

7.14 GILTERITINIB, Tablet 40 mg (as fumarate), Xospata[®], Astellas Pharma Australia Pty Ltd

1 Purpose

- 1.1 The early re-entry resubmission sought a Section 85 Authority Required (Telephone/Electronic) listing for gilteritinib for the treatment of patients with relapsed or refractory acute myeloid leukaemia (AML) with an FMS-like tyrosine kinase 3 (FLT3) mutation.
- 1.2 Listing was again requested on a cost-effectiveness basis compared with salvage chemotherapy. The key components of the previous submission were unchanged and are shown in Table 1.

Table 1: Key components of the clinical issue addressed in the submission

Component	Description
Population	FLT3 mutation-positive relapsed or refractory acute myeloid leukaemia
Intervention	Gilteritinib 120 mg (3 x 40 mg oral tablets) once daily, increased to 200 mg daily (5 x 40 mg) if no response achieved within 4 weeks, decreased to 80 mg (2 x 40 mg) daily to manage adverse events.
Comparator	Salvage chemotherapy (low intensity: low dose cytarabine or azacitidine; high intensity: MEC induction chemotherapy or FLAG-IDA induction chemotherapy).
Outcomes	Overall survival, remission rate, event free survival, HSCT rate, potential for cure.
Clinical claim	Gilteritinib is superior to salvage chemotherapy in terms of clinical efficacy and safety and tolerability.

Source: Table 1, p4 of the November 2021 submission.

FLAG-IDA; G-CSF, fludarabine, cytarabine, idarubicin; FLT3, FMS-like tyrosine kinase 3; HSCT, haematopoietic stem cell transplantation; MEC, mitoxantrone, etoposide, cytarabine.

2 Background

Registration status

- 2.1 Gilteritinib was TGA registered on 26 March 2020 for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation.

Previous PBAC consideration

- 2.2 The resubmission was based on the PBAC consideration from November 2021. This resubmission addressed the issues raised by PBAC; see Table 2 below.

Table 2: Summary of key matters to be addressed

Matter of concern	Response
<p>The PBAC considered that the economic model could be relied upon for decision making with the following amendments:</p> <ul style="list-style-type: none"> • use of the current azacitidine price • 58.9% of patients hospitalised for salvage chemotherapy • post-HSCT gilteritinib maintenance therapy costs and benefits excluded • a 25-year time horizon • a clinically appropriate and justified cure assumption (para 7.8). 	<p>Implemented all requested changes. With respect to the amendment requiring ‘a clinically appropriate and justified cure assumption’, the resubmission presented 3 scenarios:</p> <ul style="list-style-type: none"> • #1 (base case) – 3-year cure point applied (compared with 2 years in the previous submission base case) • #2 – 2-year cure point and an alternate definition of those alive and relapse free applied • #3 – 3-year cure point and an alternate definition of those alive and relapse free applied.
<p>With the changes described in row above, the PBAC considered that a price reduction would be required to achieve an acceptable ICER in the range of \$70,000 to \$80,000 per QALY gained, and to help mitigate remaining uncertainty associated with the clinical inputs and model results (para 7.8).</p>	<p>Cost per QALY gained in each scenario:</p> <ul style="list-style-type: none"> • #1: \$¹ • #2: \$² • #3: \$³. <p>These ICERs were based on a ⁴% price reduction from \$⁴ to \$⁵ (AEMP) per 28-day pack.</p>
<p>The PBAC requested revised financial estimates as presented in the pre-PBAC response updated with the price reduction in row above, reduced AML incidence and reduced gilteritinib uptake. The PBAC considered that the incidence of AML had been slightly overestimated, and that a rate of 4.2 per 100,000 was the most up-to-date estimate. The uptake was also likely to be lower than 95%, given that a proportion of patients surviving to the relapsed/refractory setting may no longer be suitable for active treatment (para 7.9-7.10).</p>	<p>Changes applied from pre-PBAC response:</p> <ul style="list-style-type: none"> • Incidence of 4.2 per 100,000 (AIHW, 2021) • Uptake of 90% • Gilteritinib price reduction incorporated.
<p>The PBAC advised that, given the overall uncertainty regarding the estimated patient numbers, an RSA would be required (para 7.9).</p>	<p>Resubmission was not able to provide a detailed RSA for the resubmission deadline but was prepared to enter an RSA.</p>

Source: Table 1, pp ii-iv of the submission, and 7.14 gilteritinib minutes, November 2021 PBAC meeting.

AEMP = approved ex-manufacturer price, AML = acute myeloid leukaemia, ICER = incremental cost-effectiveness ratio, QALY = quality-adjusted life year, RSA = risk-sharing arrangement, SMR = standardised mortality ratio.

The redacted values correspond to the following ranges:

¹ \$75,000 to < \$95,000

² \$45,000 to < \$55,000

³ \$55,000 to < \$75,000

⁴ \$15,000 to < \$25,000

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

3 Requested listing

3.1 In November 2021, with respect to the requested PBS restriction, the PBAC:

- Noted that the pre-PBAC response had withdrawn its request for use as maintenance therapy post-HSCT in patients previously treated with gilteritinib, and that these patients would need to be excluded from the restriction.
- Considered that a General Schedule Authority Required (Telephone/Electronic) listing would likely be appropriate.

- Agreed with the ESC that it would be appropriate for the initial gilteritinib listing to have zero repeats and for the continuing phase listing to have 4 repeats. The PBAC considered there would be no need to permit increases in repeats, however patients needing a 200 mg dose would require an increase to the maximum quantity (a maximum quantity multiplier of 2 applied to the continuing treatment and grandfathered treatment restrictions would provide sufficient supply).
 - Noted that the key clinical evidence in the submission (the ADMIRAL trial) included only patients with ECOG status of 0 to 2, and considered that it would be appropriate for the proposed listing to be restricted to these patients.
 - Considered that further refinements to the wording and requirements around monitoring of disease and cessation of therapy would likely be required (paragraph 7.3, gilteritinib Public Summary Document (PSD), November 2021 PBAC meeting).
- 3.2 The resubmission did not include a requested listing, but the pre-PBAC response presented the previous submission's requested listing, with the secretariat's suggested amendments.

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

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted and welcomed the input from a health care professional (1) and organisations (3) via the Consumer Comments facility on the PBS website. The health care professional considered that the role of gilteritinib in clinical practice would be to achieve remission in relapsed/refractory FLT3 positive AML, to allow these patients to receive allogeneic hematopoietic stem cell transplantation (HSCT), and also to achieve the best curative outcomes through maintenance use in the post-transplant setting.
- 4.3 The PBAC noted the comments received from Rare Cancers Australia and the Leukaemia Foundation, outlining the poor prognosis of this patient population and potential benefits associated with the oral formulation of gilteritinib. Both organisations were strongly supportive of the PBS listing. The Leukaemia Foundation also described the experience of a patient currently using the medicine in Australia, who achieved sustained remission following a dose reduction due to minor adverse events (rash and itching) and is anticipating undergoing HSCT.
- 4.4 The PBAC noted the advice received from the Australasian Leukaemia & Lymphoma Group (ALLG), which aligned with the advice received from the health care

professional, and strongly emphasised that gilteritinib was expected to reduce the risk of relapse in the post-HSCT maintenance setting. The ALLG highlighted the small number of expected patients in this group and requested that the PBAC consider extending PBS listing to this group, particularly in the absence of any other approved FLT3 inhibitors in Australia for this purpose.

Comparative effectiveness

- 4.5 In November 2021, the PBAC considered that the submission's claim of superior comparative effectiveness was likely reasonable in terms of improved overall survival (OS) over the ADMIRAL trial duration, noting that OS was statistically significantly longer for patients in the gilteritinib arm than in the salvage chemotherapy arm, with more robust results at later data cuts, and that there was consistency of benefit seen across primary and secondary outcomes. However, a range of issues noted with the ADMIRAL trial and analyses meant that the magnitude of survival benefit over the long term was uncertain, particularly in the subgroups of patients who do and do not proceed to HSCT. The PBAC also considered that the long-term remission and relapse outcomes were unclear, although there was a trend towards longer event-free survival (EFS). Importantly, in November 2021, the PBAC also agreed with the ESC that the treatment benefit in the post-HSCT maintenance setting was unsupported and considered it appropriate that the pre-PBAC response at that time had withdrawn this aspect of the requested listing (paragraph 7.6, gilteritinib PSD, November 2021).
- 4.6 The PBAC had also considered that the safety profiles of gilteritinib and salvage chemotherapy were similar in intensity but with some important differences in both type and incidence of adverse effects encountered, which meant that the claim of superior comparative safety was not adequately supported by the data presented in the submission (paragraph 7.7, gilteritinib PSD, November 2021).
- 4.7 As outlined in paragraph 4.5, the PBAC had previously noted a range of issues with the ADMIRAL trial and analyses, including: (i) concerns about the applicability of the data to the PBS population in terms of HSCT rates during the trial, prior FLT3 inhibitor use, as well as age and general fitness; (ii) the potential for confounding of OS results due to differential use of subsequent therapies; (iii) the short treatment duration in the salvage chemotherapy arm limiting the reliability of response assessments including event free survival (EFS); (iv) small numbers, a lack of documentation, and study design limitations making the post-HSCT maintenance use analysis difficult to interpret; (v) limited data to support a survival benefit in patients who did not receive HSCT during the trial follow up; and (vi) likely evidence of ongoing disease in patients whom the submission claimed were "cured".
- 4.8 Regarding applicability in terms of age, the resubmission presented PBS sample data on patients initiated on midostaurin from December 2018 to July 2021. The mean age was 58 years with a median of 60 years, which the resubmission claimed reflected the age of diagnosis for FLT3 AML that is younger than AML overall (Australian mean age 66 years, median 71 years, AIHW 2021) and similar to the ADMIRAL trial (mean age

58.5 years, median 62 years, median 5 months since diagnosis). The resubmission also presented data from Schneider et al. (2012), which analysed patients from 3 clinical trials in AML (AMLCG99, AML98, and AML04). The overall frequency of a FLT3-ITD mutation was 24.3% (353/1,450). The median age in FLT3-ITD positive patients as the most common mutation was significantly lower compared to patients with wildtype FLT3 (55 versus 61 years; $p < 0.001$). Thus, the resubmission claimed it was reasonable to assume that the age of ADMIRAL patients is representative of the proposed gilteritinib population.

- 4.9 The resubmission also re-presented data previously reviewed by PBAC with respect to the applicability of the ADMIRAL trial to the Australian population in terms of prior midostaurin use.
- 4.10 Regarding the issue of long-term survival, the resubmission presented results from a large Australian observational study in patients with a range of haematological cancers (Kliman et al., 2020). This study reported long-term survival for HSCT recipients using the Australasian Bone Marrow Transplant Recipient Registry and provided survival outcomes for those alive and relapse free at 2 years. For those remission free at >2 years after allogeneic transplant there was 78-80% survival at 10 years with 96-99% the survival risk of the general population (which the resubmission suggested indicated an SMR close to 1 as opposed to the SMR of 2.0 used in the economic analyses).
- 4.11 In addition, the pre-PBAC response argued that concerns raised regarding the likely evidence of ongoing disease in patients whom the submission claimed were “cured” have been addressed by an alternate definition for those who attain long-term survival benefit (see paragraph 4.13).

Economic analysis

- 4.12 As outlined in Table 2, the outstanding issues to be resolved in the resubmission were related to the economic model and financial estimates. In the resubmission’s base case economic model, a 3-year cure point was applied for all those alive (compared with 2 years in the previous submission’s base case). As per the November 2021 submission, these survivors are considered ‘cured’ in the sense that they have the best long-term survival of all patients. However, the resubmission stated they are not considered ‘cured’ in the commonly understood sense. Rather, the general population mortality was increased with a standardised mortality ratio (SMR) of 2.0 applied to survivors after 3 years. The resubmission’s base case incremental cost-effectiveness ratio (ICER) was \$75,000 to < \$95,000 per QALY gained. The ESC had previously advised that in clinical practice 5 years disease free is generally a more accepted definition of a cure, and that patients with ongoing disease cannot be considered cured. The ESC had noted that such patients’ morbidity and mortality will be greater than the general population due to complications of treatment (paragraph 6.55, 5.08 gilteritinib PSD, November 2021 PBAC meeting).

- 4.13 In the two sensitivity analyses presented, the resubmission applied an alternate definition of those alive and relapse free and applied a cure point of 2 and 3 years respectively. The proportion alive and relapse free at 2 years was sourced from the September 2020 data cut of ADMIRAL, where 26 patients (10.5% of ITT population) on gilteritinib lived for 2 or more years without relapse, and no salvage chemotherapy patients were alive in sustained remission by 2 years. The SMR of 2.0 was applied to 10.5% of gilteritinib patients alive at 2 years (implemented by weighting the 18.67% alive at 2 years in the base case by a value that would result in 10.55% being ‘alive and relapse free’; this was 56.5%). A similar method was used to calculate a 3-year cure point. The resulting ICERs for the sensitivity analyses undertaken were \$45,000 to < \$55,000/QALY and \$55,000 to < \$75,000/QALY for the 2-year and 3-year cure points respectively.

Drug cost/patient/year

- 4.14 The estimated drug cost/patient per course would be \$ [REDACTED], based on a mean of 5.84 cycles, a DPMQ of \$ [REDACTED] per 28-day pack, and 99.2% adherence (the mean relative dose intensity reported for the gilteritinib arm of the ADMIRAL trial).

Estimated PBS usage & financial implications

- 4.15 The resubmission provided revised financial estimates which:
- Updated the incidence of AML from 4.3 cases per 100,000 population (AIHW 2020) to 4.2 per 100,000 population (AIHW 2021)
 - Reduced the gilteritinib uptake rate from 95% (across all years) to 90%. The uptake rate was based on sponsor assumption. The resubmission maintained that uptake would be high as gilteritinib offers a targeted treatment option for patients with poor prognosis.
 - Incorporated the gilteritinib price reduction proposed in the resubmission.
- 4.16 The resubmission estimated a net cost to the RPBS of \$10 million to < \$20 million in Year 6 of listing, with a total net cost to the RPBS of \$80 million to < \$90 million over the first 6 years of listing; see Table 3 below.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of initiating patients ^a	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Number of continuing patients ^b	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Number of scripts dispensed ^c	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Cost of gilteritinib to the PBS/RPBS						
Net PBS/RPBS cost (less copay)	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³
Change in utilisation of other medicines						
Total savings to the PBS/RPBS	-\$█ ⁴	-\$█ ⁴	-\$█ ⁴	-\$█ ⁴	-\$█ ⁴	-\$█ ⁴
Net financial implications						
Net cost to the PBS/RPBS	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³
Cost to MBS	\$█ ⁵	\$█ ⁵	\$█ ⁵	\$█ ⁵	\$█ ⁵	\$█ ⁵
Net cost to PBS/RPBS/MBS	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³	\$█ ³
Net cost of gilteritinib to the PBS/RPBS (previous pre-PBAC response November 2021^d)						
Net cost to PBS/RPBS	\$█ ³	\$█ ³	\$█ ³	\$█ ⁶	\$█ ⁶	\$█ ⁶

^a Includes 18 grandfathered patients.

^b 28% discontinued treatment due to progressive disease (Table 6 ADMIRAL CSR)

^c Assuming 3 initial scripts, 3.93 continuing scripts, 100% compliance, per patient per year as estimated by the resubmission.

^d Incorporating reduced azacytidine price and overall mean 5.84 cycles

Source: Tables 14 to 16, and Table 18, pp xviii-xix of resubmission, and Xospata FLT3_Financial Estimates Early Resubmission_1.xlsx

The redacted values correspond to the following ranges:

¹ < 500

² 500 to < 5,000

³ \$10 million to < \$20 million

⁴ net cost saving

⁵ \$0 to < \$10 million

⁶ \$20 million to < \$30 million

Financial Management – Risk Sharing Arrangement

4.17 The resubmission stated the sponsor was not able to provide a detailed risk sharing arrangement (RSA) in time for the early re-entry resubmission but was prepared to discuss and enter into an RSA with the Department. The pre-PBAC response stated that the key elements for an RSA would be the special pricing arrangement for gilteritinib; annual expenditure caps based on agreed net PBS/RPBS cost to government from the financial estimates and agreed rebates for exceeding the agreed annual expenditure caps.

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

5 PBAC Outcome

- 5.1 The PBAC recommended the Authority Required (telephone/online PBS Authorities system) listing of gilteritinib for the treatment of patients with relapsed or refractory acute myeloid leukaemia (AML) with an FMS-like tyrosine kinase 3 (FLT3) mutation.
- 5.2 The PBAC is satisfied that gilteritinib provides, for some patients, a significant improvement in efficacy over salvage chemotherapy.
- 5.3 The PBAC considered that the resubmission had addressed the outstanding issues identified at the November 2021 PBAC meeting via its respecified economic model and revised financial estimates which incorporated the reduced price proposed in the resubmission. The PBAC's recommendation for listing was based on, among other matters, its assessment, as described above, that the cost-effectiveness of gilteritinib would be acceptable at the price proposed in the resubmission. In addition, the PBAC considered a Risk Sharing Arrangement (RSA) appropriate to address any residual uncertainty regarding estimated patient numbers.
- 5.4 The PBAC noted the consumer comments highlighted the poor prognosis of this patient population and potential benefits associated with the oral formulation of gilteritinib.
- 5.5 The PBAC also noted that the consumer comments had been strongly supportive of extending the listing for use as maintenance therapy post-hematopoietic stem cell transplantation (HSCT). The PBAC reiterated its November 2021 advice that the evidence to support post-HSCT maintenance use was hindered by small numbers, a lack of documentation, and study design limitations (paragraph 7.5, gilteritinib PSD, November 2021 PBAC meeting). The PBAC reaffirmed its November 2021 advice that it considered it appropriate that this aspect of the requested listing has been withdrawn by the sponsor (paragraph 7.6, gilteritinib PSD, November 2021 PBAC meeting).
- 5.6 The PBAC recalled it had considered that the claim of clinical superiority was likely reasonable for overall survival but not for safety. It remained of the view that the magnitude of long-term survival benefit was uncertain and that the new arguments made by the resubmission did not meaningfully alter its opinion.
- 5.7 The PBAC noted that the economic model had been revised in line with the PBAC's previous advice concerning certain inputs and the structure as shown in Table 2. In response to the advice that the model should incorporate a clinically appropriate and justified cure assumption, the resubmission had presented three scenarios. The PBAC noted that a 3-year cure point was applied for all those alive in scenario #1 with a resulting incremental cost-effectiveness ratios (ICER) of \$75,000 to < \$95,000 per QALY. The PBAC considered that scenarios #2 and #3, which modelled a cure in those alive and relapse free at 2 and 3 years respectively, were more likely to be clinically appropriate as they attempted to address previous concerns that patients with ongoing disease were considered cured. The ICERs in these scenarios were

\$45,000 to < \$55,000 (scenario #2) and \$55,000 to < \$75,000 (scenario #3) per QALY gained. The PBAC recalled its November 2021 advice that a price reduction to achieve an ICER in the range of \$70,000 to \$80,000 per QALY gained would be required to mitigate the remaining uncertainty associated with the clinical inputs and model results (see Table 2). The PBAC considered the price reduction proposed in the resubmission, and the resulting ICERs from the three scenarios provided, addressed the Committee’s concerns regarding the cost-effectiveness of gilteritinib.

- 5.8 The PBAC considered that the revised financial estimates incorporating the reduced price, along with an amended AML incidence and gilteritinib uptake rate, produced more plausible estimates of likely use in Australian practice and were aligned with its previous advice. The PBAC advised that the expenditure estimates should form the basis of an RSA, with a rebate of █% above the annual caps.
- 5.9 The PBAC considered the proposed restriction provided in the pre-PBAC response was consistent with the Committee’s November 2021 advice except for the provision of refinements around the monitoring of disease and cessation of therapy. In relation to the latter, the PBAC considered the Prescribing Instructions regarding progressive disease could be removed from the initial treatment restriction and amended for the Continuing treatment restriction and the grandfathered treatment restriction as per the recommended listing outlined in paragraph 6.1.
- 5.10 The PBAC advised that gilteritinib is not suitable for prescribing by nurse practitioners.
- 5.11 The PBAC recommended that the Early Supply Rule should not apply.
- 5.12 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for gilteritinib:
 - a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy over salvage chemotherapy. This is because, based on the available evidence in the submission, the magnitude of the overall survival gain was not considered substantial and in addition was uncertain over the long-term;
 - b) The treatment is not expected to address a high and urgent unmet clinical need as salvage chemotherapy regimens do provide a degree of benefit in this population, despite the ongoing need for more efficacious regimens like gilteritinib;
 - 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.
- 5.13 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
GILTERITINIB					
gilteritinib 40 mg tablet, 84	NEW	1	84	0	Xospata
Restriction Summary / Treatment of Concept:					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Telephone/electronic via Online PBS Authorities				
	Episodicity: Relapsed or refractory				
	Condition: Acute Myeloid Leukaemia				
	Indication: Relapsed or refractory Acute Myeloid Leukaemia				
	Treatment Phase: Initial treatment				
	Clinical criteria:				
	The treatment must be the sole PBS-subsidised therapy for this condition.				
	AND				
	Clinical criteria:				
	The condition must not be acute promyelocytic leukaemia.				
	AND				
	Clinical criteria:				
	The condition must be internal tandem duplication (ITD) and/or tyrosine kinase domain (TKD) FMS tyrosine kinase 3 (FLT3) mutation positive before initiating this drug for this condition, <i>confirmed through a pathology report from an Approved Pathology Authority.</i>				
	AND				
	Clinical criteria:				
	Patient must have a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score of no higher than 2 prior to treatment initiation.				
	Prescribing Instructions:				
	The prescriber must confirm whether the patient has FLT3 ITD or TKD mutation. The test result and date of testing must be provided at the time of application and documented in the patient's file.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: Special Pricing Arrangements Apply				
	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 888 333.				

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
GILTERITINIB					
gilteritinib 40 mg tablet, 84	NEW	1	84	4	Xospata
Restriction Summary / Treatment of Concept:					

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	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Telephone/electronic via Online PBS Authorities
	Episodicity: Relapsed or refractory
	Condition: Acute Myeloid Leukaemia
	Indication: Relapsed or refractory Acute Myeloid Leukaemia
	Treatment Phase: Continuing treatment
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition.
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition.
	AND
	Clinical criteria:
	Patient must not have developed disease progression while being treated with this drug for this condition.
	AND
	Clinical criteria
	Patient must not be undergoing or have undergone a stem cell transplant
	Prescribing Instructions: Progressive disease monitoring via a complete blood count must be taken at the end of each cycle. If abnormal blood counts suggest the potential for relapsed AML, following a response to gilteritinib, a bone marrow biopsy must be performed to confirm the absence of progressive disease for the patient to be eligible for further cycles. Progressive disease is defined as the presence of any of the following: •Leukaemic cells in the CSF; •Re-appearance of circulating blast cells in the peripheral blood, not attributable to overshoot following recovery from myeloablative therapy; •Greater than 5 % blasts in the marrow not attributable to bone marrow regeneration or another cause; •Extramedullary leukaemia.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements Apply
	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 888 333.

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
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Restriction Summary / Treatment of Concept:					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required – Telephone/electronic via Online PBS Authorities				
	Episodicity: Relapsed or refractory				
	Condition: Acute Myeloid Leukaemia				
	Indication: Relapsed or refractory Acute Myeloid Leukaemia				

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	Treatment Phase: Grandfathered treatment
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition.
	AND
	Clinical criteria:
	Patient must have received non-PBS subsidised treatment with this drug for this condition prior to [date of PBS listing].
	AND
	Clinical criteria:
	Patient must not have developed disease progression while receiving non-PBS subsidised treatment with this drug for this condition.
	AND
	Clinical criteria:
	The condition must have relapsed or been refractory prior to initiating non-PBS-subsidised treatment with this drug for this condition.
	AND
	Clinical criteria:
	The condition must be internal tandem duplication (ITD) and/or tyrosine kinase domain (TKD) FMS tyrosine kinase 3 (FLT3) mutation positive before initiating this drug for this condition <i>confirmed through a pathology report from an Approved Pathology Authority.</i>
	AND
	Clinical criteria:
	The condition must not be acute promyelocytic leukaemia.
	AND
	Clinical criteria:
	Patient must have had a World Health Organisation (WHO) Eastern Cooperative Oncology Group (ECOG) performance status score no higher than 2 at the time of non-PBS supply was initiated.
	AND
	Prescribing Instructions: Progressive disease monitoring via a complete blood count must be taken at the end of each cycle. If abnormal blood counts suggest the potential for relapsed AML, following a response to gilteritinib, a bone marrow biopsy must be performed to confirm the absence of progressive disease for the patient to be eligible for further cycles. Progressive disease is defined as the presence of any of the following: •Leukaemic cells in the CSF; •Re-appearance of circulating blast cells in the peripheral blood, not attributable to overshoot following recovery from myeloablative therapy; •Greater than 5 % blasts in the marrow not attributable to bone marrow regeneration or another cause; •Extramedullary leukaemia.
	Prescribing Instructions: The prescriber must confirm whether the patient has FLT3 ITD or TKD mutation. The test result and date of testing must be provided at the time of application and documented in the patient's file.
	Administrative Advice: Patients 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: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	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 888 333.
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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

Astellas Pharma Australia welcomes the positive recommendation decision by the PBAC for gilteritinib and is working with the Department of Health on the earliest possible PBS listing for patients with refractory or relapsed FLT3 mutation positive AML. As per the previous Public Summary Document for gilteritinib Astellas Pharma Australia has agreed to a PBS listing that excludes post-HSCT maintenance, solely due to the PBAC's request.