Australian Government
Department of Health

Life Saving Drugs Program (LSDP) Medicines Reviews Recommendations from the LSDP Expert Panel

Cross Program Recommendations

#	Recommendations
1	The Expert Panel recommends that a statement of rationale be developed and published, ensuring that it includes information on both the principles underpinning the program and the criteria for eligibility for a drug to be listed on the LSDP.
2	The Expert Panel recommends that the mechanisms of data collection and their management be reviewed by the Department with the aim of improving efficiency, completeness and stakeholder satisfaction. All data collected should have a predefined purpose.
3	The Expert Panel recommends that the government consider adding additional criteria that enable reasonable pricing limits to be expected at entry to the LSDP and enable adjustments in pricing over time. These pricing limits should reflect the stated principles underpinning the LSDP.

Medicine-Specific Recommendations

Fabry Disease

#	Recommendations
1	The Expert Panel considered that Fabry disease meets the prevalence criterion of less than 1:50,000 and on that criterion currently remains suitable for inclusion on the LSDP. Given the increasing prevalence of Fabry disease in Australia, the Expert Panel recommends that the prevalence of Fabry disease be reviewed within five years, or within five years post implementation of any Government agreed changes to eligibility, to determine whether Fabry disease continues to meet the definition of a rare disease for the purposes of this program.
2	The Expert Panel recognises that LSDP patient eligibility treatment criteria are not currently aligned with International Clinical Guidelines. Accordingly, the Expert Panel recommends that sponsors submit applications for the Expert Panel‘s consideration in support of amending/revising the eligibility criteria for commencement and continued access to medicines for the treatment of Fabry disease. Sponsor submissions must include an assessment of the clinical, economic and financial implications if expanded access is a likely consequence of the adoption of any proposal.
3	The Expert Panel agreed that the purpose, clinical benefits and frequency of undertaking specific diagnostic /clinical monitoring tests should be reviewed and clarified. The Expert Panel noted the importance of considering analytical validity, clinical validity, and clinical utility when assessing the value of health technologies used in the diagnosis and in monitoring patients with Fabry disease. Treating physicians are best placed to provide input on the usefulness of current tests used to diagnose, manage and monitor paediatric and adult Fabry LSDP patients. The Expert Panel recommended that a reduction in the frequency of some tests should be considered to reduce the burden on patients. The Expert Panel recommends further clinical advice be sought for review of the following diagnostic/ongoing clinical tests in relation to their places in LSDP program requirements: • Blood spot enzyme testing for diagnosis, as a replacement for the enzyme activity test • Timed overnight urine collection as an alternative to 24-hour collection for testing protein excretion in all patients with renal disease • Estimated glomerular filtration rate (eFGR) as an alternative measure of chronic kidney disease to kidney biopsy for all patients with suspected renal disease • Should there be a requirement for annual cardiac MRIs for patients entering under the cardiac criterion?

#	Recommendations
	• Should there be a requirement for respiratory function tests? • Which instruments should be used by the LSDP to assess pain and quality of life?
4	Based on the evidence identified through the Review, the Expert Panel recommended that agalsidase alfa and agalsidase beta appear to extend survival and thus remain suitable for listing on the LSDP. The Expert Panel considered that there was insufficient evidence to support any claim of a clinically important difference between agalsidase alfa and agalsidase beta, the two LSDP funded medicines for Fabry disease.
5	The availability of consistent and complete data extracted from initial and ongoing applications to the program is essential, particularly that related to patient outcomes. Consistent with recommendation 3, the Expert Panel recommended that: i. the instrument used to measure pain and quality of life be reviewed; ii. the extent and methods of data collection be revised; iii. the approach to analysis of the data be improved. The LSDP should implement a streamlined solution that enables clinicians to enter patient data both for everyday administration of the program and for future medicines reviews. The Expert Panel recommended that this revised approach should improve clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future reviews of Fabry medicines.
6	The Expert Panel noted that there appears to be a survival gain and improvement in quality of life from treatment with agalsidase alfa and agalsidase beta, and that the cost of these medicines remains very high. The Expert Panel therefore recommended that the pricing and listing arrangements for these medicines be reassessed with the goal of improving value for money when: i. current deeds of agreement with sponsors expire; and/or ii. new medicines for Fabry Disease are considered for entry onto the LSDP or other subsidy programs; and/or iii. changes in eligibility criteria are being considered. Should the value for money of any LSDP medicine approach a level that could be considered cost-effective in terms of Pharmaceutical Benefits Scheme (PBS) listing, the medicine should be reconsidered for suitability on the PBS.
7	The Expert Panel considered that the value for money aspects of weight based dosing be reconsidered. Specifically, the funding approach to treatment at above recommended and approved medicine levels should be reassessed. The Expert Panel were of the view that the Commonwealth should only be reimbursing for the dose of drug prescribed by the treating physician within the approved Product Information doses. To account for this, renegotiation of the funding arrangements with medicine sponsors may be required. The Expert Panel acknowledged the challenges for sponsors in providing product to satisfy the requirements of different international markets, but recognised the significant difference between the amount administered and the amount recommended, and the related additional cost involved in the administration of agalsidase alfa compared with agalsidase beta. The Expert Panel recommended that the sponsor of agalsidase alfa should be requested either to make a smaller vial available or to adjust pricing of the single vial to account for use of agalsidase alfa in excess of the weight-based dose approved in the product information.
8	The Expert Panel noted that novel therapies are in development and their availability may impact the LSDP and patients in the future, however none of these therapies were imminent.

Gaucher Disease

#	Recommendations
1	The Expert Panel considered that Gaucher disease meets the prevalence criterion of less than 1:50,000 and currently remains suitable on this criterion for inclusion on the LSDP. In light of the increasing prevalence of Gaucher disease in Australia, and anticipated increased access to genetic testing, the Expert Panel recommends that the prevalence of Gaucher disease be reviewed in five years, or within five years post implementation of any Government agreed changes to eligibility, to determine whether Gaucher disease continues to meet the prevalence criterion for inclusion on the LSDP (prevalence ≤ 1 in 50,000 considering all stages and genetic subtypes of the condition).
2	The Expert Panel recognises that LSDP patient eligibility treatment criteria are currently narrower than applied in some other international jurisdictions. In order to evaluate whether Type 3 Gaucher Disease is appropriate for inclusion on the LSDP, the Expert Panel recommends that sponsors submit applications for consideration of amending/revising the eligibility criteria for commencement and for continued access to treatment for Gaucher disease. Sponsor submissions must include an assessment of the clinical, economic and financial implications if expanded access is a likely consequence of adoption of any proposal.
3	The Expert Panel considers that the burden of testing be reduced where appropriate. To enable this, the purpose, clinical benefits and frequency of specific diagnostic /clinical monitoring tests needs to be clarified. Treating physicians are best placed to specify which currently LSDP-required tests are part of routine care and provide input on the usefulness of LSDP-required tests for diagnosis and management of Gaucher LSDP patients. The Expert Panel recommends further expert advice be sought for review of the requirements for the following tests related to either diagnosis or treatment continuation of LSDP medicines for Gaucher disease: • Which is the most appropriate biomarker to determine Gaucher disease severity and monitor progression? Glucosylsphyngose (lyso-Gb-1) and chitotriosidase are currently used, but should CCL18, TRAP or ACE test results also be included in the criteria? • Is there an appropriate requirement for annual skeletal MRIs? • Which instruments should be used in the LSDP criteria to assess quality of life, pain and fatigue?
4	On the basis of the evidence identified through the Review, the Expert Panel recommended that imiglucerase, velaglucerase and taliglucerase remain suitable for inclusion on the LSDP. The Expert Panel considered that there was insufficient evidence to support any claim of a clinically important difference between the three Gaucher disease medicines.
5	In light of the international clinical guidelines recommending the down-titration of doses after 12 months in stable patients, the Expert Panel recommended that this guidance be included in the LSDP Guidelines for clinicians to consider in stable adult patients. Dosage adjustments should be made on an individual basis, and may increase or decrease, based on achievement of therapeutic goals as assessed by routine comprehensive evaluations of the patient's clinical manifestations.
6	The Expert Panel noted that the extent and methods of data collection and the approach to analysis of the data require 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 clinicians to enter patient data both for everyday administration of the program and for future medicines reviews. The Expert Panel recommended that this revised approach should improve clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future review of Gaucher disease medicines.

#	Recommendations
7	The Expert Panel noted that there appears to be a survival gain and improvement in quality of life from treatment with the three medicines, and that the cost of these medicines remains very high. The Expert Panel therefore recommended that the pricing and listing arrangements for these medicines be reassessed with the goal of improving value for money when: i. current deeds of agreement with sponsors expire; and/or ii. new medicines for Gaucher disease are considered for entry onto the LSDP or other subsidy programs; and/or iii. changes in eligibility criteria are being considered.
8	The Expert Panel acknowledged the challenges for sponsors in providing product to satisfy the requirements of different international markets but recognised the significant excess costs to government due to dispensing of greater than approved doses of treatments for Gaucher disease. The Expert Panel recommended that the value for money aspects of a weight-based dosing be reconsidered. Specifically, the funding approach to treatment at above recommended and approved medicine levels should be reassessed. The Expert Panel were of the view that the Commonwealth should only be reimbursing for the dose of drug prescribed by the treating physician within the approved Product Information doses. To account for this, renegotiation of the funding arrangements with medicine sponsors may be required. The Expert Panel recommended that the sponsors of these medicines should be requested either to make a smaller vial available or to adjust pricing of the single vial to account for use of the medicines in excess of the weight-based dose considered appropriate by the prescriber within the dose limits approved in the Product Information.
9	The Expert Panel noted that novel therapies and diagnostic methods are in development and their availability may impact the LSDP and patients in the future, however none were imminent. The Expert Panel also noted that the existing TGA registered product Cerdelga (eliglustat) is not included in this review but is an approved option for some patients with Gaucher Disease.

Mucopolysaccharidosis Type I (MPS I)

#	Recommendations
1	The Expert Panel considered that MPS I meets the prevalence criterion of less than 1:50,000 and currently remains suitable for inclusion on the LSDP. The Expert Panel advises that the prevalence of MPS I be reviewed five years post implementation of Government agreed changes to determine whether it continues to meet the definition of a rare disease.
2	The Expert Panel recognises that the current LSDP patient eligibility treatment criteria are narrower than current expert opinion. Accordingly, the Expert Panel recommends that sponsors submit applications for the Expert Panel's consideration in support of amending/revising the eligibility criteria for commencement and continued access to treatment for MPS I. Submissions must include an assessment of the clinical, economic and financial implications if expanded access is a likely consequence of adoption of any proposal by the sponsor.

#	Recommendations
3	The Expert Panel acknowledged the importance of analytical validity, clinical validity, and clinical utility when considering the value of health technologies, particularly in this context for the purpose initial and ongoing eligibility requirements. The Expert Panel agreed that the purpose, clinical benefits and frequency of undertaking additional specific clinical monitoring tests for initial and ongoing subsidy compared with routine clinical care needs to be clarified. Treating physicians are best placed to provide input on any discordance between the tests required for initial ongoing eligibility, and that which are used in routine clinical practice, and a formal Health Technology Assessment (HTA) should be conducted for any tests that are required solely for eligibility purposes. The Expert Panel recommends that further clinical advice be sought for review of the following ongoing clinical tests: • Imaging requirements • Cognitive testing • Ophthalmological assessments • Sleep studies • Functional tests.
4	The Expert Panel noted the limitations of the available evidence regarding the conclusion that laronidase extends survival for MPS I patients. The Expert Panel noted that maintenance or slowing of deterioration in clinical outcomes through the use of laronidase is an important outcome. Therefore, on the basis of the evidence identified through the Review, the Expert Panel advises that laronidase remains suitable for inclusion on the LSDP.
5	The Expert Panel noted that data available to estimate the survival benefit observed in LSDP patients treated with laronidase is limited, although there is evidence demonstrating a delay in deterioration. Some patients experience a decline in precent predicted forced vital capacity (ppFVC), although considerable uncertainty about the impact on survival exists. The Expert Panel advises that a price reduction be negotiated with the sponsor on this basis.
6	The availability of consistent and complete data extracted from initial and ongoing applications to the program is essential, particularly that related to patient outcomes. Consistent with recommendation 3, the Expert Panel recommended that: i. the instrument used to measure pain and quality of life be reviewed ii. the extent and methods of data collection be revised iii. the approach to analysis of the data be improved. The LSDP should implement a streamlined solution that enables clinicians to enter patient data both for everyday administration of the program and for future medicines reviews. The Expert Panel recommended that this revised approach should improve clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future reviews of MPS I medicines.
7	The Expert Panel noted that there appears to be a survival gain and improvement in quality of life from treatment with the laronidase, and that the cost of this medicine remains very high. Due to uncertainty of survival gains as a result of limited data, costs associated with laronidase treatment may be even higher than current estimates. The Expert Panel therefore recommended that the pricing and listing arrangements for laronidase be reassessed with the goal of improving value for money when: i. current deeds of agreement with sponsors expire; and/or ii. new medicines for MPS I are considered for entry onto the LSDP or other subsidy programs; and/or iii. changes in eligibility criteria are being considered.
8	The Expert Panel advised that should the Product Information be formally updated to allow for home infusions of laronidase, the Expert Panel and LSDP would be in support of amending the MPS I LSDP Guidelines to include this service to potentially improve care for patients.

#	Recommendations
9	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.

Mucopolysaccharidosis Type II (MPS II)

#	Recommendations
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.
2	The Expert Panel recommends that the MPS II LSDP Guidelines be amended to allow patients with the severe (neurological) form of the disease access to treatment.
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 recommends 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.
4	Consistent with international guidelines the Expert Panel recommends that, at the time of onset of treatment, clinicians and patients should jointly agree on criteria for cessation of the ERT using indicators that reflect lack of response to therapy or deterioration in somatic or neurological disease despite therapy.
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.
6	The Expert Panel noted that the extent and methods of data collection and the approach to analysis of the data require 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 clinicians 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 clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future review of MPS II disease medicines.

#	Recommendations
7	The Expert Panel noted that there appears to be a survival gain and improvement in quality of life 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: i. current deeds of agreement with sponsors expire; and/or ii. new medicines for MPS II are considered for entry onto the LSDP or other subsidy programs; and/or iii. changes in eligibility criteria are being considered.
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.

Mucopolysaccharidosis Type VI (MPS VI)

#	Recommendations
1	The Expert Panel considered that MPS VI meets the prevalence criterion of less than 1:50,000 and currently remains suitable on this criterion for inclusion on the LSDP.
2	The Expert Panel agreed that the purpose, clinical benefits and frequency of undertaking specific diagnostic/clinical monitoring tests needs to be clarified. The Expert Panel noted the importance of considering analytical validity, clinical validity, and clinical utility when assessing the value of health technologies used in the diagnosis and in monitoring patients with MPS VI. Treating physicians are best placed to provide input on the usefulness of current tests used to diagnose, manage and monitor MPS VI LSDP patients. The Expert Panel recommended that further clinical advice be sought for review of the following diagnostic/ongoing clinical tests: • Urinary GAG (glycosaminoglycans analysis) • Liver and spleen size • Ophthalmology and neurological examination • Sleep study
3	The Expert Panel noted the limitations of the available evidence regarding the conclusion that galsulfase likely extends survival for some MPS VI patients. However, on the basis of the evidence identified through the Review, including data on the improvement to patients' quality of life, the Expert Panel advised that galsulfase remains suitable for inclusion on the LSDP.
4	The Expert Panel noted that the extent and methods of data collection and the approach to analysis of the data require 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 clinicians to enter patient data both for everyday administration of the program and for future medicines reviews. The Expert Panel recommended that this revised approach should improve clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future reviews of galsulfase.
5	The Expert Panel noted that a survival gain is plausible, with maintenance of function and improvement in quality of life from treatment with the medicine in some patients, and that the cost of this medicine remains very high. The Expert Panel therefore recommended that the pricing and listing arrangements for this medicine be reassessed with the goal of improving value for money when: i. current deeds of agreement with the sponsor expires; and/or ii. new medicines for MPS VI are considered for entry onto the LSDP or other subsidy programs; and/or

#	Recommendations
	iii. changes in eligibility criteria are being considered.
6	The Expert Panel acknowledged the challenges for sponsors in providing product to satisfy the requirements of different international markets, but recognised the significant excess costs to government due to dispensing of greater than approved doses of treatments for MPS VI disease. The Expert Panel recommended that the value for money aspects of a weight-based dosing be reconsidered. Specifically, the funding approach to treatment at above recommended and approved medicine levels should be reassessed. The Expert Panel were of the view that the Commonwealth should only be reimbursing for the dose of drug prescribed by the treating physician within the approved Product Information doses. To account for this, renegotiation of the funding arrangements with medicine sponsors may be required. The Expert Panel recommended that the sponsors of these medicines should be requested either to make a smaller vial available or to adjust pricing of the single vial to account for use of the medicines in excess of the weight-based dose considered appropriate by the prescriber within the dose limits approved in the Product Information.
7	The Expert Panel advised that should the Product Information be formally updated to allow for home infusions of galsulfase, the Expert Panel and LSDP would be in support of amending the MPS VI LSDP Guidelines to include this service to potentially improve care for patients.

Pompe Disease

#	Recommendations
1	The Expert Panel considered that Pompe disease meets the prevalence criterion of less than 1:50,000 and currently remains suitable for inclusion on the LSDP. Due to the increasing prevalence of Pompe disease in Australia, the Expert Panel recommends that the prevalence of Pompe disease be reviewed within five years post implementation of Government agreed changes to determine whether Pompe disease continues to meet the definition of a rare disease.
2	The Expert Panel noted that the international classification of Pompe disease is for classic and later-onset disease. The Expert Panel advised that the current classification of Infantile Onset Pompe Disease (IOPD), Juvenile Onset Pompe Disease (JOPD) and Adult Onset Pompe Disease (AOPD) should be revised to include only IOPD and Later Onset Pompe Disease (LOPD).
3	The Expert Panel advised that the initial LSDP patient eligibility requirements appear to be suitable for appropriate patient access to treatment.
4	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 diagnostic /clinical monitoring tests needs to be clarified. Treating physicians are best placed to provide input on any discordance between the tests required for initial ongoing eligibility, and that which are used in routine clinical practice, and a formal Health Technology Assessment (HTA) should be conducted for any tests that are required solely for eligibility purposes. The Expert Panel recommends that further clinical advice be sought for review of the following ongoing clinical tests: • For infantile-onset Pompe Disease (IOPD): the need for annual psychometric testing, full neurological testing and testing of haemoglobin, platelets, alanine amino transferase, aspartate amino transferase and lactate dehydrogenase. • For IOPD: clarification on what constitutes ‘invasive ventilation’. • For children under the age of 12: remove requirement for Forced Vital Capacity (FVC – respiratory function test) and 6 Minute Walk Test (6MWT). • For AOPD: need for manual muscle testing.
5	The Expert Panel advised that on the basis of the evidence identified through the Review, alglucosidase alfa remains suitable for listing on the LSDP.
6	The Expert Panel noted that the extent and methods of data collection and the approach to analysis of the data require 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 clinicians to enter patient data both for everyday administration of the program and for future medicines reviews. The Expert Panel recommended that this revised approach should see a future review of alglucosidase alfa with complete and comprehensive data resubmitted for its consideration.
7	The Expert Panel noted that there appears to be a survival gain and improvement in quality of life from treatment with the alglucosidase alfa, and that the cost of this medicine remains very high. Due to uncertainty of survival gains as a result of limited data, costs associated with alglucosidase alfa treatment may be even higher than current estimates. The Expert Panel therefore recommended that the pricing and listing arrangements for alglucosidase alfa be reassessed with the goal of improving value for money when: i. current deeds of agreement wtih sponsors expire; and/or ii. new medicines for Pompe disease are considered for entry onto the LSDP or other subsidy programs; and/or iii. changes in eligibility criteria are being considered.

#	Recommendations
8	The Expert Panel advised that the current weight based dose approved in the LSDP Pompe disease Guidelines remains suitable as it is in line with the Product Information and patients appear to respond positively to treatment.
9	The Expert Panel acknowledged that it can be difficult to maintain an accurate weight based dose for young growing patients. These patients, their families/carers and the healthcare staff providing the subsidised alglucosidase alfa to patients on a fortnightly basis should be mindful of a patient's changing weight and advise the treating physician of any changes. The Expert Panel noted that the current LSDP approval process for dose adjustments is administratively simple and that any improvements to the administration process (such as advised in Recommendation 6) should continue to incorporate a practical process for dose adjustment approvals.
10	The Expert Panel advised that should the Product Information be formally updated to allow for home infusions of alglucosidase alfa, the Expert Panel and LSDP would be in support of amending the Pompe disease LSDP Guidelines to include this service to potentially improve care for patients.

Hereditary Tyrosinaemia Type I (HT1)

#	Recommendations
1	The Expert Panel considered that HT1 meets the prevalence criterion of less than 1:50,000 and currently remains suitable for inclusion on the LSDP.
2	The Expert Panel recommended amending eligibility guidelines to exclude use in patients post liver transplant.
3	The Expert Panel noted that there is evidence that nitisinone extends survival for patients with HT1, although the extent is unclear. On the basis of the evidence identified through the Review, the Expert Panel advises that nitisinone remains suitable for listing on the LSDP.
4	The Expert Panel noted that the approach to data collection and analysis 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 clinicians to enter patient data both for everyday administration of the program and for future reviews new medicines. The Expert Panel recommended that this revised approach should improve clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future review of nitisinone.
5	The Expert Panel considered that clinicians should be made aware of the process for dose adjustments outside of the annual reapplication process.
6	The Expert Panel noted that there appears to be a survival gain and improvement in quality of life from treatment with nitisinone, and that the cost of nitisinone remains very high. The Expert Panel therefore recommended that pricing and listing arrangements for these medicines be reassessed with the goal of improving value for money when: i. current deeds of agreement with sponsors expire; and/or ii. new medicines for HT1 are considered for entry onto the LSDP or other subsidy programs; and/or iii. changes in eligibility criteria are being considered.

Paroxysmal Nocturnal Haemoglobinuria (PNH)

The recommendations relating to eculizumab (Soliris®) for the treatment of PNH will not be actioned by the LSDP. At the July 2021 Pharmaceutical Benefits Advisory Committee (PBAC) Meeting, ravulizumab (Ultomiris®) received a positive recommendation for the treatment of PNH. A medicine is ineligible for inclusion on the LSDP where an alternative is available on the PBS. Eculizumab (Soliris®), for PNH, is now listed on the PBS as of 1 March 2022. Access via the LSDP remains for a three-month transitional period until 1 June 2022. See www.health.gov.au/news/solirisr-eculizumab-available-on-pbs-from-1-march-2022.

#	Recommendations
1	The Expert Panel considered that PNH meets the prevalence criterion of less than 1:50,000 and on that criterion currently remains suitable for inclusion on the LSDP. In light of the increasing number of PNH patients in Australia, the Expert Panel recommends that the prevalence of PNH be reviewed again within five years to determine whether PNH continues to meet the definition of a rare disease for the purposes of this program.
2	The Expert Panel advised that to improve care for patients, the LSDP Guidelines for PNH be adjusted to specify that the frequency of dosing of eculizumab can be +/- 2 days from the 14 day interval, as outlined in the Product Information.
3	The Expert Panel advises that the Product Information should be updated to include guidance on the use of eculizumab doses greater than 900mg per infusion in patients with PNH (notably, in the event of breakthrough intravascular haemolysis). If the Product Information is updated, then it would be appropriate for this guidance to be incorporated in the LSDP Guidelines for PNH. This will require reconsideration of costs and renegotiation of price.
4	The Expert Panel noted that the extent and methods of data collection and the approach to analysis of the data require 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 clinicians to enter patient data both for everyday administration of the program and for future medicines reviews. The Panel recommended that this revised approach should improve clinician and patient satisfaction and facilitate availability of complete and comprehensive data for any future review of any medicines for treating PNH.
5	The Expert Panel noted that although there appears to be a survival gain and improvement in quality of life associated with eculizumab treatment, the cost of eculizumab is extremely high in absolute terms and relative to other drugs on the LSDP. The Expert Panel could identify no specific justification for this extremely high cost and considered that the cost per patient should reduce to levels more aligned with costs paid for similar health gains generated by treatments for other rare diseases on the LSDP and in other subsidy schemes. This would improve equity and sustainability in the system. The Expert Panel therefore recommended that the listing arrangements be reassessed with the goal of improving value for money when: i. current deeds of agreement with the sponsor expire; and/or ii. new medicines for PNH are considered for entry onto the LSDP or other subsidy programs; and/or iii. changes in maximum maintenance dose of eculizumab are implemented for patients experiencing breakthrough haemolysis.
6	The Expert Panel recommended that there be reconsideration of the appropriateness of inclusion on the LSDP of any drug that has a listing on the PBS for another condition resulting in a total patient market in Australia that exceeds the threshold for medicines to be eligible for inclusion on the LSDP (i.e. prevalence < 1:50,000).
7	The Expert Panel noted that the utilisation of eculizumab has exceeded the initial estimates and advised that Department of Health should review current arrangements.

Note: Recommendations were made based on the information available to the Expert Panel at the time of the reviews.