretta O'Grady	*LO'G*	*Chief Medical Scientist, National Newborn Bloodspot Screening Laboratory, Children's Health Ireland at Temple Street*
Paul Marsden	*PM*	*Project Manager for Child Health Screening Programmes, HSE*
Joanne Uí Chrualaoich	*JUC*	*Principal Officer, Population Health Screening, Department of Health.*
Grainne Ryan	*GR*	*National Lead for Public Health Nursing Service, HSE*
Alana Ward	*AW*	*Information Scientist, National Rare Diseases Office, HSE.*
Máirín Ryan (Chair)	*MR*	*Director of Health Technology Assessment and Deputy Chief Executive Officer, HIQA*
Patricia Harrington	*PH*	*Deputy Director, Health Technology Assessment, HIQA*

Susan Spillane	*SS*	*Deputy Director, Health Technology Assessment, HIQA*

In attendance

Name	Initials	Details
Eanan Finnegan	*EF*	*HTA Analyst, Health Information and Quality Authority*
Arielle Maher	*AM*	*Health Services Researcher, Health Information and Quality Authority*
Helen O'Donnell	*HO'D*	*Senior HTA Analyst, Health Information and Quality Authority*
Michelle O'Neill	*MO'N*	*Deputy Director, Health Technology Assessment, HIQA*
Michelle O'Shea	*MO'S*	*Programme Administrator, Health Information and Quality Authority*
Conor Teljeur	*CT*	*Chief Scientist, Health Technology Assessment, HIQA*

Apologies

Name	Initials	Details
Andrew Green	*AG*	*Consultant in Clinical Genetics and Professor of Medical Genetics, Children's Health Ireland at Crumlin*
Catherine Harvey	*CH*	*Clinical Liaison Officer, National Newborn Bloodspot Screening Laboratory, Children's Health Ireland at Temple Street*
Sue Jameson	*SJ*	*Cuidiú*
Sinéad Lawlor	*SLa*	*National Practice Development Co-Ordinator (Public Health Nursing Service), Office of Nursing and Midwifery Services Director, HSE*
Sinéad Lucey	*SLu*	*Chief II Pharmacist, Medicines Management Programme, HSE*
John Murphy	*JM*	*Clinical Lead for Neonatology, National Clinical Programme for Paediatrics and Neonatology, HSE*
Denise McDonald	*DMcD*	*Consultant in Paediatric Neurodisability, Children's Health Ireland at Tallaght*
Ellen McGrath	*EMcG*	*Head of Corporate Pharmaceutical Unit, Primary Care Eligibility & Reimbursement Service, HSE*

Margaret O'Brien	*MO'B*	*Consultant Neurologist, Beaumont Hospital*
Declan O'Rourke	*DO'R*	*Consultant Paediatric Neurologist, Children's Health Ireland at Temple Street*

1. Welcome (MR)

   MR welcomed the attendees to the second meeting of the group and thanked everyone for their support with this health technology assessment (HTA).

2. Apologies and introductions (MR)

   MR invited Expert Advisory Group (EAG) members to introduce themselves to the group.

   Apologies were noted.

3. Group management and protocols (MR)

   MR reminded the Group that their confidentiality declarations extend to the date of report publication on the HIQA website. Any media enquiries before that date should be forwarded to HIQA for fielding.

4. Minutes of the meeting 3 May 2023

   Approved.

5. Presentation of draft chapters for Health Technology Assessment of the addition of spinal muscular atrophy (SMA) to the National Newborn Bloodspot Screening Programme (NNBSP)

   - Group review of draft report

     HO'D and AM provided an overview on the updated draft chapters and new draft chapters of the HTA of the addition of SMA to the NNBSP. EAG members were asked to consider the following questions in providing feedback;

     - Was the information reported and interpreted it accurately?
     - Were there other sources of data we should have included – is what we have done complete?
     - Do the key points accurately reflect the findings of each chapter?
     - Are there any issues regarding readability?

<u>Chapters 1-2, 4-6 - Changes since last EAG</u>

- Regarding Chapters 2 and 5, it was clarified that while stakeholders led by NNBSP are involved in the implementation process, treatment pathways are a responsibility for the relevant clinical programmes and the treating clinicians. The choice of pathway would however have an impact on the budget impact associated with the introduction of SMA screening.
- Additional clarity is required in defining the scope and limitations of SMA screening, particularly with respect to the definition of screen positivity, which may be defined on the basis of survival motor neuron 2 *(SMN2)* copy number. In terms of access routes to treatment, it was suggested that recommendations of the National Screening Advisory Committee (NSAC) should align with the availability of treatment.
- It was noted that the outcome of the risdiplam (Evrysdi®) reimbursement process has been published, and it is anticipated that the license for risdiplam will be extended to include infants under two months of age in the coming months. However, further details cannot be included in the report until the exact criteria are published.
- It was queried whether the proposed treatment pathway in this HTA could be amended to indicate immediate treatment for those screened positive and found to hold four *SMN2* copies, instead of 'watchful waiting'. In response, it was noted that the proposed pathway was based upon international guidelines and consultation with specialist clinicians. In the event of a decision to add SMA to the NNBSP, further work would be required to establish the appropriate treatment pathway in Ireland. An action was taken to follow up with specialist clinicians to confirm that the pathway outlined in the report was still relevant for the purposes of this HTA.
- It was queried whether families with known cases of SMA in parents or siblings fall within this treatment pathway, as some of these families may present with cases of SMA arising from compound heterozygous mutations which the proposed screening test is not designed to detect. A sentence will be included in the report to indicate that this suggested pathway is not applicable to families with known cases. Alternative routes for people with a family history of disease are often considered when planning for the implementation of modifications to screening programmes.

<u>Chapter 3 – Epidemiology and burden of disease</u>

- It was suggested again that the approach of 'watchful waiting' for individuals with four copies may be an outdated clinical recommendation. It was noted that the limitations of this approach are detailed in the ethical and social considerations chapter of the report, but it was necessary to detail a potential pathway to provide a basis for budget impact analyses. Scenario analyses

were undertaken to also provide the budget impact in the event of immediate treatment for these patients.

- It was suggested that it would enhance the clarity of the report if the correlation between phenotype and genotype in this chapter were presented in reverse order. This suggestion will be implemented in the next draft.
- Some readability concerns were raised regarding the complex descriptions of inheritance pattern and carrier status in subsections 3.1.1 and 3.1.2. Email correspondence has been issued to HO'D with suggested rewording and MR confirmed that the next iteration of the report will consider these changes.

Chapter 7 - Organisational and budgetary implications

- It was proposed to consider including the budgetary implications for referrals to genetic counsellors and cascade testing in the analysis. It was noted that there may be a frontloading of cases rather than an ongoing increase in referrals.
- It was raised that program elements identified in the previous HTA of the addition of Severe Combined Immunodeficiency to the NNBSP remain unfunded. Implementation of recommendations from this HTA will depend on securing funding for these elements.
- It was suggested to consider accounting in the analysis for data specialist resources that would allow for clinical outcomes to be captured and used to confirm clinical benefits if screening is implemented
- It was queried whether the current scenarios presented sufficient variability in terms of the potential for discounts associated with drug prices. It was clarified that a scenario with a 50% reduction from base case is provided. It was noted that while it is difficult to capture all possible discount combinations, some additional scenarios will be considered for inclusion here.
- It was recommended to reconsider the assumption that treatment is a one-time event, as patients may require additional treatments if they do not have the expected or desired response to the initial treatment.
- Regarding implementation, it was noted that the current lab infrastructure in place is not suitable. Additional resources including personnel, equipment, and stronger IT infrastructure would be required for successful implementation. While screening for SMA could be implemented in the current laboratory, it may be more appropriate to wait until the laboratory moves to the New Children's Hospital.
- For confirmatory and diagnostic testing a number of factors were noted as important considerations for the choice of site. These included the turnaround time and workforce resilience. Splitting diagnostic testing across multiple sites may pose challenges due to the relatively small number of tests and the speciality equipment required, as well as difficulties for quality control.

- It was requested that the presented costings be based on genotype rather than phenotype. Also, it was requested that the costs of increased monitoring be taken into account for patients who would be expected to develop type IV SMA in the absence of screening.
- It was noted that the costs of capillary electrophoresis instruments differ depending on the instrument type. For those used by the Department of Clinical Genetics at CHI Crumlin, the cost is estimated to be around €250,000 per instrument. Estimated costs for the types of instruments considered by the National Newborn Bloodspot Screening Laboratory were provided for in an email sent by the laboratory to HIQA.

Chapter 8 – Ethical and social considerations associated with the addition of newborn screening for SMA

- It was raised that the use of the term bi-allelic pathogenic variations is potentially misleading, as bi-allelic may imply homozygous or heterozygous forms of SMA. It was advised that the use of this terminology was informed by previous EAG feedback, but advice will be sought again to ensure accuracy.

Chapter 9 - Discussion

- A potential bias was raised regarding the cost-effectiveness studies as they were supplied by pharmaceutical manufacturers. It was questioned whether conducting these analyses independently would be worth considering to ensure fairness and to mitigate any potential bias. In response, it was advised that the HTA found the cost-effectiveness of screening was inconclusive given the broad range of incremental cost-effectiveness ratios (ICERs) observed across studies. Conducting the analysis again independently would be unlikely to change these conclusions. This approach taken is highlighted as a limitation in the report.
- There was a query regarding the possibility of further consideration being given to the implications of being diagnosed as a carrier, along with the counselling, educational support, and associated costs. Further feedback on this topic to follow over email correspondence.
- It was requested that this chapter establish a clear definition of screen positive as the ethical implications and subsequent decision-making rely heavily on this definition. Further feedback on this topic to follow over email correspondence.
    - A discussion was held regarding the ethical considerations in disclosing of the results, particularly for those with higher copy numbers. Some members considered that SMA is a binary condition, meaning an individual either has it or does not. However, the severity of the

disease can vary. Given that many affected children may not exhibit symptoms early on, it becomes paramount to carefully consider the ethical implications of identifying the condition and deciding whether to disclose this information or not.

- It was requested that additional information be included regarding the implications of the definition of screen positive for the identification of carriers given that one out of every 40 to 50 people in Ireland are estimated to be carriers. Withholding this information may be ethically problematic as it may impact reproductive choices.

6. Next steps

   - HO'D requested that any additional feedback on the report be forwarded as soon as possible to ensure necessary changes could be incorporated. HO'D then provided an overview of the next steps.

7. AOB

   - Nothing raised.

8. Meeting Close

   - MR thanked attendees for their time and ongoing contributions.