Nusinersen for spinal muscular atrophy in adults: utilisation analysis

Drug utilisation sub-committee (DUSC)

June 2025

Abstract

Purpose

To review the utilisation of nusinersen for spinal muscular atrophy (SMA) in adult patients as requested by the PBAC at its March 2022 meeting.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Nusinersen was PBS listed for the treatment of SMA in adult patients on 1 August 2022.

Data Source / methodology

Data extracted from the PBS database maintained by Department of Health, Disability and Ageing, processed by Services Australia were used for the analyses.

Key Findings

- In 2023, 93 adult patients were supplied 314 prescriptions for the treatment of SMA.
- In 2024, 80 adult patients were supplied 230 prescriptions for the treatment of SMA.
- The median age of initiating nusinersen patients was 37 years.
- The data was too immature to analyse the time on nusinersen treatment, the median treatment duration was not reached by the analysis end date.
- A greater number of adult patients have been treated with risdiplam compared to nusinersen.

Purpose of analysis

At its March 2022 meeting, the PBAC recommended the listing of nusinersen for the treatment of adult patients (older than 18 years of age) diagnosed with spinal muscular atrophy (SMA) with symptom onset before 19 years of age (primarily SMA Types II and III), on the basis that it should be available only under special arrangements under Section 100.

The PBAC considered that given the remaining uncertainty regarding potential uptake and continuation rates in adult SMA patients, a review should take place within three years after listing. The PBAC noted that the sponsor would need to provide relevant data from the SMA registry to inform the review of uptake and continuation rates. The PBAC considered that review of the rates of treatment continuation may also be informative in assessing the ongoing effectiveness of nusinersen in the adult population as perceived by patients and clinicians.

Background

Clinical situation

Spinal muscular atrophy (SMA) is a genetic condition affecting skeletal motor neurons responsible for controlling muscle movement. These motor neurons degenerate, leading to muscle weakness, hypotonia and atrophy of skeletal muscles.[1] SMA is an autosomal recessive progressive neuromuscular disease due to mutations in chromosome 5q. It has a carrier frequency of one in 35 and an incidence of one in 10,000 live births in Australia.[2]

Most patients with SMA have low levels of survival-of-motor-neuron (SMN) protein in their spinal cord motor neurons.[3] The SMN protein is produced by survival motor neuron 1 (SMN1) and survival motor neuron 2 (SMN2) genes. SMA patients have no functioning copies of the SMN1 gene, due to a homozygous deletion of the SMN1 gene on chromosome 5q. Therefore, SMA patients are dependent on the SMN2 gene for production of SMN protein. The SMN2 gene is a pseudogene of SMN1, but differs in exon 7 where the 840th nucleotide is a C in SMN1 and T in SMN2. This difference results in splicing out of exon 7 in SMN2 messenger ribonucleic acid (mRNA) and the production of rapidly degrading SMN proteins.[4] Consequently, SMA patients have limited quantities of SMN protein. The phenotypic severity of SMA is associated with the number of SMN2 genes

[1] Lunn M R, Wang CH. Spinal muscular atrophy. Lancet 2008; 371: 2120-33 https://doi.org/10.1016/S0140-6736(08)60921-6
[2] Farrar M.A, Park S.B, Vucic S, Carey K.A, Turner BJ, Gillingwater TH et al. Emerging therapies and Challenges in Spinal Muscular Atrophy. Annals of Neurology 2017; 81:355-368 doi: 10.1002/ana.24864
[3] Farrar M.A, Kiernan M.C. The Genetics of Spinal Muscular Atrophy: Progress and Challenges. Neurotherapeutics 2015; 12: 290-302
[4] Kolb S.J, Kissel J.T. Spinal Muscular Atrophy: A Timely Review. Archives of Neurology 2011; 68(8) doi:10.1001/archneurol.2011.74.

available. Fewer SMN2 gene copies are generally associated with an earlier age of onset and increased severity of symptoms.[5]

At the time of this review, nusinersen is PBS-listed for the treatment of:

- Children with symptomatic SMA (Type I, II, IIIa and Type IIIb, IIIc)
- Children with presymptomatic SMA (≤3 copies of SMN2 gene)
- Adults with SMA with symptom onset before 19 years of age.

There are also currently two other therapies for the treatment of SMA.

- Risdiplam is indicated for the same populations as nusinersen.
- Onasemnogene abeparvovec (ONA) is indicated for Type I and presymptomatic SMA (≤3 copies of SMN2 gene).

Pharmacology

Nusinersen is an antisense oligonucleotide (ASO) which increases the proportion of exon 7 inclusion in SMN2 mRNA transcripts by binding to an intronic splice silencing site (ISS-N1) in intron 7 or binding to SMN2 pre-mRNA. Exon 7 remains in SMN2 mRNA and can be translated to functional full length SMN protein.[6]

Therapeutic Goods Administration (TGA) approved indications

Nusinersen was ARTG approved on 2 November 2017. Nusinersen is only indicated for the treatment of 5q Spinal Muscular Atrophy.

Dosage and administration

The recommended dosage of nusinersen is 12 mg (5 mL) per administration. Four loading doses are administered on days 0, 14, 28 and 63. A maintenance dose is administered once every four months thereafter.

If a loading dose is delayed or missed, nusinersen should be administered as soon as possible with at least 14 days between doses, and dosing continued at the prescribed dosing frequency. If a maintenance dose is delayed or missed, nusinersen should be administered as soon as possible and dosing continued at the prescribed dosing frequency. Nusinersen is administered intrathecally by lumbar puncture. It should be administered by health care professionals experienced in performing lumbar punctures.

[5] Feldkötter M, Schwarzer V, Wirth R, Wienker T.F, Wirth B. Quantitative Analyses of SMN1 and SMN2 Based on Real-Time LightCycler PCR: Fast and Highly Reliable Carrier Testing and Prediction of Severity of Spinal Muscular Atrophy. The American Journal of Human Genetics; 70 (2): 358-368. https://doi.org/10.1086/338627.
[6] Spinraza®(nusinersen). Australian Approved Product Information. Macquarie Park: Biogen Australia Pty Ltd. Approved 3 November 2017, updated 31 January 2024. Available from < https://www.tga.gov.au/product-information-pi.>

The current Product Information (PI) and Consumer Medicine Information (CMI) are available from the TGA (Product Information) and the TGA (Consumer Medicines Information).

PBS listing details (as at March 2025)

Table 1: PBS listing details of nusinersen for SMA in adults

Item code	Name, form & strength, pack size	Max. qty.	Rpts	DPMQ	Brand name and manufacturer
13052Y	nusinersen 12 mg/5 mL intrathecal injection, 5 mL vial	1	3	$104,500.00	Spinraza® Biogen Australia Pty Ltd
13068T	nusinersen 12 mg/5 mL intrathecal injection, 5 mL vial	1	0	$104,500.00	
13064N	nusinersen 12 mg/5 mL intrathecal injection, 5 mL vial	1	3	$104,548.67	
13045N	nusinersen 12 mg/5 mL intrathecal injection, 5 mL vial	1	0	$104,548.67	

Notes:

- No increase in the maximum quantity or number of units may be authorised.
- No increase in the maximum number of repeats may be authorised.
- Special Pricing Arrangements apply.

Restriction (abridged)

Patients must:

- have genetic confirmation of 5q homozygous deletion of the SMN1 gene or deletion of one copy of the SMN1 gene in addition to a pathogenic/likely pathogenic variant in the remaining single copy of the SMN1 gene.
- not be receiving invasive permanent assisted ventilation in the absence of a potentially reversible cause while being treated.
- be treated by:
    - a specialist medical practitioner experienced in the diagnosis/management of SMA; OR
    - a medical practitioner who has been directed to prescribe this benefit by a specialist medical practitioner experienced in the diagnosis/management of SMA

If a patient continues treatment with nusinersen beyond the first 104 weeks of treatment, a comprehensive assessment must be undertaken periodically (at least every six months) and documented, involving the patient and the treating physician to establish agreement that treatment is continuing to produce a clinically meaningful response.

A clinically meaningful response is present where an improvement, stabilisation or minimal decline in symptoms has occurred as a result of this drug treatment and where there is agreement between the treating physician and patient over what constitutes improvement, stabilisation, or minimal decline.

PBS subsidy must cease if there is no agreement on whether a clinically meaningful response is present.

In undertaking comprehensive assessments, where practical, a clinically meaningful response assessment encompasses the patient's motor function as assessed using an instrument like the Revised Upper Limb Module (RULM), Hammersmith Functional Motor Scale - Expanded (HFMSE) or 6-minute walk test (6MWT), and the patient's quality of life including, but not limited to, level of independence. Quality of life may be informed by use of the SMA Health Index (SMA-HI) or SMA Functional Rating Scale (SMAFRS).

For details of the current PBS listing refer to the PBS website.

Changes to listing

Table 2: Chronology of PBS-listings for SMA

Date	Change to listing
1 June 2018	Nusinersen was listed for Type I, II, IIIa SMA
1 December 2020	Nusinersen listed for pre-symptomatic SMA (1 or 2 copies of the SMN2 gene)
1 August 2021	Risdiplam listed for Type I, II, IIIa SMA
1 May 2022	ONA listed for Type I and presymptomatic (1 or 2 copies of the SMN2 gene)
1 August 2022	Nusinersen listed for adult patients with SMA
1 October 2023	Risdiplam listed for adult patients with SMA, presymptomatic SMA (1 or 2 copies of the SMN2 gene)
1 August 2024	ONA listed for presymptomatic SMA (3 copies of the SMN2 gene)
1 November 2024	Risdiplam listed for presymptomatic SMA (3 copies of the SMN2 gene)

Current PBS listing details are available from the PBS website.

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

November 2020

The PBAC did not recommend extending the listing of nusinersen to include the treatment of SMA in patients with symptom onset prior to 19 years of age, and removal of the age limit of 18 years for initiation of treatment. The PBAC recognised the high clinical need for effective treatments for adults with SMA. However, the PBAC considered that the resubmission had not adequately defined the appropriate adult population for nusinersen and proposed convening a consultation with experts in the clinical management of adult

SMA to help resolve the specific issues associated with use of nusinersen in adult patients. The PBAC considered the magnitude of the effect was difficult to quantify and the incremental cost effectiveness ratio (ICER) was >$1,055,000 per QALY and likely underestimated.

For further details refer to the Public Summary Document from the November 2020 PBAC meeting.

July 2021

The PBAC did not recommend extending the listing of nusinersen to include the treatment of SMA in patients with symptom onset prior to 19 years of age, and removal of the age limit of 18 years for initiation of treatment. The PBAC recognised the clinical need for effective treatments for adult SMA. However, the PBAC considered that the adult population most likely to benefit from treatment with nusinersen remained inadequately defined in the resubmission. The PBAC noted that the magnitude and durability of the treatment benefit remained uncertain and considered that the ICER was exceptionally high at the price proposed. The PBAC advised that a substantial price reduction commensurate with the benefit of treatment in adult SMA patients, a Risk Sharing Arrangement (RSA), and a Managed Access Program (MAP) which accounts for the number of patients treated and the number of patients who respond to treatment, would be required to achieve a cost-effective listing for adult SMA patients.

For further details refer to the Public Summary Document from the July 2021 PBAC meeting.

March 2022

The PBAC recommended the listing of nusinersen for the treatment of adult patients (older than 18 years of age) diagnosed with SMA with symptom onset before 19 years of age (primarily SMA Types II and III), on the basis that it should be available only under special arrangements under Section 100. The PBAC is satisfied that nusinersen provides, for some patients, a significant improvement in efficacy over standard care. The PBAC recognised the clinical need for effective treatments for adults with SMA. The PBAC noted that the changes to the restrictions proposed in the resubmission were based on consultation with patients and clinicians and considered this helped to ensure the adult population most likely to benefit from treatment was sufficiently defined. The PBAC also noted that the sponsor proposed a substantial price reduction in the pre-PBAC response to better reflect the benefit of treatment in adult SMA patients. The sponsor also proposed a RSA which accounts for the number of patients treated and the number of patients who respond to treatment. The PBAC considered that a review of uptake and continuation rates in adult SMA patients should take place within three years after listing.

The PBAC noted that the same approach was used for the financial estimates as in the July 2021 resubmission, with changes to the effective price and the increased discontinuation rate consistent with the restriction requirements for ongoing assessment of response for continuing treatment. The PBAC recalled it previously considered the financial estimates were uncertain and associated with a low level of confidence (paragraph 7.13, nusinersen

PSD, July 2021 PBAC meeting). The PBAC noted that the pre-PBAC response (p3) stated that the uptake is expected to be limited and tempered by patient choice, suitability of spinal access for intrathecal administration and the overall risk-benefit assessment between patient and clinician. The PBAC noted that this was consistent with the modest uptake in the nusinersen access program and with clinical input from the sponsor hearing.

The PBAC considered that given the remaining uncertainty regarding potential uptake and continuation rates in adult SMA patients, a review should take place within three years after listing. The PBAC noted that the sponsor would need to provide relevant data from the SMA registry to inform the review of uptake and continuation rates. The PBAC considered that review of the rates of treatment continuation may also be informative in assessing the ongoing effectiveness of nusinersen in the adult population as perceived by patients and clinicians.

For further details refer to the Public Summary Document from the March 2022 PBAC meeting.

Previous reviews by the DUSC

DUSC reviewed the use of nusinersen for the treatment of Type I, II, IIIa SMA at its February 2021 meeting. In 2018, 140 patients were dispensed 591 nusinersen scripts. In 2019, 160 patients were dispensed 514 nusinersen scripts. Type II SMA was the most common type of SMA in patients receiving nusinersen treatment. The data was too immature to analyse the time on nusinersen treatment, the median treatment duration was not reached by the analysis end date. DUSC advised that a further analysis of the time on nusinersen treatment should be undertaken when sufficient data was available.

For details of the DUSC consideration of nusinersen for SMA refer to the Public Release Document from the February 2021 DUSC meeting.

Methods

Data extracted from the PBS claims database maintained by the Department of Health, Disability and Ageing and processed by Services Australia were used for the analyses. Prescription data were extracted from 1 June 2018 up to and including 31 December 2024.

This data was used to determine the number of incident and prevalent patients, number of prescriptions supplied and to analyse patient demographics such as age and gender. Initiating and prevalent patients were counted by quarter of supply. An initiating patient was defined based on their first date of supply of nusinersen. Utilisation of initial and continuing listings were based on the respective item code. Additional analyses were conducted to examine the overall SMA market as well as the adult SMA market.

A drug sequence analysis was conducted to examine the pattern of utilisation of adult SMA listings: nusinersen and risdiplam. The first prescribed drug was recorded and if patients were subsequently supplied other drugs, these were noted to form the patient's chronological drug sequence.

The Kaplan-Meier method was used to analyse treatment duration with nusinersen, censoring patients that were still continuing treatment at the analysis end date (31 December 2024). The median standard treatment days were 116 days. Patients were censored if they received a supply within three sets of standard treatment days before the analysis end date.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Services Australia Medicare date of processing data.[7] The publicly available Services Australia Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included. The Services Australia Medicare data used in this report includes under co-payment prescriptions which became available from 1 April 2012.

[7] PBS statistics. Australian Government Services Australia. Canberra. Available from <http://www.medicareaustralia.gov.au/provider/pbs/stats.jsp>.

Results

Analysis of drug utilisation

Overall utilisation

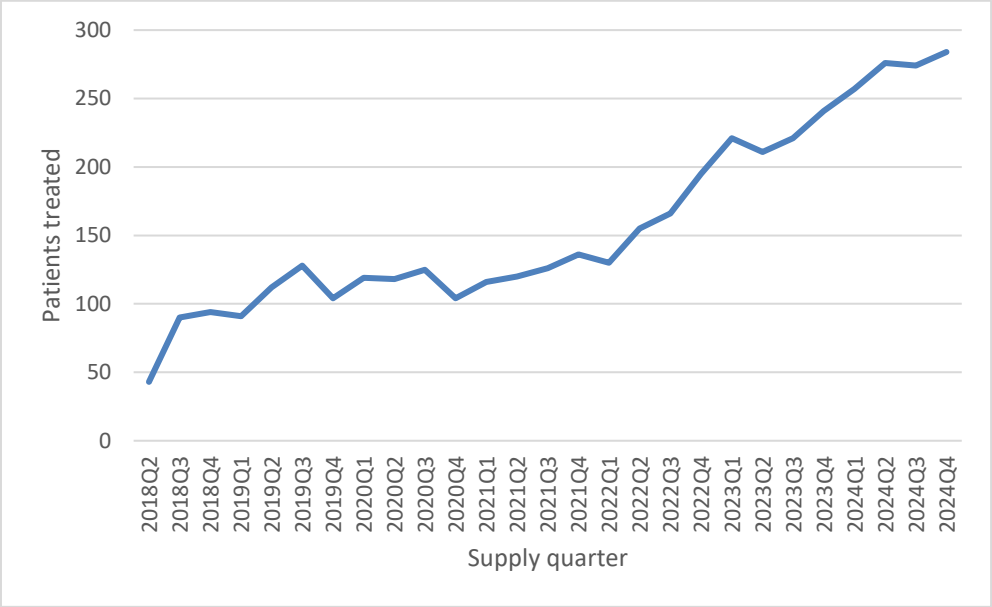

Figure 1: Number of SMA patients treated with PBS-listed therapies by supply quarter

Figure 1 shows the number of patients treated with PBS-listed therapies for SMA has increased over time, particularly from 2022Q2 onwards.

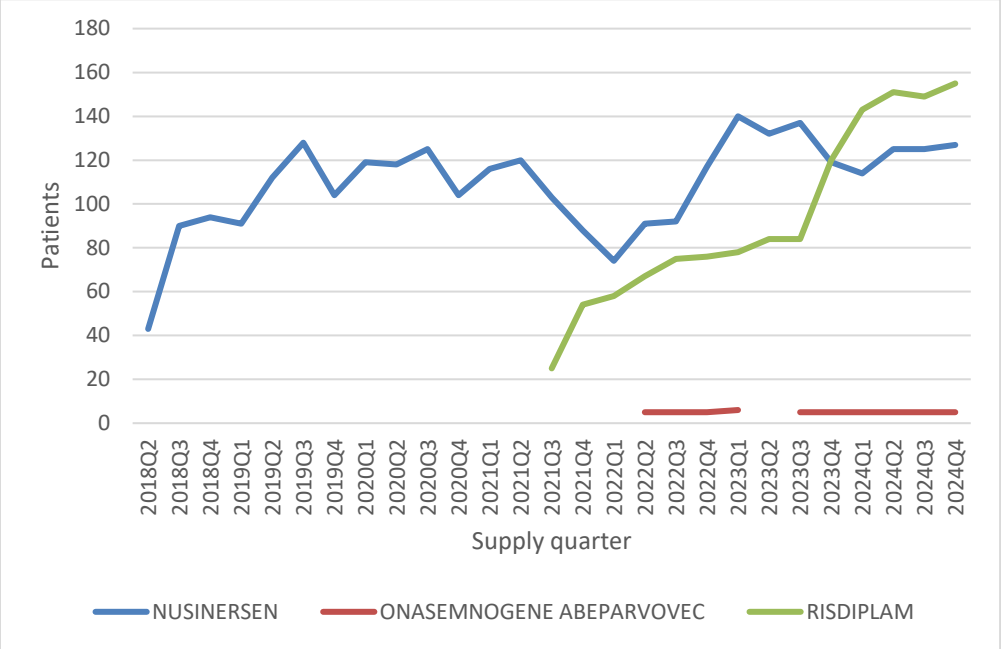

Figure 2: Number of SMA patients treated by drug and supply quarter

Note: Patient counts of less than 5 were denoted by 5 to reduce the risk of patient identification.

Figure 2 shows the number of SMA patients treated by drug. Prior to 2024Q1, most patients were treated with nusinersen for SMA. However, from 2024Q1 onwards most patients were been treated with risdiplam.

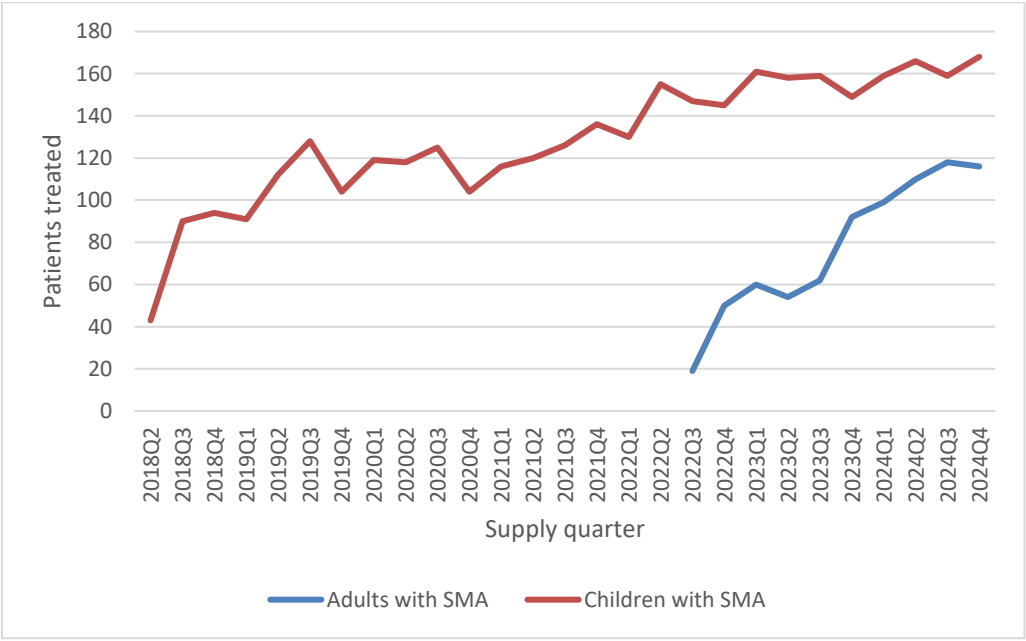

Figure 3: Number of SMA patients treated by age group and supply quarter

Figure 3 shows the majority of patients treated for SMA were children.

Utilisation of nusinersen for SMA in adults

Table 3 and Figures 4 and 5 show the utilisation of nusinersen in adult patients. At listing, there was high initial uptake of nusinersen, however the number of initiating patients has decreased, with a lower number of patients treated with nusinersen in 2024 compared to 2023.

Table 3: Utilisation of nusinersen for SMA in adults by calendar year

	2022	2023	2024
Patients treated	57	93	80
Prescriptions supplied	106	314	230

Note: Figures for 2022 represent five months of data from August 2022 to December 2022, inclusive.

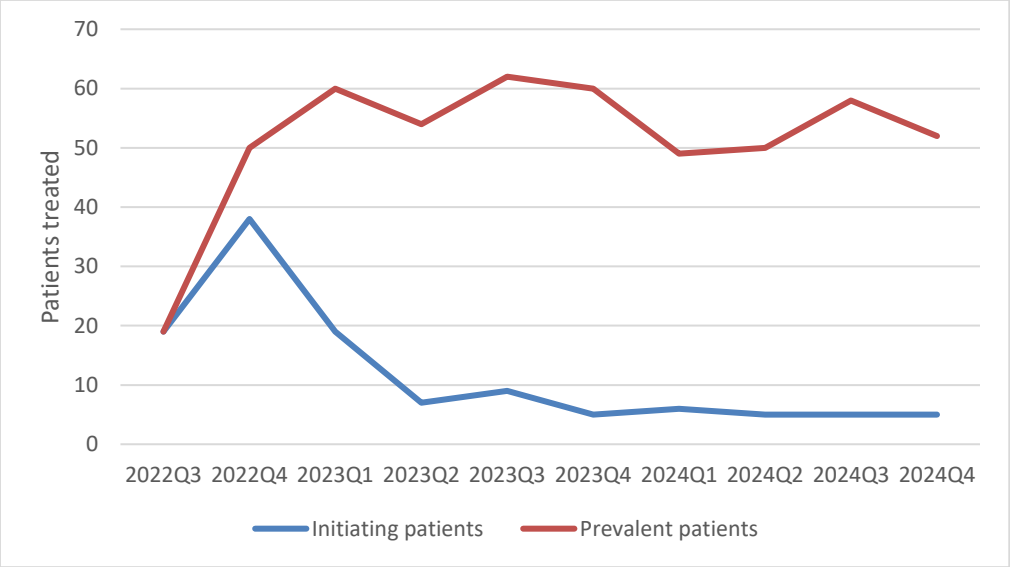

Figure 4: Number of adult SMA patients treated with nusinersen by supply quarter

Note: Patient counts of less than 5 were denoted by 5 to reduce the risk of patient identification.

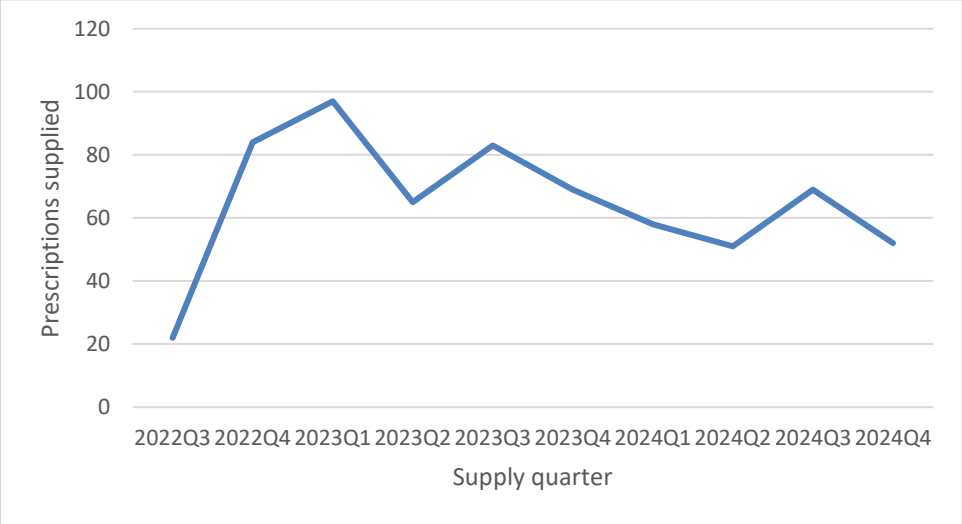

Figure 5: Nusinersen SMA prescriptions supplied by quarter

Utilisation by relevant sub-populations/regions or patient level analysis

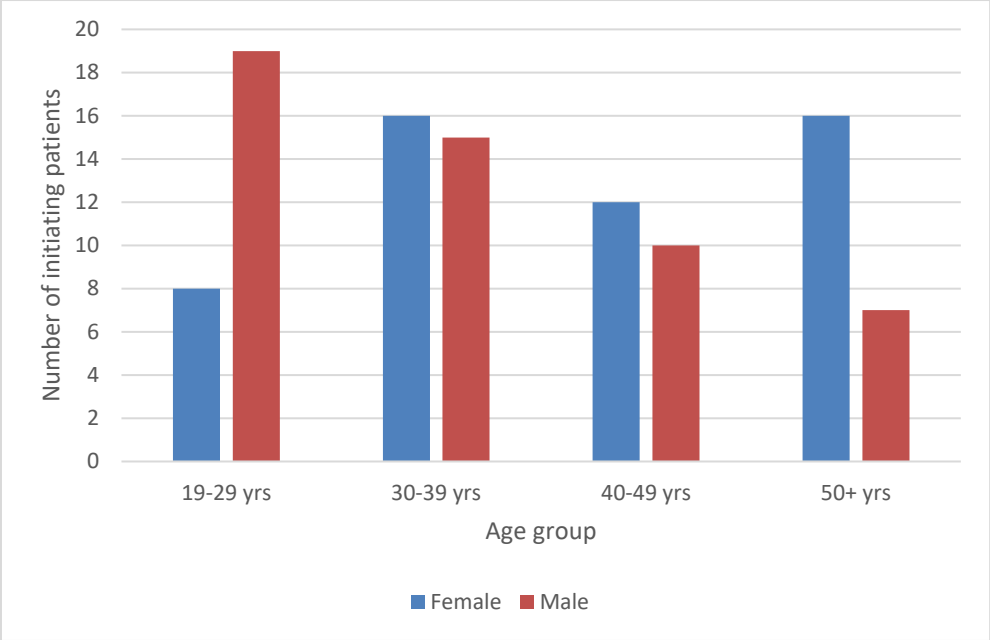

Figure 6: Age and gender distribution of initiating adult nusinersen patients for SMA

Note: Less than 5 patients were less than 19 years of age.

Figure 6 shows the most common age group to initiate treatment for adult SMA was between 30-39 years. Males accounted for a greater proportion of initiation in the 19-29 year age group, whereas females accounted for a greater proportion in the older age groups. The median age of initiating female nusinersen patients was 42 years and for males was 34 years. Overall, the median age of initiating nusinersen patients was 37 years.

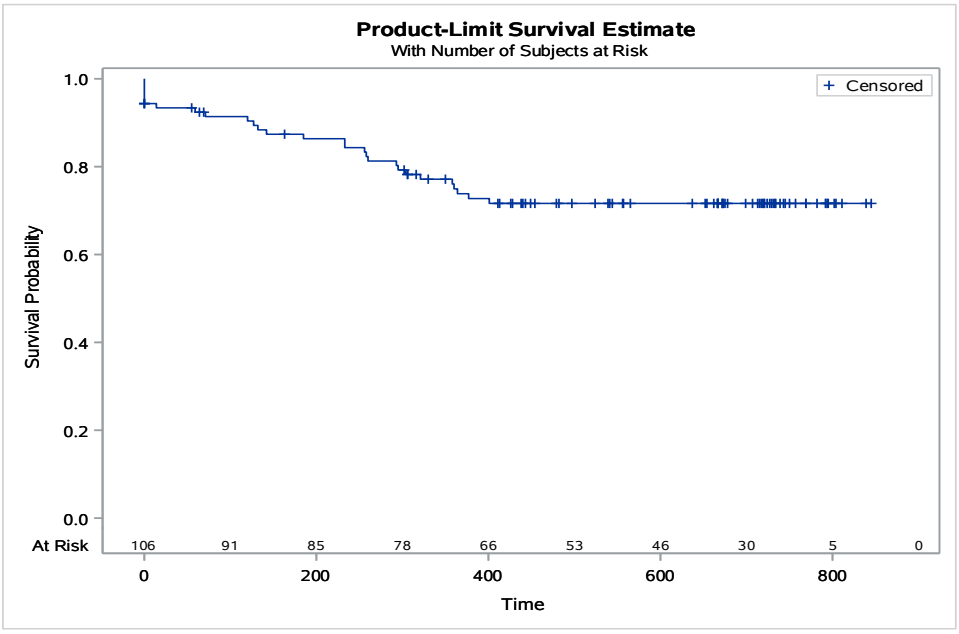

Figure 7: Treatment duration of adult nusinersen patients

The data was too immature to fully analyse the time of treatment on nusinersen, with the median time on therapy not being reached at analysis end date. Of the 106 patients who have initiated treatment with nusinersen, 73.58% of these patients were censored at 31 December 2024 and were identified as continuing on treatment.

Changes in the use of other drugs

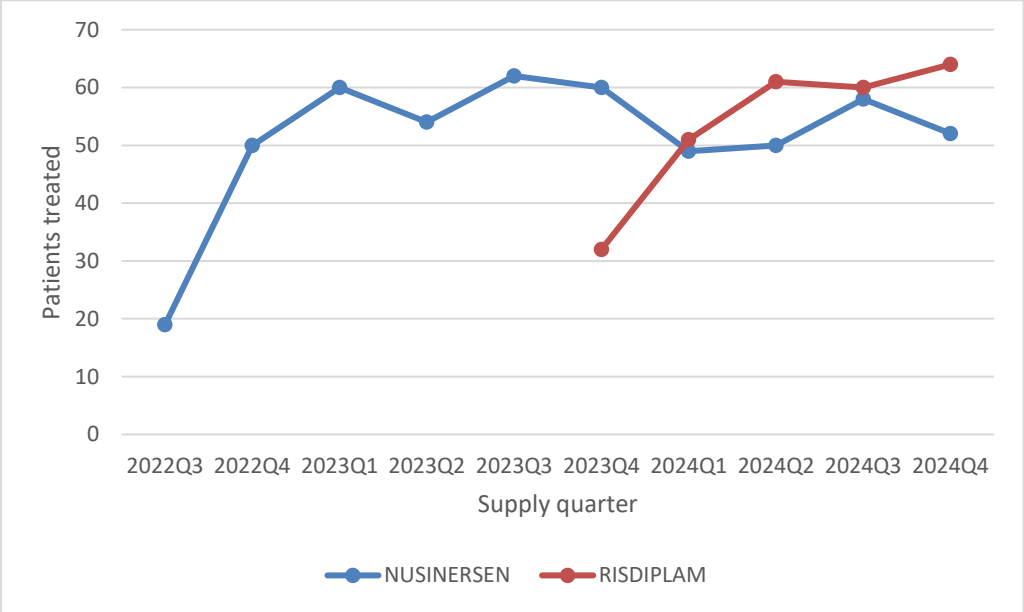

Figure 8: Utilisation of medicines for the treatment of SMA in adults

Figure 8 shows utilisation of medicines for SMA in adults. Most patients were treated with nusinersen up until 2023Q4, however from 2024Q1 onwards, a greater number of patients were treated with risdiplam compared to nusinersen.

Table 4: Treatment sequence of adult SMA listings

Sequence	Proportion of patients
NUSINERSEN	51%
RISDIPLAM	27%
NUSINERSEN→RISDIPLAM	21%
RISDIPLAM→NUSINERSEN	1%

As shown in Table 4, the majority of adult patients have only been treated with nusinersen for SMA (51%). Approximately 48% of patients have initiated therapy with risdiplam or have switched to risdiplam from nusinersen.

Discussion

As part of the PBAC's consideration of nusinersen at its March 2022 meeting, the sponsor's pre-PBAC response (p3) noted that the uptake is expected to be limited and tempered by patient choice, suitability of spinal access for intrathecal administration and the overall risk-benefit assessment between patient and clinician. The Pre-PBAC response also stated that a modest uptake rate has been observed in the nusinersen access program. The PBAC noted that this was consistent with clinical input from the sponsor hearing and considered that the uptake rates appeared to be reasonable (paragraph 6.83, nusinersen PSD March 2022 PBAC meeting).

As shown in Figure 8, there were more patients treated with risdiplam compared to nusinersen. As part of the PBAC's consideration of risidiplam, the PBAC acknowledged that there is a clinical need for an orally administered treatment for SMA, noting the important factors for patients and carers associated with the less invasive route of administration. As identified in consumer comments, risdiplam has advantages in reducing the treatment burden for patients in terms of increasing independence and reducing the need for patients to travel to specialist hospitals for administration of treatment. The PBAC also noted that there are likely to be patients for whom intrathecal administration of nusinersen is not feasible due to high grade scoliosis (paragraph 7.3, risdiplam PSD March 2023 PBAC meeting).

As part of its recommendation, the PBAC considered the restrictions should require that assessment of suitability for continuation of treatment takes place every 6 months after 2 years of treatment (paragraph 7.4, nusinersen PSD March 2022 PBAC meeting). At the time of this review, the data was not mature to see the effects of the continuation rule or to examine the median treatment duration.

DUSC consideration

DUSC noted the differences in mechanism of action between nusinersen, risdiplam and onasemnogene abeparvovec and noted the adverse events associated with these medicines.[8,9,10]

DUSC noted the utilisation of PBS-listed for spinal muscular atrophy in adults: nusinersen and risdiplam. DUSC noted nusinersen and risdiplam were initially listed for the treatment of Type I, II, IIIa SMA in children in June 2018 and August 2021 respectively, and their listings were extended to include adult patients in August 2022 and October 2023

[8] Onasemnogene abeparvovec for spinal muscular atrophy. Aust Prescr 2022;45:140-1. First published 7 July 2022.https://doi.org/10.18773/austprescr.2022.044
[9] Risdiplam for spinal muscular atrophy. Aust Prescr 2022;45:142-3. First published 7 July 2022.https://doi.org/10.18773/austprescr.2022.041
[10] Nusinersen for spinal muscular atrophy. Aust Prescr 2019;42:75-6. First published 28 February 2019.https://doi.org/10.18773/austprescr.2019.019

respectively. DUSC noted the increase in the size of the SMA market following extension to include adult patients.

DUSC noted most adult patients were treated with risdiplam and noted the differences in the mode and frequency of administration between nusinersen and risdiplam. DUSC noted an increase in the number of initiating SMA treatment following risdiplam listing and noted 21% of patients had switched from nusinersen to risdiplam.

DUSC noted the data were too immature to determine median duration of treatment. DUSC noted the Pre-Sub-Committee Response (PSCR, p3) provided SMA registry data as requested by the PBAC as part of its recommendation in order to inform uptake and continuation rates (paragraph 7.12 nusinersen PSD, March 2022 PBAC meeting). The sponsor noted registry data only represents aggregate data and PBS data would be more appropriate to inform continuation and persistence.

DUSC actions

DUSC requested that the report be provided to the PBAC for consideration.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Biogen Australia Pty Ltd: The sponsor has no comment.

Disclaimer

The information provided in this report does not constitute medical advice and is not intended to take the place of professional medical advice or care. It is not intended to define what constitutes reasonable, appropriate or best care for any individual for any given health issue. The information should not be used as a substitute for the judgement and skill of a medical practitioner.

The Department of Health, Disability and Ageing has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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Appendices

Appendix A: PBS listing details of risdiplam for SMA in adults as at March 2025

Item code	Name, form & strength, pack size	Max. qty.	Rpts	DPMQ	Brand name and manufacturer
13632L	risdiplam 750 microgram/ml powder for oral liquid, 80 ml	3	7	$32,574.33	Evrysdi® Roche Products Pty Ltd
13654P	risdiplam 750 microgram/ml powder for oral liquid, 80 ml	3	7	$32,525.67	
13646F	risdiplam 750 microgram/ml powder for oral liquid, 80 ml	3	5	$32,574.33	
13656R	risdiplam 750 microgram/ml powder for oral liquid, 80 ml	3	5	$32,525.67	