

7.04 MIGALASTAT, Capsule containing migalastat hydrochloride 150 mg, Galafold[®], Amicus Therapeutics

1 Purpose

- 1.1 In response to a referral from the Life Saving Drugs Program (LSDP) Expert Panel (EP), the PBAC considered the PBS listing of migalastat for the treatment of Fabry disease in patients 16 years of age and older who have an amenable mutation.

2 Background

- 2.1 Migalastat was included on the LSDP in November 2018 for the treatment of Fabry disease in patients 16 years of age and older with an amenable mutation who have been treated with enzyme replacement therapy (ERT) for at least 12 months.
- 2.2 In June 2022, as part of its consideration of the sponsor's request to remove the requirement for at least 12 months of ERT prior to commencing treatment with migalastat, the LSDP EP advised it:
- was supportive of having migalastat available for patients with amenable mutations without the requirement for 12 months of ERT prior to commencing treatment;
 - has determined, based on recently available evidence, that Fabry disease no longer meets the prevalence criterion for the LSDP; and
 - will refer migalastat to PBAC for consideration noting the EP's support for making it a first line treatment for Fabry disease, assuming cost-effectiveness can be satisfied.

TGA registration

- 2.3 Migalastat was TGA registered on 11 August 2017 for the long-term treatment of adult and adolescent patients 16 years and older with a confirmed diagnosis of Fabry disease (alpha-galactosidase A deficiency) and who have an amenable mutation. In its pre-PBAC response, the sponsor advised the TGA registration was updated in November 2022 to include adult and adolescent patients 12 years and older. The PBAC noted the updated Product Information recommended a dose of one capsule every other day (the same as the adult dose) for adolescents 12 to < 18 years of age and weighing ≥ 45 kg.

PBAC consideration

2.4 The PBAC has previously considered migalastat in March 2017, July 2017 and November 2017. A summary of each consideration is provided in Table 1.

Table 1: Previous PBAC considerations of migalastat

	March 2017 (major submission)	July 2017 (minor submission)	November 2017 (minor submission)
Clinical evidence	Migalastat vs ERT in treatment-experienced patients: ATTRACT study (n=52 patients with amenable mutations). Migalastat vs placebo in treatment-naïve patients: FACETS study (n=50 patients with amenable mutations).	Unchanged	Some additional longer term data for ATTRACT, FACETS was presented.
Clinical claim	Migalastat is non-inferior in terms of comparative effectiveness and safety over the primary comparator, ERT The PBAC considered that the outcomes of the trials did not provide confidence in the superior effectiveness of migalastat compared to placebo or equivalent effectiveness of migalastat compared to ERT. The PBAC considered....it was reasonable to accept the claim of non-inferior comparative safety compared to ERT.	Unchanged	Unchanged
Economic evaluation	Cost minimisation approach	Unchanged	Unchanged
Cost per patient per year	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Financial estimates	[REDACTED] ¹ to [REDACTED] ¹ treated patients per year	Unclear from PSD	Unclear from PSD
Outcome	Deferred pending the outcome of TGA consideration	The PBAC did not recommend the listing of migalastat for the treatment of Fabry disease. In making this decision, the PBAC was uncertain about the submission's clinical claim of non-inferior comparative effectiveness compared with ERT.	The PBAC did not recommend the listing of migalastat for the treatment of Fabry disease. In making this decision the PBAC considered that the submission's clinical claim of non-inferior comparative effectiveness compared with ERT remained uncertain and could not be supported.

ERT = enzyme replacement therapy, PSD = Public Summary Document

The redacted values correspond to the following ranges:
¹< 500

LSDP EP consideration

- 2.5 The LSDP EP completed a review of Fabry disease in October 2020 and the EP evaluation overview was provided to the PBAC. Migalastat was not included in the protocol for the review as it had only recently become available on the LSDP at the time of protocol development.
- 2.6 The LSDP EP completed a 24 month review of the listing of migalastat on the LSDP and the overview of the review was provided to the PBAC. As part of this review, the EP discussed the sponsor’s request to allow use of migalastat as a first line treatment (i.e., removal of the requirement for 12 months of ERT prior to accessing migalastat). The sponsor of migalastat provided a response to a draft version of the review and this was provided to the PBAC.
- 2.7 The LSDP EP further considered the sponsor request to amend the criteria for migalastat at its June 2022 meeting. The minutes of the meeting were provided to the sponsor and the PBAC. The Fabry Australia Treatment Review White Paper referred to by the LSDP EP as part of its consideration is available on the Fabry Australia website¹.

3 Proposed listing

3.1 The proposed PBS restriction criteria based on the current LSDP guidelines is provided below. The Secretariat has proposed:

- A listing that provides for 28 days of treatment per script with 5 repeats, providing a total of 6 months of treatment
- A General Schedule listing
- Authority Required (written) criteria for initial treatment
- Authority Required (telephone/ online) criteria for continuing treatment
- Authority Required (written) criteria to allow patients currently being treated with migalastat to transition to PBS-funded treatment

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
MIGALASTAT					
Migalastat 123 mg capsules, 14	NEW	1	14	5	Galafold

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: Medical Practitioners

¹ <https://www.fabry.com.au/preventing-the-consequences/>

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Restriction type Authority Required (in writing only via post/HPOS upload)
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: Special Pricing Arrangements apply.
Indication: Fabry disease
Treatment Phase: Initial treatment
Clinical criteria: Patient must have at least one of (i) documented specific deficiency of alpha- galactosidase enzyme activity in blood or white cells, (ii) presence of genetic mutations known to result in deficiency of alpha-galactosidase enzyme activity.
AND
Clinical criteria: Patient must have a documented migalastat amenable GLA gene variant with an eGFR of at least 30 mL/m ² .
AND
Clinical criteria: Patient must have been treated with Enzyme Replacement Therapy (ERT) for at least 12 months prior initiating treatment with this drug
AND
Clinical criteria: Patient must be male, have Fabry related renal disease confirmed by at least one of the following: (i) abnormal albumin (> 20µg/min), as determined by 2 separate samples at least 24 hours apart, (ii) abnormal protein excretion (>150mg/24 hours), (iii) albumin: creatinine ratio greater than upper limit of normal in 2 separate samples at least 24 hours apart, (iv) renal disease due to long-term accumulation of glycosphingolipids in the kidneys. OR
Patient must be female, have Fabry related renal disease confirmed by at least one of the following: (i) proteinuria >300mg/24 hours with clinical evidence of progression, (ii) renal disease due to long-term accumulation of glycosphingolipids in the kidneys. OR
Patient must have Fabry-related cardiac disease confirmed by at least one of the following: (i) Left ventricular hypertrophy, as evidenced by cardiac MRI or echocardiogram data, in the absence of hypertension, (ii) Significant life-threatening arrhythmia or conduction defect. OR
Patient must have ischaemic vascular disease as shown on objective testing with no other cause or risk factors identified. OR
Patient must have uncontrolled chronic pain despite the use of maximum doses of appropriate analgesia and antiepileptic medications for peripheral neuropathy.
Treatment criteria: Must be treated by a physician with expertise in the management of Fabry disease
Population criteria: Patient must be at least 16 years of age.
Prescribing Instructions: If hypertension is present in patients with Fabry-related cardiac disease, the prescriber must treat it optimally for at least 6 months prior to submitting PBS application.

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<p>Administrative Advice: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).</p>
<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Category / Program: GENERAL – General Schedule (Code GE)</p>
<p>Prescriber type: Medical Practitioners</p>
<p>Restriction type: Authority Required (telephone/online PBS Authorities system)</p>
<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p>
<p>Administrative Advice: Special Pricing Arrangements apply.</p>
<p>Indication: Fabry disease</p>
<p>Treatment Phase: Continuing treatment</p>
<p>Clinical criteria: Patient must have received prior PBS-subsidised treatment with this drug for this condition.</p>
<p>AND</p>
<p>Clinical criteria: Patient must have demonstrated clinical improvement or stabilisation of this condition.</p>
<p>AND</p>
<p>Clinical criteria: Patient must have not developed another life threatening or severe disease where long term prognosis is unlikely to be influenced by migalastat.</p>
<p>AND</p>
<p>Clinical criteria: The patient must have not developed another medical condition that might reasonably be expected to compromise a response to migalastat.</p>
<p>Treatment criteria: Must be treated by a physician with expertise in the management of Fabry disease</p>

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<p>Administrative advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).</p>
<p>Category / Program: GENERAL – General Schedule (Code GE)</p>
<p>Prescriber type: Medical Practitioners</p>
<p>Restriction type: Authority Required (in writing only via post/HPOS upload)</p>
<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p>
<p>Administrative Advice: Special Pricing Arrangements apply.</p>
<p>Indication: Fabry disease</p>
<p>Treatment Phase: Grandfather treatment (transition from LSDP-funded migalastat)</p>
<p>Clinical criteria: Patient must have previously received this drug for this condition funded under the Australian Government's Life Saving Drugs Program (LSDP)</p>
<p>AND</p>
<p>Clinical criteria: Patient must have at least one of (i) documented specific deficiency of alpha- galactosidase enzyme activity in blood or white cells, (ii) presence of genetic mutations known to result in deficiency of alpha-galactosidase enzyme activity.</p>
<p>AND</p>
<p>Clinical criteria: Patient must have a documented migalastat amenable GLA gene variant</p>
<p>AND</p>
<p>Clinical criteria: Patient must have an eGFR of at least 30 mL/m².</p>
<p>AND</p>
<p>Clinical criteria: Patient must have been treated with Enzyme Replacement Therapy (ERT) for at least 12 months prior to initiating treatment with this drug</p>
<p>AND</p>
<p>Clinical criteria: Patient must have had at least one of (i) Fabry related renal disease, (ii) Fabry-related cardiac disease, (iii) ischaemic vascular disease, (iv) uncontrolled chronic pain confirmed prior to initiating treatment with this drug.</p>
<p>Treatment criteria: Must be treated by a physician with expertise in the management of Fabry disease</p>
<p>Prescribing Instructions: If hypertension is present in patients with Fabry-related cardiac disease, the prescriber must treat it optimally for at least 6 months prior to submitting PBS application.</p>
<p>Prescribing Instructions: A patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p>

Administrative Advice:

The authority application must be made in writing and must include:

- (1) a completed authority prescription form; and
- (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).

Administrative advice:

Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au

Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos

Or mailed to:

Services Australia

Complex Drugs

Reply Paid 9826

HOBART TAS 7001

- 3.2 In its consideration in June 2022, the LSDP EP was supportive of removing the following clinical criteria from the LSDP criteria:

‘Patients must have been treated with agalsidase alfa or agalsidase beta for at least 12 months or must be intolerant to agalsidase alfa or agalsidase beta’

- 3.3 Additionally, the LSDP EP has previously recommended the initial and continuing restriction criteria be brought into line with current International Clinical Guidelines for Fabry disease (as outlined in the Fabry Australia Treatment Review White Paper).

For more detail on PBAC’s view, see section 5 PBAC outcome.

4 Consideration of the evidence

Clinical evidence

- 4.1 The PBAC previously considered the clinical claim that migalastat is of non-inferior comparative effectiveness compared with ERT was uncertain and could not be supported with the available clinical evidence (paragraph 6.1, migalastat Public Summary Document (PSD), November 2017 PBAC meeting).
- 4.2 The LSDP EP 24-month review did not identify any additional clinical evidence for migalastat. The review found that no important evidence has come to light that clearly establishes migalastat as non-inferior to ERT for all (migalastat-amenable) patients needing treatment, and there remains no direct evidence that migalastat improves survival. However, the review acknowledged that clinical experience with migalastat has grown considerably since PBAC’s review of migalastat in 2017, as more patients have been exposed to migalastat (in both trial and non-trial settings), and there has been longer follow-up of patients in early trials.
- 4.3 The PBAC previously raised concerns regarding the determination of amenability for migalastat (using the Galafold Amenability Table, GAT) as discussed in paragraph 6.10

of the November 2017 PBAC meeting PSD. The LSDP EP 24-month review stated “The key concern with the GAT is that it may be identifying patients with in vitro amenability who are not clinically amenable to migalastat. The review report suggested an option to address this concern is to ensure patients starting on LSDP migalastat have an early review of all clinically relevant information, at around 3 to 6 months”. The pre-PBAC response stated the GAT reduces uncertainty by ruling out patients who almost certainly would not respond to migalastat.

Clinical claim

- 4.4 The PBAC recalled it had previously not accepted the claim of non-inferior comparative effectiveness of migalastat compared to ERT in either treatment naïve or treatment experienced patients (paragraph 6.4, migalastat PSD, November 2017 PBAC meeting). The PBAC noted there was no additional clinical evidence available and the claim remained uncertain.
- 4.5 The PBAC recalled it had previously considered the claim of non-inferior comparative safety of migalastat compared to ERT was reasonable (paragraph 6.5, migalastat PSD, November 2017 PBAC meeting).

Economic analysis

- 4.6 The previous submissions to PBAC were based on a cost minimisation approach to ERT.
- 4.7 However, as the PBAC did not accept the clinical claim of non-inferiority versus ERT, the basis for determining the equi-effective doses and the cost-minimisation approach were also not accepted (paragraph 6.7, migalastat PSD, November 2017 PBAC meeting).
- 4.8 The PBAC previously advised that the cost of migalastat should not be greater than the cost of the form of agalsidase which has the lowest cost to the Commonwealth, measured over a one to two year time period, with a further significant price reduction reflective of the uncertainty around the claim of non-inferiority to ERT (paragraph 6.10, migalastat PSD, November 2017 PBAC meeting).
- 4.9 The PBAC has previously noted that the two ERTs are not cost-effective (paragraph 6.2, migalastat PSD, November 2017 PBAC meeting).

Drug cost/patient/year

- 4.10 Assuming a dose of 150 mg every second day and the current LSDP price of \$ [REDACTED] per 14 capsules, the drug cost per patient per year for migalastat is \$[REDACTED].

Estimated PBS usage & financial implications

- 4.11 The number of patients treated and expenditure on the LSDP is summarised for migalastat in Table 2.

Table 2: Number of treated patients per year and expenditure on migalastat

Financial year	2018/2019 (listed Nov 2018)	2019/2020	2020/ 2021	2021/2022
Number of patients treated	1	1	1	1
Expenditure on the LSDP	\$ 2	\$ 2	\$ 2	\$ 2

LSDP = Life Saving Drugs Program

The redacted values correspond to the following ranges:

¹< 500

²\$0 to < \$10 million

4.12 In its submission to the LSDP EP in May 2022, the sponsor stated that most eligible patients with Fabry disease are currently being treated with either migalastat or ERT. The submission stated removing the requirement for 12 months ERT prior to accessing migalastat would allow up to < 500 patients per year to be treated with migalastat 1 to 12 months earlier than they are currently able to (Table 3).

Table 3: Additional patients to be treated if requirement for 12 months of ERT is removed

Financial year	2022/2023	2023/2024	2024/2025	2025/2026	2026/2027
Treated patients	1	1	1	1	1
Additional patients if 12 month ERT requirement removed	1	1	1	1	1
Total treated patients	1	1	1	1	1

Source: Sponsor response to draft 24 month review

ERT = enzyme replacement therapy

The redacted values correspond to the following ranges:

¹< 500

For more detail on PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended the Authority Required listing of migalastat on the Pharmaceutical Benefits Scheme (PBS) for the treatment of Fabry disease in patients aged 16 years of age and older who have an amenable mutation. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of migalastat would be acceptable if it was less expensive than the lowest cost available enzyme replacement therapy (ERT) on the LSDP for Fabry disease for all patients aged 16 years of age and older. The PBAC considered that this could be achieved with a cost per patient per year no higher than the cost of ERT for a patient weighing 45 kg.
- 5.2 The PBAC noted the request from the LSDP Expert Panel (EP) to reconsider a PBS listing of migalastat, including the LSDP EP support for the removal of the requirement of 12 months of ERT prior to accessing migalastat.
- 5.3 The PBAC acknowledged the importance of patients with Fabry disease having ongoing access to effective therapies.
- 5.4 The PBAC recalled that it had previously found the available evidence for migalastat insufficient to support a claim of non-inferior effectiveness compared to ERT. The

PBAC noted the 24-month review by the LSDP EP stated there was no substantive additional evidence available. However, the PBAC agreed with the LSDP EP that clinical experience with migalastat since its LSDP listing supported its continued availability for eligible patients.

- 5.5 The PBAC recalled that it had previously considered the claim of non-inferior comparative safety of migalastat compared to ERT was reasonable.
- 5.6 The PBAC recalled its previous consideration that the cost of migalastat should not be greater than the cost of the form of agalsidase which has the lowest cost to the Commonwealth, with a further significant price reduction reflective of the uncertainty around the claim of non-inferiority to ERT. The PBAC noted the cost per patient for the ERTs is highly variable due to the use of weight-based dosing and that migalastat was more costly than the ERTs at the lower end of the range of likely patient weights. Therefore, the PBAC considered migalastat would be appropriate for PBS listing at a price that ensured it was less expensive than the lowest cost available ERT on the LSDP for Fabry disease for all patients aged 16 years of age and older, and that this could be achieved with a cost per patient per year no higher than the cost of ERT for a patient weighing 45 kg.
- 5.7 The PBAC considered that, under the parameters outlined in paragraph 5.6 and noting the reduced cost of migalastat and the ERTs since its consideration in November 2017, the cost effectiveness of migalastat would be acceptable.
- 5.8 The PBAC noted the number of patients treated with migalastat in the most recent full financial year (2021/2022) was < 500 and the sponsor's response to the draft 24-month review estimated there would be < 500 patients treated in 2026/2027 (including < 500 additional patient if the requirement for 12 months of ERT is removed). The PBAC noted the number of patients treated with migalastat has been higher than was estimated at the March 2017 meeting (< 500 patients in Year 1 increasing to < 500 patients in Year 5) but considered that, overall, the utilisation of migalastat since it was first included on the LSDP has been reasonably stable. The PBAC advised the utilisation of migalastat be reviewed after 24 months of PBS listing.
- 5.9 The PBAC noted financial estimates for the transitioning of migalastat from the LSDP to the PBS will need to be finalised by the Department, based on the estimated total number of patients likely to be treated with migalastat previously provided by the sponsor (refer to Table 3).
- 5.10 The PBAC advised a General Schedule Authority Required (Written) listing for initial and Grandfather (patients transitioning from LSDP-funded migalastat) treatment phases and an Authority Required (telephone/ online) listing for continuing treatment phase was appropriate. The PBAC considered the restriction wording proposed by the Secretariat based on the current LSDP guidelines (as outlined in Section 3) was appropriate with the following amendments:

- The clinical criterion “Patient must have been treated with Enzyme Replacement Therapy (ERT) for at least 12 months prior initiating treatment with this drug” should be removed (consistent with advice from the LSDP EP, see paragraph 5.2);
 - The clinical criterion “Patient must have a documented migalastat amenable GLA gene variant with an eGFR of at least 30 mL/m²” should be split into two separate criteria;
 - Amend the prescribing instruction “If hypertension is present in patients with Fabry-related cardiac disease, the prescriber must treat it optimally for at least 6 months prior to submitting PBS application” to “If hypertension is present in patients relying their eligibility on Fabry-related cardiac disease, the prescriber must treat it optimally for at least 6 months prior to submitting PBS application”.
 - Addition of prescribing instruction “Confirmation of eligibility for treatment with diagnostic reports including the confirmed mutations must be documented in the patient's medical records”.
- 5.11 The PBAC noted the LSDP EP support for changing the restriction criteria to be consistent with International Clinical Guidelines for Fabry disease (see paragraph 3.3) but advised it would be appropriate to consider any substantial changes to the PBS criteria separately.
- 5.12 The PBAC considered that while there was a moderate risk of use outside the restriction criteria, this could be managed by monitoring utilisation 24 months after PBS listing.
- 5.13 The PBAC recommended that migalastat should not be treated as interchangeable with any other drugs.
- 5.14 The PBAC advised that migalastat is not suitable for prescribing by nurse practitioners.
- 5.15 The PBAC recommended that the Early Supply Rule should apply to migalastat.
- 5.16 The PBAC found that the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022 for Pricing Pathway A were not met. Specifically the PBAC found that in the circumstances of its recommendation for migalastat:
- a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over alternative treatments for Fabry disease;
 - b) The treatment is not expected to address a high and urgent unmet clinical need because of the availability of alternative treatments for Fabry disease;

- c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

Outcome:

Recommended

6 Recommended listing

6.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
MIGALASTAT					
Migalastat 123 mg capsules, 14	NEW	1	14	5	Galafold

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: Medical Practitioners
Restriction type Authority Required (in writing only via post/HPOS upload)
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: Special Pricing Arrangements apply.
Indication: Fabry disease
Treatment Phase: Initial treatment
Clinical criteria: Patient must have at least one of (i) documented specific deficiency of alpha- galactosidase enzyme activity in blood or white cells, (ii) presence of genetic mutations known to result in deficiency of alpha-galactosidase enzyme activity.
AND
Clinical criteria: Patient must have a documented migalastat amenable GLA gene variant
AND
Clinical criteria: Patient must have an eGFR of at least 30 mL/m ² .
AND
Clinical criteria: Patient must be male, have Fabry related renal disease confirmed by at least one of the following: (i) abnormal albumin (> 20µg/min), as determined by 2 separate samples at least 24 hours apart, (ii) abnormal protein excretion (>150mg/24 hours), (iii) albumin: creatinine ratio greater than upper limit of normal in 2 separate samples at least 24 hours apart, (iv) renal disease due to long-term accumulation of glycosphingolipids in the kidneys. OR

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Patient must be female, have Fabry related renal disease confirmed by at least one of the following: (i) proteinuria >300mg/24 hours with clinical evidence of progression, (ii) renal disease due to long-term accumulation of glycosphingolipids in the kidneys. OR
Patient must have Fabry-related cardiac disease confirmed by at least one of the following: (i) Left ventricular hypertrophy, as evidenced by cardiac MRI or echocardiogram data, in the absence of hypertension, (ii) Significant life-threatening arrhythmia or conduction defect. OR
Patient must have ischaemic vascular disease as shown on objective testing with no other cause or risk factors identified. OR
Patient must have uncontrolled chronic pain despite the use of maximum doses of appropriate analgesia and antiepileptic medications for peripheral neuropathy.
Treatment criteria:
Must be treated by a physician with expertise in the management of Fabry disease
Population criteria:
Patient must be at least 16 years of age.
Prescribing Instructions: If hypertension is present in patients relying their eligibility on Fabry-related cardiac disease, the prescriber must treat it optimally for at least 6 months prior to submitting PBS application.
Prescribing Instructions: Confirmation of eligibility for treatment with diagnostic reports including the confirmed mutations must be documented in the patient's medical records.
Administrative Advice: The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: Medical Practitioners
Restriction type: Authority Required (telephone/online PBS Authorities system)
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: Special Pricing Arrangements apply.

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Indication: Fabry disease
Treatment Phase: Continuing treatment
Clinical criteria:
Patient must have received prior PBS-subsidised treatment with this drug for this condition.
AND
Clinical criteria:
Patient must have demonstrated clinical improvement or stabilisation of this condition.
AND
Clinical criteria:
Patient must have not developed another life threatening or severe disease where long term prognosis is unlikely to be influenced by migalastat.
AND
Clinical criteria:
The patient must have not developed another medical condition that might reasonably be expected to compromise a response to migalastat.
Treatment criteria:
Must be treated by a physician with expertise in the management of Fabry disease
Administrative advice:
Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

Category / Program:
GENERAL – General Schedule (Code GE)
Prescriber type: Medical Practitioners
Restriction type:
Authority Required (in writing only via post/HPOS upload)
Administrative Advice:
No increase in the maximum quantity or number of units may be authorised.
Administrative Advice:
No increase in the maximum number of repeats may be authorised.
Administrative Advice:
Special Pricing Arrangements apply.
Indication: Fabry disease
Treatment Phase: Grandfather treatment (transition from LSDP-funded migalastat)
Clinical criteria:
Patient must have previously received this drug for this condition funded under the Australian Government's Life Saving Drugs Program (LSDP)
AND
Clinical criteria:
Patient must have at least one of (i) documented specific deficiency of alpha- galactosidase enzyme activity in blood or white cells, (ii) presence of genetic mutations known to result in deficiency of alpha-galactosidase enzyme activity.
AND
Clinical criteria:
Patient must have a documented migalastat amenable GLA gene variant with an eGFR of at least 30 mL/m ² .

AND
Clinical criteria:
<i>Patient must have met all other PBS eligibility criteria that a non- 'Grandfather' patient would ordinarily be required to meet, meaning that at the time LSDP supply was commenced, the patient had at least one of</i>
(i) Fabry-related renal disease, (ii) Fabry-related cardiac disease, (iii) ischaemic vascular disease, (iv) uncontrolled chronic pain
Treatment criteria:
Must be treated by a physician with expertise in the management of Fabry disease
Prescribing Instructions: If hypertension was present in patients relying their eligibility on Fabry-related cardiac disease, the prescriber must have treated it optimally for at least 6 months prior to commencing LSDP subsidised treatment with this drug.
Prescribing Instructions: A patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.
Administrative Advice:
The authority application must be made in writing and must include: (1) a completed authority prescription form; and (2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice).
Administrative advice:
Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available

through the PBS. The PBAC welcomes applications containing new information at any time.

8 Sponsor's Comment

Amicus Australia welcomes the opportunity to make migalastat more easily available to Australian patients with Fabry disease. We look forward to working with the PBAC on an arrangement that is equitable for patients, the Commonwealth and Amicus.