



# Life Saving Drugs Program (LSDP): Review of Medicines for Mucopolysaccharidosis Type II (MPS II)

## Review summary and Expert panel recommendations

### Purpose of the MPS II Review

Idursulfase (Elaprase®) was listed on the LSDP for MPS II on 28 August 2008. The Expert Panel considered this review at its October 2020 meeting.

This review of idursulfase sought to develop a better understanding of this medicine by comparing its current use against the recommendations and expectations at the time of listing.

The review further aimed to assess the clinical benefits achieved through the use of idursulfase; ensure the ongoing viability of the LSDP; and ensure testing and access requirements for idursulfase remained appropriate. It identified immediate and future changes that may be required to the funding criteria for idursulfase and to the LSDP more broadly.

The review of each of the LSDP medicines was supported by an approved disease specific Review Protocol, which was structured around seven Terms of Reference (ToRs). The ToRs were tailored specifically to each disease and the relevant medicine(s).

### MPS II Medicine Review Terms of Reference

1. Review the prevalence of MPS II in Australia.
2. Review evidence for the management of MPS II and compare to the LSDP treatment guidelines, patient eligibility and testing requirements for the use of idursulfase on the program (including the validity of the tests).
3. Review clinical effectiveness and safety of idursulfase, including analysis of LSDP patient data and international literature to provide evidence of life extension.
4. Review relevant patient-based outcomes that are most important or clinically relevant to patients with MPS II.
5. Assess the value for money of idursulfase under the current funding arrangements by evaluating the benefit of its treatment outcomes and cost.
6. Review the utilisation of idursulfase including storage, dispensing and evidence of patient compliance to treatment.
7. Investigate developing technologies that may impact future funded access.

## Key Findings and Recommendations from the Expert Panel

### ToR 1 – Review the prevalence of MPS II within Australia

The Expert Panel noted the best prevalence estimate for MPS II in Australia is between 0.13 and 0.3 per 50,000 people. While there was uncertainty about this estimate, the Expert Panel noted it is below the 1:50,000 threshold and MPS II therefore continued to meet this criterion as a rare disease under the LSDP.

According to MPS II treating physicians, approximately 90 percent of patients with MPS II in Australia were estimated to have symptoms of end-organ damage and were therefore eligible for access to LSDP-subsidised treatment under current eligibility criteria. The majority (85 percent) of these eligible patients accessed treatment on the LSDP.

The Expert Panel noted the annual increase in the number of patients accessing the LSDP for MPS II treatment was likely due to increasing recognition of the disease in the clinical setting.

#### **Recommendation 1:**

The Expert Panel considered that MPS II meets the prevalence criterion of less than 1:50,000 and currently remains suitable for inclusion on the LSDP.

### ToR 2 – Review evidence for the management of MPS II and compare to the LSDP treatment guidelines, patient eligibility and testing requirements for the use of idursulfase on the program (including the validity of the tests)

The Expert Panel noted the main difference between the LSDP criteria and the international clinical guidelines was the inclusion of patients with the severe (neurological) form of MPS II. There was a temporary clause in the LSDP Guidelines permitting these patients access to treatment. The Review had identified that approximately two thirds of current LSDP patients had been identified as having this severe presentation. The Expert Panel considered that amending the LSDP Guidelines to remove the temporary nature of the clause would likely have minimal impact on uptake and expenditure.

The Expert Panel acknowledged the difficulty faced by treating physicians in engaging patients and their families in discussions around stopping treatment when the disease has progressed to a stage where the patient is no longer benefiting in receiving idursulfase. The LSDP Guidelines could be amended to include a 'stopping clause'. This clause may help treating physicians in discussions with patients and their families about ceasing treatment. Cessation of treatment when no longer providing clinical benefit may result in reduced expenditure to the Commonwealth.

The Expert Panel discussed the high burden placed on patients and treating physicians through the annual patient assessment and application process. The Expert Panel noted the assessment and application process can be invasive, which is a concern for young children, and may be unnecessary in many adults.

Conversely, some treating physicians reported the testing requirements for the LSDP were useful in monitoring their patients' symptom progression.

**Recommendation 2:**

The Expert Panel recommended that the MPS II LSDP Guidelines be amended to allow patients with the severe (neurological) form of the disease access to treatment.

**Recommendation 3:**

The Expert Panel acknowledged the importance of analytical validity, clinical validity, and clinical utility when considering the value of health technologies. The Expert Panel agreed that the purpose, clinical benefits and frequency of undertaking specific tests to monitor clinical outcomes, and hence inform management and cessation decisions, needs to be clarified. Treating physicians are best placed to provide input on the usefulness of current tests used to diagnose, manage and monitor MPS II LSDP patients. The Expert Panel recommended that further clinical advice be sought as to whether blood spot enzyme testing is a valid method for diagnosing MPS II, and to review the following ongoing clinical tests:

- Imaging requirements
- Cognitive testing
- Ophthalmological assessments
- Sleep studies
- Functional tests.

**Recommendation 4:**

Consistent with international guidelines the Expert Panel recommended that, at the time of onset of treatment, treating physicians and patients should jointly agree on criteria for cessation of the enzyme replacement therapy (ERT) using indicators that reflect lack of response to therapy or deterioration in somatic or neurological disease despite therapy.

**ToR 3 – Review clinical effectiveness and safety of idursulfase, including analysis of LSDP patient data and international literature to provide evidence of life extension**

The Expert Panel noted LSDP patient data was consistent with both pre-LSDP listing and more recently published evidence indicating that idursulfase was effective and likely prolonged survival in MPS II patients. Small patient numbers in the literature and the lack of deaths in the LSDP cohort (or small number of deaths according to treating physician consultation) made it difficult to draw accurate conclusions regarding life extension.

**Recommendation 5:**

The Expert Panel noted the limitations of the available evidence regarding the conclusion that idursulfase extends survival for MPS II patients. However, on the basis of the evidence identified through the Review, the Expert Panel advised that idursulfase remains suitable for inclusion on the LSDP.

## ToR 4 – Review relevant patient-based outcomes that are most important or clinically relevant to patients with MPS II

The Expert Panel noted there were many positive aspects to idursulfase treatment as experienced by patients, their families and treating physicians. Important outcomes for adult and paediatric patients with MPS II were stabilisation and reduction of respiratory symptoms, improved mobility and range of motion, improved tolerance for and reduced need for surgery, reduced liver size, improved quality of life (QoL), improved sleep, and increased life expectancy.

The Expert Panel also noted stakeholders wanted to reduce the annual testing burden as noted in the discussion of ToR 2.

**Recommendation 6:**

The Expert Panel noted the extent and methods of data collection and the approach to analysis of the data requires improvement. The availability of consistent and complete data extracted from initial and ongoing applications to the program is essential. The LSDP should implement a streamlined solution that enables treating physicians to enter patient data both for everyday administration of the program and for future medicines reviews. Data collected must be clinically meaningful (e.g. to guide therapy or discussions on cessation of therapy) and/or relevant to the LSDP (including adverse events, compliance). The Expert Panel recommended that this revised approach should improve treating physician and patient satisfaction and facilitate availability of complete and comprehensive data for any future review of MPS II disease medicines.

## ToR 5 – Assess the value for money of idursulfase under the current funding arrangements by evaluating the benefit of its treatment outcomes and cost

The Expert Panel noted the average annual cost for idursulfase per recipient was approximately \$ [REDACTED] per year.

In the short-term studies of MPS II patients treated with idursulfase presented to the Pharmaceutical Benefits Advisory Committee (PBAC), there were improved QoL outcomes. The Expert Panel noted this finding was supported by recent data reported in the Review.

The Review found there was indirect evidence of increased survival for patients treated with idursulfase (approximately three years). The Expert Panel noted the cost per Life Year Gained was estimated to be approximately \$ [REDACTED], which was significantly more expensive than other drugs listed on the LSDP.

**Recommendation 7:**

The Expert Panel noted that there appears to be a survival gain and improvement in QoL from treatment with idursulfase, and that the cost of idursulfase remains very high. The Expert Panel therefore recommended that the pricing and listing arrangements for idursulfase be reassessed with the goal of improving value for money when:

current deeds of agreements with sponsors expire; and/or

new medicines for MPS II are considered for entry onto the LSDP or other subsidy programs; and/or

changes in eligibility criteria are being considered.

## ToR 6 – Review the utilisation of idursulfase, including the way it is stored and dispensed, and evidence of patient compliance to treatment

The Expert Panel noted the actual utilisation of idursulfase (patient numbers and vials used) was higher than expected at the time of LSDP listing, likely due to the inclusion of patients with the severe form of the disease. The Expert Panel noted the average patient weight had increased with age, leading to the increase in vials used per person. However, the total expenditure on idursulfase was less than expected due to price reductions.

While 64 percent of patients have had a treatment break, it is unclear whether these were related to patient compliance or adverse events or were due to gaps in the dispensing data.

The Review found idursulfase was being stored and dispensed as outlined in the LSDP Guidelines.

## ToR 7 – Investigate developing technologies that may impact future funded access

The Expert Panel noted there were new therapies in clinical development for MPS II. However, it was unclear what their impact would be on the usage of idursulfase and the MPS II patient population.

The Panel also noted stakeholders expressed a need for changes to exclusion criteria to allow patients who are participating in clinical trials to also be eligible for idursulfase.

**Recommendation 8:**

The Expert Panel recommended that the exclusion criterion that prevents patients being treated with LSDP funded medicines whilst participating in clinical trials should be removed.

## Next Steps

The then Minister for Health, the Hon Greg Hunt MP, agreed to these recommendations on 29 March 2022. The implementation of these recommendation is currently being considered and progressed by the Department of Health and Aged Care in consultation with sponsors, treating physicians and patient advocacy groups.