Ruxolitinib for Disease Related Splenomegaly or Symptoms in Adults with Primary Myelofibrosis (Chronic Idiopathic Myelofibrosis), Post-Polycythaemia Vera Myelofibrosis or Post-Essential Thrombocythaemia Myelofibrosis

Ruxolitinib **WILL BE** routinely funded on the NHS for use as an option for treating splenomegaly or symptoms in adults with primary myelofibrosis (or chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis, in patients who have **intermediate-2 risk disease** (see definition at end of paper).

This recommendation is based on evidence of clinical effectiveness (improvement in symptom score, reduction in spleen size and overall survival) and cost-effectiveness. NICE concluded that the most likely incremental cost effectiveness ratio (ICER) compared to existing treatments would be £26,000 per QALY.

Stopping criteria as set out on page 2 to be applied.

Ruxolitinib **WILL NOT** be routinely funded for use in patients with **HIGH-RISK** disease. CRC and DHSC acknowledge that there is evidence of clinical effectiveness (improvement in symptom score, reduction in spleen size and overall survival) in this patient group. However, the ICER for ruxolitinib in patients with high-risk disease is £38,000 per QALY. It is therefore considered not sufficient value for money given all other calls on DHSC resources.

Ruxolitinib will **NOT** be routinely funded for use in patients with low risk or **intermediate-1 risk disease** since these patients were not included in the scope of the evidence review and there is a lack of evidence to support the use of ruxolitinib in these patient groups.

**Summary:** Ruxolitinib has been shown to reduce spleen size in two RCTs and to improve symptom scores in one RCT (with supporting evidence from four non-randomised studies). Evidence from follow up of two RCTs indicates a survival benefit from ruxolitinib compared to either placebo or standard treatment.

Ruxolitinib meets the standard threshold for cost effectiveness in patients with intermediate-2 risk myelofibrosis but not in patients with high-risk myelofibrosis. However, high-risk myelofibrosis met the criteria for life extending, end of life treatment which have been agreed for use by NICE.
**Stopping criteria:** Treatment may be continued as long as the benefit-risk remains positive. However, the treatment should be discontinued after 6 months if there has been no reduction in spleen size or improvement in symptoms since initiation of therapy.

In patients who have demonstrated some degree of clinical improvement, ruxolitinib therapy should be discontinued if they sustain an increase in their spleen length of 40% compared with baseline size (roughly equivalent to a 25% increase in spleen volume) and no longer have tangible improvement in disease-related symptoms.

**NOTE:**

**Risk stratification in myelofibrosis:** The Dynamic International Prognostic Scoring System-plus (DIPSS-plus) uses eight predictors of inferior survival: age >65 years, hemoglobin <10 g/dL, leukocytes >25 × 10⁹ /L, circulating blasts ≥1%, constitutional symptoms, red cell transfusion dependency, platelet count <100 × 10⁹ /L, and unfavorable karyotype (i.e., complex karyotype or sole or two abnormalities that include +8, -7/7q-, i(17q), inv(3), -5/5q-, 12p-, or 11q23 rearrangement). The presence of 0, 1, "2 or 3," and ≥4 adverse factors defines low, intermediate-1, intermediate-2, and high-risk disease with median survivals of approximately 15.4, 6.5, 2.9, and 1.3 years, respectively. High risk disease is also defined by CALR(-)/ASXL1(+) mutational status. (Tefferi, A, ‘Primary Myelofibrosis: 2014 update on diagnosis, risk-stratification and management’, Am J Haematol, 2014 Sep;89(9):915-25. doi: 10.1002/ajh.23703.

**Summary of evidence:**


**Reason for policy:**

Replaces CRC Recommendation CRC16-07: Ruxolitinib for disease-related splenomegaly or symptoms in adults with primary myelofibrosis (chronic idiopathic myelofibrosis), post-polycythaemia vera myelofibrosis or post-essential thrombocythaemia myelofibrosis.

Where a patient is considered to have exceptional need for and capacity to benefit from a treatment that is not routinely funded, a request for individual funding may be made to the Individual Funding Requests Panel. The patient must be made aware that the Panel may not support the request and must not be given any expectation that they will be able to have the treatment until a decision to fund has been received in writing from the Panel.

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