# Health Technology Briefing
# November 2025

# Gilteritinib with chemotherapy for treating newly diagnosed FLT3 positive acute myeloid leukaemia

| Company/Developer | Astellas Pharma Ltd |
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☐ New Active Substance ☒ Significant Licence Extension (SLE)

| NIHRIO ID: 27575 | NICE ID: Not available | UKPS ID: 668225 |
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## Licensing and Market Availability Plans

Currently in phase III clinical trial.

## Summary

Gilteritinib with chemotherapy is in development for newly diagnosed FLT3 positive acute myeloid leukaemia (AML). AML is a type of cancer affecting young blood cells in the bone marrow, which is the soft inner part of the bone. In healthy individuals these young blood cells, known as stem cells, develop into red blood cells, platelets, and some types of white blood cell. In AML, some of these stem cells do not develop fully and instead become abnormal leukaemia cells. These can stop the bone marrow from working properly and can also spread to other parts of the body. Symptoms can include looking pale, feeling tired or weak, breathlessness, frequent infections, unusual and frequent bruising or bleeding. The exact cause of AML is unknown, but the risk of developing AML increases with age. Some individuals with AML may have alterations (changes to) FLT3 which encourages cells in the bone marrow to multiply uncontrollably. Patients with AML positive for alterations in FLT3 are more likely to have poorer outcomes than those who do not. Initial treatment for AML depends on whether patients are fit enough to have intensive chemotherapy, or whether lower dosage treatment is recommended. For AML positive for FLT3 alterations, targeted medicines may be given to help kill the leukaemia cells and reduce the risk of the cancer coming back.

Gilteritinib is designed to selectively target AML positive for FLT3 alterations and is taken orally (by mouth). If licensed gilteritinib, administered alongside chemotherapy, will offer an additional treatment for newly diagnosed patients with AML.

## Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Treatment of adults with newly diagnosed acute myeloid leukaemia (AML) with FMS-like tyrosine kinase-3 (FLT3) mutations who are eligible for intensive chemotherapy, in addition to standard chemotherapy.[1,2]

## Technology

### Description

Gilteritinib (Gilteritinib fumarate)is a small-molecule FLT3/AXL inhibitor with activity against both internal tandem duplication (ITD) and tyrosine kinase domain (TKD) FLT3 mutations.[3] Mutations in FLT3 seen in AML lead to constitutive phosphorylation of FLT3 and activation of its downstream signalling cascades, resulting ultimately in aberrant proliferation, and survival of haematopoietic progenitors.[4] While, AXL, is an oncogenic tyrosine kinase frequently overexpressed in AML and facilitates FLT3 activation, which is known to be a mechanism of FLT3 TKI resistance.[3-5] Therefore inhibition of both tyrosine kinases impairs downstream signal transduction, and consequently inhibits AML cell proliferation.[3]

Gilteritinib is in clinical development for adults with newly diagnosed FLT3 positive AML who are eligible for intensive chemotherapy. In the ongoing phase III clinical trial, (NCT4027309) gilteritinib 120mg is administered orally, once daily, in combination with standard chemotherapy in induction and consolidation therapy followed by one-year maintenance therapy..[1]

### Key Innovation

Currently treatment for adults with newly diagnosed AML with a FLT3 gene mutation is induction and consolidation chemotherapy with the FLT3 kinase inhibitors. Current treatment options have limited specificity for FLT3 and/or the FLT3-TKD subtypes.[6] Further, individuals positive for FLT3 mutations tend to have lower survival rates than those without the mutation and their disease is more likely to return, or relapse, after treatment. Further treatment may be required with stem cell transplantation in suitable patients.[7] Gilteritinib exhibits specificity for inhibition of both ITD and TKD FLT3 mutations,[3] as well as activity against AXL, a mechanism of resistance.[4]

If licensed gilteritinib will offer an additional treatment for newly diagnosed patients with FLT3 positive AML in adults.

### Regulatory & Development Status

Gilteritinib fumarate currently has Marketing Authorisation in the EU/UK for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation.[8]

Gilteritinib is also in phase I/II clinical development for broader populations of patients with AML.[9]

## Patient Group

### Disease Area and Clinical Need

AML is an aggressive cancer of the monocyte or granulocyte cells, which come from myeloid stem cells, and usually requires immediate treatment. Symptoms may include fatigue, breathlessness, weakness, fever, unintentional weight loss and frequent infections.[10] It is not clear what causes AML, and in most cases there is no identifiable cause, although some factors can increase the risk of getting AML including previous chemotherapy/radiotherapy; smoking; exposure to benzene; having a blood disorder; having

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certain genetic conditions such as Down's syndrome.[10] Multiple factors influence how the disease progresses, including the presence of specific genetic mutations. In AML there are two recognised types of mutations: FLT3-ITD, which occurs in 20-25% of individuals with AML, and FLT3-TKD. Under normal circumstances, FLT3 stimulates growth, division and survival of young cells in the bone marrow. Changes in this gene encourages these cells to multiply uncontrollably and is highly unfavourable for survival outcomes.[7]

In the UK between 2017 and 2019, approximately 2,900 new cases of AML each year on average were reported, accounting for less than 1% of all new cancer cases in the UK approximately.[11] Each year 40% new cases are in people aged 75 years and over (2017-2019).[11] In England (2024-25), there were 64,055 finished admission episodes and 68,293 finished consultant episodes (FCE) for AML (ICD-10: C92.0), resulting in 129,201 FCE bed days and 56,878 day cases.[12]

### Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends:

- Midostaurin for newly diagnosed acute FLT3-mutation-positive myeloid leukaemia with standard daunorubicin and cytarabine as induction therapy, with high-dose cytarabine as consolidation therapy, and alone after complete response as maintenance therapy.[13]
- Quizartinib for newly diagnosed FLT3-ITD-positive AML in adults, when used with standard cytarabine and anthracycline chemotherapy as induction treatment, then with standard cytarabine chemotherapy as consolidation treatment, then alone as maintenance treatment.[6]

## Clinical Trial Information

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| Trial | NCT04027309; **EudraCT**-2018-000624-33; A Phase 3, Multicenter, Open-label, Randomized, Study of Gilteritinib Versus Midostaurin in Combination With Induction and Consolidation Therapy Followed by One-year Maintenance in Patients With Newly Diagnosed Acute Myeloid Leukemia (AML) or Myelodysplastic Syndromes With Excess Blasts-2 (MDS-EB2) With FLT3 Mutations Eligible for Intensive Chemotherapy (HOVON 156 AML / AMLSG 28-18)<br>**Phase III:** Active, not recruiting<br>**Location(s):** 10 EU countries and other countries<br>**Primary completion date:** October 2025 |
| Trial Design | Randomised, parallel assignment, open-label |
| Population | N=777 (actual); adults with newly diagnosed AML or MDS Excess Blasts-2 (MDS-EB2) with FLT3 mutations eligible for intensive chemotherapy; 18 years and older |
| Intervention(s) | Gilteritinib, administered orally, in addition to standard induction and consolidation chemotherapy |
| Comparator(s) | Midostaurin, administered orally, in addition to standard induction and consolidation chemotherapy |
| Outcome(s) | Primary outcome: overall survival<br><br>See trial record for full list of other outcomes |
| Results (efficacy) | - |

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| Results (safety) | - |

## Estimated Cost

The list price of gilteritinib is £14,188.00 per pack of 84 x 40mg tablets.[14] A confidential simple Patient Access Scheme has been agreed with NHS England.

## Relevant Guidance

### NICE Guidance

- NICE technology appraisal. Quizartinib for induction, consolidation and maintenance treatment of newly diagnosed FLT3-ITD-positive acute myeloid leukaemia (TA1013). October 2024.
- NICE technology appraisal. Midostaurin for untreated acute myeloid leukaemia (TA523). June 2018.
- NICE quality standard. Haematological cancers (QS150). June 2017.
- NICE quality standard. Suspected cancer (QS124). June 2016.

### NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Sorafenib maintenance for adults with FLT3-internal tandem duplication (FLT3-ITD) acute myeloid leukaemia (AML) undergoing allogeneic haematopoietic stem cell transplantation (allo-HSCT). November 2023.
- NHS England. Clinical Commissioning Policy: Clofarabine for refractory or relapsed acute myeloid leukaemia (AML) as a bridge to stem cell transplantation (all ages). 170080P. November 2018.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

### Other Guidance

- All Wales Therapeutics and Toxicology Centre. Sorafenib. OW18. June. 2023.[15]
- Döhner et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the European LeukemiaNet (ELN). 2022.[16]
- European Society for Medical Oncology (ESMO) Clinical practice guidelines for diagnosis, treatment and follow-up of AML in adult patients. 2020.[17]
- West Midlands Cancer Alliance (NHS). West midlands guidelines for the treatment of adult acute myeloid leukaemia. 2020.[18]

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