AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

One Wales Medicine Assessment Group summary of decision rationale

Medicine: gilteritinib (Gilteritinib Astellas®)
Indication: For maintenance therapy after haematopoietic stem cell transplant for acute myeloid leukaemia in adults with FLT3-ITD mutation and evidence of measurable residual disease before or after transplant (OW36).

Meeting date: **05 October 2026**

Criteria	OWMAG opinion
Clinical effectiveness	OWMAG were presented with the Evidence Status Report (ESR) and noted the rationale for use of gilteritinib for maintenance therapy after haematopoietic stem cell transplant (HCT) for acute myeloid leukaemia (AML) in adults with FLT3 internal tandem duplication (ITD) mutation and evidence of measurable residual disease (MRD) before or after transplant. The group noted the rationale from clinicians that gilteritinib is better tolerated and has fewer adverse effects than sorafenib. The group noted the current treatment option for maintenance therapy after haematopoietic stem cell transplant for acute myeloid leukaemia in adults with FLT3-ITD mutation is off-label sorafenib following One Wales assessment in 2022. This advice covers patients who have MRD positive and those who are MRD negative. The group noted that clinicians expect that if gilteritinib were to be made available for this subset of MRD-positive patients that sorafenib would no longer be considered as an option for maintenance treatment in FLT3-ITD AML patients, irrespective of MRD status. OWMAG acknowledge the proposed place of gilteritinib for a subset of patients with MRD detected either pre- or post-HCT. OWMAG considered the available evidence, including the pre-planned subgroup analysis of the MORPHO clinical trial (Levis et al., 2024), additional post hoc analysis of this trial by Levis et al. (2025), and retrospective studies by Liang et al. (2021,2025). Across these studies, gilteritinib demonstrated an improvement in relapse free survival and in overall survival compared with placebo or no maintenance treatment. The MORPHO trial demonstrated significant benefit of gilteritinib over placebo in MRD

	positive patients (HR 0.515; 95% CI: 0.316 to 0.838; p = 0.0065), no benefit was shown in MRD negative patients (HR, 1.213 [95% CI: 0.616 to 2.387]; p = 0.575). The studies by Liang et al. demonstrated benefit compared with no maintenance independent of MRD status. In the absence of direct comparison between gilteritinib and sorafenib, OWMAG considered 3 studies for sorafenib efficacy. Of these, SORMAIN (Burchet et al., 2020) was the main study used in the One Wales assessment. An exploratory post-hoc analysis of MRD status pre- and post-HCT showed significantly improved relapse-free survival (RFS) compared with placebo for patients who were MRD-negative before HCT (p = 0.028), and for those who were MRD-positive after HCT (p = 0.015). The group acknowledge the limitations of this study for comparison as stated by the clinician. They accept that due to improved sensitivity of modern MRD testing it is likely that MRD negative patients could have had low levels of MRD. The group noted the poor tolerability in real world data provided by Cardiff and Vale University Health Board haematology department. They recognised the number of patients discontinuing treatment due to adverse effects and that no patients receive the full dose of sorafenib in practice due to toxicity, in particular gastrointestinal effects. OWMAG considered the safety profile of gilteritinib and that no new safety signals had been noted in the MORPHO trial. Comparative data on safety is lacking, supporting studies showed a trend for discontinuation of treatment to be higher for sorafenib than for gilteritinib. OWMAG considers that, clinical evidence for post-HCT gilteritinib maintenance treatment for MRD positive FLT3-ITD AML is limited but has a beneficial effect on RFS and overall survival when compared with placebo and a similar efficacy when compared with sorafenib. Whilst the available real-world data suggest sorafenib may be more poorly tolerated than is suggested in the literature.
Cost-effectiveness	There is no published cost-effectiveness evidence comparing this treatment with the relevant standard of care. Therefore, OWMAG considered the de-novo stepwise cost-effectiveness and threshold analysis, presented in the ESR. OWMAG accepted that the stepwise approach adopted by AWTTC was a suitable assessment of cost-effectiveness.

	The group acknowledged the limitations of the analyses in terms of uncertainty due to naïve comparison between heterogeneous studies for gilteritinib and sorafenib (MORPHO and Massoud et al., 2026). OWMAG noted that the adverse event profile, treatment discontinuations and dose reductions were taken from the broader post HCT FLT3-ITD AML population and acknowledge clinical expert opinion that adverse effects are not expected to differ in the MRD positive group when compared to the MRD negative group. The group recognised the immature overall survival data for gilteritinib and the resultant uncertainty in survival estimates and consequently in cost, threshold and plausibility estimates. Limited evidence on continued care and future treatments were noted by the group. OWMAG consider that the expected clinical benefit of gilteritinib compared to sorafenib is uncertain. This uncertainty, alongside limitations in data quality (for gilteritinib and sorafenib), discontinuation rates and adverse events, makes assessment of value difficult. Threshold analysis indicates that a gain of [confidential data removed] QALYs is required over a three-year time horizon, for gilteritinib to be considered cost-effective. OWMAG consider the required QALY gain to be implausible based on current available evidence. AWTTC considers the most plausible QALY gain to be between 0.02 and 0.03, over the three-year time horizon, with the range reflecting the base-case and scenario analysis utility value inputs. OWMAG consider this to be a reasonable assumption. Longer term modelling, particularly the 40-year horizon, aligned with the implausible cost-effectiveness status observed in the base case. On consideration of these factors OWMAG consider it unlikely that gilteritinib would be considered cost-effective compared with sorafenib.
Budget impact	OWMAG considers the clinical estimate of patient numbers to be reasonable. The group considers that the clinical assumptions underlying the budget impact estimates are generally

	reasonable. The group recognise the range of relevant cost components included. The main driver of the budget impact is the cost of gilteritinib. OWMAG notes that minor changes in patient numbers, time to relapse, dose reductions and discontinuation rates could have a significant impact on the budget impact. OWMAG considers that, based on the estimated number of eligible patients and the expected treatment pathway, the overall budget impact of gilteritinib is likely to be much higher when compared to standard of care.
Resource use	Based on clinical expert opinion, OWMAG note that treatment with gilteritinib may be less resource intensive due to a more favourable adverse event profile. Monitoring and administration requirements are not expected to differ between treatments. MRD testing is routine for all patients and is not an additional cost. The group considers that resource use with gilteritinib is acceptable, as it may be offset by lower inpatient requirements and reduced management needs for serious treatment-related adverse events.
Other factors	The group understand that the risk of relapse is greater for patients with FLT3-ITD AML compared with wild-type FLT3 AML and that relapse risk is higher for patient with MRD positivity. A targeted approach will ensure that only those with the highest risk of relapse receive treatment.
Final recommendation	OWMAG does not recommend the use of gilteritinib for maintenance therapy after haematopoietic stem cell transplant for acute myeloid leukaemia in adults with FLT3-ITD mutation and evidence of measurable residual disease before or after transplant.
Summary of rationale	There is a lack of robust clinical evidence comparing gilteritinib and sorafenib for maintenance treatment of FLT3-ITD AML pre- or post-HCT. Naïve treatment comparisons indicate that these treatments are likely to be similar in terms of clinical outcomes however real world evidence indicates that sorafenib may be more poorly tolerated than gilteritinib. Overall, the extent of additional clinical benefit with gilteritinib when compared with sorafenib remains uncertain. OWMAG consider that this treatment is unlikely to be cost effective based on conventional thresholds when compared with sorafenib. The significantly higher cost of gilteritinib compared with sorafenib is not considered to be a reasonable use of NHS resources.