# CLINICAL PRIORITIES ADVISORY GROUP
# 6th September 2023

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| **Agenda Item No** | 2.5 |
| **National Programme** | Blood and Infection |
| **Clinical Reference Group** | Blood and Marrow Transplantation |
| **URN** | 2262 |

| **Title** |
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| Sorafenib maintenance for adults with FLT3-internal tandem duplication (FLT3-ITD) acute myeloid leukaemia (AML) undergoing allogeneic haematopoietic stem cell transplantation (allo-HSCT) |

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| **Actions Requested** | • Support the adoption of the policy proposition |
| | • Recommend its approval as an IYSD |

| **Proposition** |
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| Acute myeloid leukaemia (AML) is a type of cancer affecting young blood cells in the bone marrow. One of most common mutations in AML is a change to the genetic instructions for producing a protein called fms-like tyrosine kinase 3 (FLT3). The FLT3 protein is part of a family of proteins called receptor tyrosine kinases (RTKs). Under normal circumstances, FLT3 stimulates growth, division (proliferation) and survival of young cells in the bone marrow. Changes in this gene encourages these cells to multiply uncontrollably and is highly unfavourable.<br><br>FLT3-ITD Acute myeloid leukaemia (AML) is an aggressive haematological malignancy, and individuals with this condition are rarely cured by chemotherapy alone. Current standard treatment is with chemotherapy, and further treatment may be required with stem cell transplantation in suitable patients. Allogeneic haematopoietic stem-cell transplantation (allo-HSCT) uses healthy blood stem cells from a donor to replace bone marrow that's not producing enough healthy blood cells. Allo-HSCT improves the survival of these individuals, however, leukaemia relapse remains high, occurring in 30-59% of patients (Bazarbachi et al, 2020). These individuals have a very poor prognosis with predicted 1-year overall survival rates after relapse of less than 20%. There is currently no alternative treatment to prevent disease relapse in individuals with FLT3-ITD AML who have undergone allo-HSCT.<br><br>Sorafenib is a multikinase inhibitor which blocks the action of the abnormal FLT3 protein. It has been proposed as a potential maintenance therapy in patients with |

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| FLT3-ITD AML who have undergone allo-HSCT. It is administered as daily tablets. It is currently licenced for use in the treatment of adults with hepatocellular carcinoma, advanced renal cell carcinoma and thyroid carcinoma (SmPC).<br>It is proposed that sorafenib is prescribed in NHS England commissioned allo-HSCT centres only. |

| **Clinical Panel recommendation** |
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| The Clinical Panel recommended that the policy proposition progress as a routine commissioning policy proposition. |

| **The committee is asked to receive the following assurance:** | |
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| 1. | The Head of Clinical Effectiveness confirms the proposition has completed the appropriate sequence of governance steps and includes an: Evidence Review; Clinical Panel Report. |
| 2. | The Head of Acute Programmes confirms the proposition is supported by an: Impact Assessment; Engagement Report; Equality and Health Inequalities Impact Assessment; Clinical Policy Proposition. The relevant National Programme of Care has approved these reports. |
| 3. | The Director of Finance (Specialised Commissioning) confirms that the impact assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal. |
| 4. | The Clinical Programmes Director (Specialised Commissioning) confirms that the service and operational impacts have been completed. |

| **The following documents are included (others available on request):** | |
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| 1. | Clinical Policy Proposition |
| 2. | Engagement Report |
| 3. | Evidence Summary |
| 4. | Clinical Panel Report |
| 5. | Equality and Health Inequalities Impact Assessment |

## In the Population what is the clinical effectiveness and safety of the Intervention compared with Comparator?

| **Outcome** | **Evidence statement** |
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| **Clinical effectiveness** | |
| **Critical outcomes** | |
| **Relapse free Survival** | This outcome is important to patients as it represents the time for which their disease is not progressing. Stable disease might |

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| **Certainty of evidence:** High to moderate | represent longer survival and that patients experience less symptoms from the disease itself.<br><br>In total, two RCTs provided evidence relating to relapse free survival (RFS) in patients with FTL3-ITD AML who have undergone allo-HSCT. RFS, calculated as time from randomisation to the first occurrence of either AML relapse[1] or death from any cause, was reported in one RCT comparing sorafenib to placebo. RFS, calculated as time from transplantation to relapse[2] or death from any cause, was reported in a second RCT3 comparing sorafenib to no maintenance therapy. This second RCT also reported cumulative incidence of relapse.<br><br>*Sorafenib vs placebo*<br><br>**At median 42 months:**<br>• One RCT (Burchert et al 2020) reported statistically significantly fewer relapse events for sorafenib (10/43, 23.3%) vs placebo (19/40, 47.5%) at median (IQR) follow-up of 41.8 months (24.1 to 42.5) (HR for relapse or death at median follow-up: 0.39 (95%CI 0.18 to 0.85), p=0.013). Median RFS was not reached for sorafenib and was 30.9 months (CI not reported) for placebo. **(MODERATE)**<br><br>**At 21-24 months:**<br>• One RCT (Burchert et al 2020) reported statistically significantly higher RFS at 24 months with sorafenib (85.0% (95%CI 70 to 93)) vs placebo (53.3% (95%CI 36 to 68)) (HR for relapse or death at 24 months: 0.26 (95%CI 0.10 to 0.65), p=0.002). **(HIGH)**<br><br>*Sorafenib vs no maintenance therapy*<br><br>**At 3 years:**<br>• One RCT (Xu et al 2022) reported statistically significantly higher RFS at three years with sorafenib (75.9% (95%CI 66.2 to 83.1)) vs no maintenance therapy (52.5% (95%CI 42.2 to 61.7)) (HR: 0.41 (95%CI 0.25 to 0.67), p<0.001). **(HIGH)**<br>• Xu et al also reported statistically significantly lower cumulative incidence of relapse at three years with sorafenib (13.0% (95%CI 7.3 to 20.4)) vs no maintenance |

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| | therapy (34.8% (95%CI 25.5 to 44.2)) (HR: 0.31 (95%CI 0.16 to 0.58), p<0.001). **(HIGH)**<br><br>**At 21-24 months:**<br>• One RCT (Xuan et al 2020) reported statistically significantly higher RFS at two years with sorafenib (78.9% (95%CI 69.0 to 85.9)) vs no maintenance therapy (56.6% (95%CI 46.1 to 65.8)) (HR: 0.37 (95%CI 0.22 to 0.63), p<0.0001). **(HIGH)**<br>• Xuan et al also reported 11/100 (11.0%) relapses with sorafenib and 32/102 (31.4%) relapses with no maintenance therapy at a median (IQR) follow-up of 21.3 months (15.0 to 37.0). The groups were not statistically compared. Median RFS was not reached for sorafenib or no maintenance therapy. **(MODERATE)**<br>• Xuan et al also reported statistically significantly lower cumulative incidence of relapse at two years with sorafenib (11.9% (95%CI 6.2 to 19.6)) vs no maintenance therapy (31.6% (95%CI 22.6 to 41.1)) (HR: 0.29 (95%CI 0.15 to 0.58), p<0.0001). **(HIGH)**<br><br>**At 1 year:**<br>• Xuan et al (2020) reported statistically significantly lower cumulative incidence of relapse at one year with sorafenib (7.0% (95%CI 3.1 to 13.1)) vs no maintenance therapy (24.5% (95%CI 16.6 to 33.2)) (HR: 0.25 (95%CI 0.11 to 0.57), p=0.001). **(HIGH)**<br><br>**One RCT provided high certainty evidence of statistically significantly higher RFS at 24 months for sorafenib compared to placebo and moderate certainty evidence of statistically significantly fewer relapse events for sorafenib compared to placebo at a median follow-up of 42 months. A second RCT provided high certainty evidence of statistically significantly higher RFS with sorafenib compared to no maintenance therapy at two years and three years. The same RCT also provided high certainty evidence of statistically significantly lower cumulative incidence of relapse with sorafenib compared to no maintenance therapy at one, two and three years.** |
| **Overall survival**<br><br>**Certainty of evidence:** | Overall survival is important to patients as individuals with relapsed AML have a high mortality rate due to disease. Improvement in survival is an important marker of effective treatment. |

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| High to moderate | In total, two RCTs provided evidence relating to overall survival in patients with FTL3-ITD AML who have undergone allo-HSCT. Overall survival, calculated as time from randomisation to death from any cause, was reported in one RCT comparing sorafenib to placebo. Overall survival, calculated as time from transplantation to death from any cause, was reported in a second RCT comparing sorafenib to no maintenance therapy.<br><br>*Sorafenib vs placebo*<br><br>**At median 55 months:**<br>• One RCT (Burchert et al 2020) reported no statistically significant difference in deaths between sorafenib (11/43, 25.6%) and placebo (16/40, 40.0%) at median follow-up of 55.1 months (IQR for follow-up not reported) (HR for death at median follow-up: 0.52 (95%CI 0.24 to 1.11), p=0.086). Median overall survival was not reached for sorafenib or placebo. **(MODERATE)**<br><br>**At 21-24 months:**<br>One RCT (Burchert et al 2020) reported statistically significantly higher overall survival at 24 months with sorafenib (90.5% (95%CI 77 to 96)) vs placebo (66.2% (95%CI 49 to 79)) (HR for death at 24 months: 0.24 (95%CI 0.08 to 0.74), p=0.007). **(HIGH)**<br><br>*Sorafenib vs no maintenance therapy*<br><br>**At 3 years:**<br>One RCT (Xu et al 2022) reported statistically significantly higher overall survival at three years with sorafenib (79.5% (95%CI 69.6 to 85.8)) vs no maintenance therapy (61.4% (95%CI 51.1 to 70.1)) (HR: 0.48 (95%CI 0.28 to 0.82), p=0.005). **(MODERATE)**<br>Xu et al also reported 21/100 (21.0%) deaths with sorafenib and 39/102 (38.2%) deaths with no maintenance therapy at a median<br>(IQR) follow-up of 36.8 months (2.5 to 67.1). The groups were not statistically compared. **(MODERATE)**<br><br>**At 21-24 months:**<br>One RCT (Xuan et al 2020) reported statistically significantly higher overall survival at two years with sorafenib (82.1% (95%CI 72.6 to 88.5)) vs no maintenance therapy (68.0% (95%CI 57.8 to 76.2)) (HR: 0.48 (95%CI 0.27 to 0.86), p=0.012). **(MODERATE)**<br>Xuan et al also reported 17/100 (17.0%) deaths with sorafenib and 32/102 (31.4%) deaths with no maintenance therapy at a median (IQR) follow-up of 21.3 months (15.0 to 37.0). The |

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| | groups were not statistically compared. Median overall survival was not reached for sorafenib or no maintenance therapy. **(MODERATE)**<br><br>**One RCT provided high certainty evidence of statistically significantly higher overall survival at 24 months for sorafenib compared to placebo. In this RCT there was moderate certainty evidence that the difference in number of deaths between the groups was not statistically significant at a median follow-up of 55 months. A second RCT provided moderate certainty evidence of statistically significantly higher overall survival for sorafenib compared to no maintenance therapy at two and three years.** |
| **Quality of life**<br><br>**Certainty of evidence:**<br>Not applicable | Quality of life is important to patients as it provides an indication of an individual's general health and self-perceived well-being and their ability to participate in activities of daily living. Measurement of quality of life can help inform patient-centred decision making and inform health policy.<br><br>**No evidence was identified for this outcome.** |
| **Important outcomes** | |
| **Hospitalisation**<br><br>**Certainty of evidence:**<br>Not applicable | This outcome is important to patients as it may represent either disease progression or treatment toxicity. It may have a bearing on the patient's quality of life and inform their treatment decision making.<br><br>**No evidence was identified for this outcome.** |
| **Treatment Adherence**<br><br>**Certainty of evidence:**<br>Moderate | Adherence to treatment is important to patients as it provides an indication of how the treatment is tolerated. If a treatment has adherence challenges, it can increase the risk of treatment failure and add to relapse risk.<br><br>In total, two RCTs provided evidence for treatment adherence related outcomes in patients with FTL3-ITD AML who have undergone allo-HSCT.<br><br>One RCT compared sorafenib to placebo. A second RCT compared sorafenib to no maintenance therapy, but only reported adherence to treatment for sorafenib patients. Treatment adherence related outcomes reported were duration of therapy, dose reductions and dose interruptions.<br><br>*Sorafenib vs placebo*<br><br>**At median 42 months:**<br>• One RCT (Burchert et al 2020) reported the median (range) duration of therapy as 34.6 weeks (1.3 to 106.9) for sorafenib patients and 54.4 weeks (1.7 to 128.3) for |

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| | placebo patients at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The groups were not statistically compared. **(MODERATE)**<br>• One RCT (Burchert et al 2020) reported dose reductions for 21 of 43 (49%) sorafenib patients and 16 of 40 (40%) placebo patients at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The groups were not statistically compared. **(MODERATE)**<br><br>*Sorafenib (no comparator)*<br><br>**At median 21 months:**<br>• One RCT (Xuan et al 2020) reported the median (IQR) duration of therapy as 134 days (116 to 150) for sorafenib patients at a median (IQR) follow-up of 21.3 months (15.0 to 37.0). **(MODERATE)**<br>• One RCT (Xuan et al 2020) reported dose reductions due to adverse events for 42 of 100 (42%) sorafenib patients at a median (IQR) follow-up of 21.3 months (15.0 to 37.0). **(MODERATE)**<br>• One RCT (Xuan et al 2020) reported dose interruptions due to adverse events for 12 of 100 (12%) sorafenib patients at a median (IQR) follow-up of 21.3 months (15.0 to 37.0). **(MODERATE)**<br><br>**One RCT provided moderate certainty evidence that sorafenib patients had a shorter duration of therapy and a higher proportion of dose reductions than placebo patients at a median follow-up of 42 months. The groups were not statistically compared. A second RCT reported moderate certainty evidence that patients received sorafenib for a median of 134 days with dose reductions and dose interruptions due to adverse events in 42% and 12% respectively.** |
| **Graft-versus host-disease (GVHD)**<br><br>**Certainty of evidence:** Moderate | This is important to patients since acute or chronic GVHD is a potentially serious complication of allogeneic stem cell transplantation and reduced intensity allogeneic stem cell transplantation which requires further management.<br><br>In total, two RCTs provided evidence relating to GVHD in patients with FTL3-ITD AML who have undergone allo-HSCT. Acute and chronic GVHD4 were reported by one RCT comparing sorafenib to placebo. Acute and chronic GVHD5 were also reported by a second RCT comparing sorafenib to no maintenance therapy. |

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| | *Sorafenib vs placebo*<br><br>**At median 42 months:**<br>• One RCT (Burchert et al 2020) reported acute GVHD (Grade ≥2) for 10 of 42 (24%) sorafenib patients and seven of 39 (18%) placebo patients at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The groups were not statistically compared. **(MODERATE)**<br>• One RCT (Burchert et al 2020) reported severe chronic GVHD for 8 of 42 (19%) sorafenib patients and 4 of 39 (10%) placebo patients at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The groups were not statistically compared. **(MODERATE)**<br>• One RCT (Burchert et al 2020) reported mild/moderate chronic GVHD for 18 of 42 (43%) sorafenib patients and 14 of 39 (36%) placebo patients at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The groups were not statistically compared. **(MODERATE)**<br><br>*Sorafenib vs no maintenance therapy*<br>**At up to 210 days:**<br>• One RCT (Xuan et al 2020) reported acute GVHD (Grade ≥2) for 23 of 100 (23%) sorafenib patients and 21 of 102 (21%) no maintenance therapy patients at up to 210 days post-transplantation. The groups were not statistically compared. **(MODERATE)**<br>• One RCT (Xuan et al 2020) reported acute GVHD (Grade 1) for eight of 100 (8%) sorafenib patients and six of 102 (6%) no maintenance therapy patients at up to 210 days post-transplantation. The groups were not statistically compared. **(MODERATE)**<br>• One RCT (Xuan et al 2020) reported moderate/severe chronic GVHD for 18 of 99 (18%) sorafenib patients and 17 of 99 (17%) no maintenance therapy patients at up to 210 days post-transplantation. The groups were not statistically compared. **(MODERATE)**<br>• One RCT (Xuan et al 2020) reported mild chronic GVHD for five of 99 (5%) sorafenib patients and five of 99 (5%) no maintenance therapy patients at up to 210 days post-transplantation. The groups were not statistically compared. **(MODERATE)**<br><br>**One RCT provided moderate certainty evidence that a higher proportion of sorafenib patients had acute and chronic GVHD than placebo patients at a median follow-up** |

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| | **of 42 months. A second RCT provided moderate certainty evidence that sorafenib and no maintenance therapy patients had similar proportions of acute and chronic GVHD at up to 210 days post-transplantation. The groups were not statistically compared in either RCT.** |
| **Activities of daily living (ADLs)**<br><br>**Certainty of evidence:**<br>Not applicable | ADLs are important outcomes to patients as they facilitate enablement and independence, allowing individuals to function in education, work, home and recreational settings. They encompass patients' individual needs and facilitate inclusion and participation. The complications of recurrence can lead to progressively worsening physical symptoms and altered ability to complete ADLs without assistance.<br><br>**No evidence was identified for this outcome.** |
| **Safety** | |
| **Safety**<br><br>**Certainty of evidence:**<br>Moderate | Safety of sorafenib is important to patients as it allows comparison of interventional approaches.<br><br>In total, two RCTs provided evidence relating to safety outcomes in patients with FTL3-ITD AML who have undergone allo-HSCT. Adverse events[6] and drug discontinuation due to toxicity were reported by one RCT comparing sorafenib to placebo. Adverse events[7] and drug discontinuation due to adverse events were reported by a second RCT comparing sorafenib to no maintenance therapy.<br><br>*Sorafenib vs placebo*<br><br>**At median 42 months:**<br>One RCT (Burchert et al 2020) reported study drug discontinuation due to toxicity for nine of 42 (21%) sorafenib patients and two of 39 (5%) placebo patients at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The groups were not statistically compared. **(MODERATE)**<br><br>Burchert et al also reported adverse events of Grade ≥3 for each group at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The proportion of patients in each group with any adverse event of Grade ≥3 was not reported and the groups were not statistically compared. The most common (>10% of patients) adverse events with sorafenib were infections (26%), GI toxicity (14%), electrolyte alterations (14%), skin toxicity (12%), cardiotoxicity and renal insufficiency (10%) and other (not further defined) (79%). The most common (>10% of patients) adverse events with placebo were infections (23%), GI toxicity (15%) and other (not further defined) (56%). **(MODERATE)**<br><br>Burchert et al also reported drug-related adverse events of Grade ≥3 for each group at a median (IQR) follow-up of 41.8 months (24.1 to 42.5). The proportion of patients in each group |

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| | with any drug-related adverse event of Grade ≥3 was not reported and the groups were not statistically compared. The most common (>5% of patients) drug-related adverse events with sorafenib were electrolyte alterations (7%), skin toxicity (5%), GI toxicity (5%) and other (not further defined) (19%). The most common (>5% of patients) drug-related adverse events with placebo were GI toxicity (8%), infections (5%), liver toxicity (5%) and other (not further defined) 10%. **(MODERATE)**<br><br>*Sorafenib vs no maintenance therapy*<br><br>**At up to 210 days:**<br>• One RCT (Xuan et al 2020) reported study drug discontinuation due to adverse events for five of 100 (5%) sorafenib patients at up to 210 days post-transplantation. **(MODERATE)**<br>• Xuan et al also reported deaths due to adverse events for four of 100 (4%) sorafenib patients and five of 102 (5%) no maintenance therapy patients at up to 210 days post-transplantation. The groups were not statistically compared. **(MODERATE)**<br>Xuan et al also reported that 50/100 (50%) sorafenib patients and 47/102 (46%) no maintenance therapy patients experienced at least one adverse event of Grade 3 or 4, at up to 210 days post- transplantation. The groups were not statistically compared. **(MODERATE)**<br>• In Xuan et al the most common (>10% of patients) Grade 3-4 adverse events with sorafenib were infections (25%), haematologic toxicity (15%) and gastrointestinal (11%). The most common (>10% of patients) Grade 3-4 adverse event with no maintenance therapy was infections (24%). Adverse events were assessed up to 210 days post-transplantation. **(MODERATE)**<br>• In Xuan et al the most common (>10% of patients) Grade 1-2 adverse events with sorafenib were gastrointestinal (25%), renal or<br>• genitourinary (23%), skin related (20%), hepatobiliary or pancreatic (16%) and cardiac (14%). The most common (>10% of patients) adverse events with no maintenance therapy were renal or genitourinary (25%), gastrointestinal (20%), hepatobiliary or pancreatic (17%) and cardiac (12%). Adverse events were assessed up to 210 days post-transplantation. **(MODERATE)**<br>• Xuan et al also stated that the most common Grade 3-4 treatment related adverse events with sorafenib were |

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| | skin-related (7%) or haematological (5%) and that no patients died from treatment-related adverse events. Adverse events were assessed up to 210 days post-transplantation. The proportion of patients in each group with any drug-related adverse events was not reported. **(MODERATE)**<br><br>**One RCT provided moderate certainty evidence of higher drug discontinuation due to toxicity with sorafenib than placebo at a median follow-up of 42 months. The groups were not statistically compared. The same RCT specified adverse events and drug-related adverse events of Grade ≥3 experienced by each group at a median follow-up of 42 months. However, the proportion of patients in each group with any adverse event of Grade ≥3 was not reported and the groups were not statistically compared. A second RCT provided moderate certainty evidence of similar proportions of deaths due to adverse events and patients experiencing at least one Grade 3 or 4 adverse event with sorafenib or no maintenance therapy, assessed up to 210 days post-transplantation. The groups were not statistically compared. The same RCT reported discontinuation of sorafenib due to adverse events in 5% of patients. This RCT also specified adverse events and treatment-related adverse events experienced by each group.** |

**Abbreviations**

ADLs: activities of daily living; Allo-HSCT: allogeneic haematopoietic stem cell transplantation; AML: acute myeloid leukaemia; CI: confidence intervals; FLT3-ITD: fms-like tyrosine kinase 3-internal tandem duplication; GI: gastrointestinal; GVHD: graft-versus-host-disease; HR: hazard ratio; HSCT: haematopoietic stem cell transplantation; IQR: interquartile range; RCT: randomised controlled trial; RFS: relapse free survival

## In the Population what is the cost effectiveness of the Intervention compared with Comparator?

| Outcome | Evidence statement |
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| **Cost effectiveness** | No evidence was identified for cost effectiveness. |

**From the evidence selected, are there any subgroups of patients that may benefit from the intervention more than the wider population of interest?**

| Outcome | Evidence statement |
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| **Subgroups** | Subgroup results comparing sorafenib and placebo for relapse free survival were reported by one RCT. A second RCT reported cumulative incidence of relapse separately by age group. Neither RCT reported outcomes according to whether patients had received one, or more than one, allo-HSCT. The subgroup analyses were exploratory and post-hoc.<br><br>**Relapse free survival (RFS)**<br>*Sorafenib vs placebo*<br>• One RCT (Burchert et al 2020) reported that RFS was statistically significantly higher with sorafenib than placebo for the following subgroups:<br>  ○ Patients with undetectable minimal residual disease (MRD) before allo-HSCT (0/9 relapsed or died with sorafenib vs 5/12 with placebo, p=0.028)<br>  ○ Patients with detectable MRD after allo-HSCT (p=0.015) (n not reported)<br>Median follow-up was 41.8 months (24.1 to 42.5).<br><br>*Sorafenib vs no maintenance therapy*<br>• One RCT (Xuan et al 2020) reported a statistically significantly lower cumulative incidence of relapse at two years for sorafenib (8.0% (95%CI 2.5 to 17.7)) vs no maintenance therapy (38.7% (95%CI 24.4 to 52.7)) for patients aged ≥35 years (n=99) (HR 0.17 (95%CI 0.06 to 0.50), p not reported). For patients aged <35 years (n=103) the difference between sorafenib (16.1% (95%CI 6.8 to 28.9)) and no maintenance therapy (25.1% (95%CI 14.2 o 37.7)) was not statistically significant (HR 0.45 (95%CI 0.18 to 1.11), p not reported).<br><br>**One RCT reported that RFS was statistically significantly higher for sorafenib vs placebo for patients with undetectable MRD before allo-HSCT and patients with detectable MRD after allo-HSCT. A second RCT reported that cumulative incidence of relapse at two years was statistically significantly lower for sorafenib vs no maintenance therapy for patients aged ≥35 years, but not for patients aged <35 years.** |

| Patient Impact Summary |
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| **The condition has the following impacts on the patient's everyday life:**<br><br>• **mobility:** Patients have severe problems in walking about<br>• **ability to provide self-care:** Patients have severe problems in washing or dressing<br>• **undertaking usual activities:** Patients are unable to do their daily activities<br>• **experience of pain/discomfort:** Patients have severe pain or discomfort<br>• **experience of anxiety/depression:** Patients are extremely anxious or depressed |
| **Further details of impact upon patients:**<br>Patients with AML are severely impacted by both the disease and the treatments. The disease causes fever, bone pain, fatigue, frequent infections, easy bruising, unusual bleeding, and ultimately death without successful treatment. The standard treatment options of chemotherapy and stem cell transplant cause extremely low immunity, sickness, and pain, with considerable hospitalisation. This leads to exclusion from normal family, social and work life, with potentially significant financial impact. Social exclusion and low mood are frequently reported.<br><br>**Further details of impact upon carers:**<br>The impact of the disease and the treatments on patients is debilitating. Carers are required to perform and support nearly all aspects of the patient's life, from feeding, bathing, clothing etc to transport to and support at frequent hospital visits and stays. The caring role is full time and impacts on the carer's social and work life, and carers can become socially excluded and anxious in the same way as patients. |

| Considerations from review by Rare Disease Advisory Group |
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| Not applicable. |

| Pharmaceutical considerations |
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| This clinical commissioning policy proposition recommends sorafenib as a maintenance treatment for adults with FLT3-internal tandem duplication (FLT3-ITD) AML undergoing allo-HSCT. This recommendation is outside of the marketing authorisation for sorafenib. Sorafenib is categorised as a high-cost drug to be reimbursed under the cost and volume process. Post pubescent children will be able to access sorafenib under the Medicines for Children Policy. |

| Considerations from review by National Programme of Care |
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| The proposal received the full support of the Blood and Infection PoC on the 23 May 2023 |