midostaurin (Rydapt®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO094

Description

Midostaurin (Rydapt) is an orally administered tyrosine kinase inhibitor (TKI) targeting FLT3 and KIT D816V receptors to induce cell apoptosis.

Length of Authorization

- Initial: Six months
- Renewal:
    i. AML: Cannot be renewed
    ii. Systemic mast cell disease: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
midostaurin (Rydapt)	25 mg capsule	Acute myeloid leukemia, newly diagnosed, FLT3 mutation-positive, in combination with cytarabine/daunorubicin induction and cytarabine consolidation	56 capsules/28 days
		Systemic mast cell disease: aggressive systemic mastocytosis, systemic mastocytosis with hematological neoplasm, mast cell leukemia	224 capsules/28 days

Initial Evaluation

I. Midostaurin (Rydapt) may be considered medically necessary when the following criteria below are met:
    A. Member is 18 years of age or older; **AND**
    B. Medication is prescribed by, or in consultation with an oncologist; **AND**
    C. A diagnosis of one of the following:
        1. **Acute myeloid leukemia (AML)**; **AND**
            i. The member has FLT3 mutation-positive AML; **AND**
            ii. Will be used in combination with standard cytarabine and daunorubicin induction AND cytarabine consolidate therapy; **AND**
            iii. Will not be used with any other oncolytic therapy outside of cytarabine and daunorubicin; **AND**
            iv. The member has received no prior therapy for AML; **OR**

2. **Systemic mast cell disease**; **AND**
    i. Systemic mast cell disease is characterized by one of the following: aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL); **AND**
    ii. Midostaurin (Rydapt) will not be used in combination with any other oncolytic medication.

II. Midostaurin (Rydapt) is considered investigational when used for all other conditions, including but not limited to:
    A. Pediatric leukemia
    B. Rectal cancer
    C. Acute myeloid leukemia in absence of FLT3 mutation

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Midostaurin (Rydapt) is prescribed by, or in consultation with an oncologist; **AND**
    A. For **acute myeloid leukemia**:
        a. No renewal, one 6-month (initial) approval per lifetime.
    B. For **systemic mast cell disease**;
        a. Midostaurin (Rydapt) will not be used in combination with any other oncolytic medication; **AND**
        b. Clinical documentation of response to treatment, such as stabilization or improvement of disease, and absence of unacceptable toxicity from the medication.

Supporting Evidence

I. Midostaurin (Rydapt) was evaluated in three trials. Trial 1: in combination with chemotherapy in a randomized, double-blind, placebo-controlled trial in adults with FLT3-mutated AML. Subjects received 50 mg twice daily on days 8-21 for up to two cycles, followed by up to 12 months of midostaurin (Rydapt) therapy. Although evaluated for up to one year of therapy, the FDA-

approval for midostaurin (Rydapt) indicates combination therapy with cytarabine and daunorubicin for two cycles of induction and four cycles of consolidation - for a complete total of six 28-day cycles. The primary outcome was overall survival (OS) which was statistically in favor of midostaurin (Rydapt) [HR 0.77; 95% CI 0.63-0.95, p=0.016]; however, OS data plateaued before reaching the median. Median survival could not be reliably estimated.

II. Midostaurin (Rydapt) has not been sufficiently evaluated for safety and/or efficacy in combination with any other oncolytic medication outside of cytarabine and daunorubicin in the setting of AML.

III. In Trial 2, midostaurin (Rydapt) was evaluated in a single-arm, open-label trial in ASM, SM-AHN, and MCL, collectively referred to as advanced SM. The trial included 116 adult subjects that had relapsed or progressed on or after 0-2 prior therapies. The primary outcome was complete remission (CR) plus incomplete remission (ICR) by six cycles via the Valent criteria for ASM and SM-AHN, with twenty-one percent of subjects meeting the primary endpoint (16-38%, depending on the specific type of SM). The median duration of CR+ICR was not reached at time of evaluation, and the median time to CR+ICR was 0.5 months.

IV. Trial 3 was a single-arm, open-label trial of 26 subjects with advanced SM. By Valent criteria, 10 achieved a response by two cycles that was sustained for at least eight weeks.

V. Midostaurin (Rydapt) is available in 25 mg capsules to be given as 50 mg twice daily on days 8-21 of each 28-day cycle for a total of six cycles in AML or, given as 100 mg twice daily continuously for SM.

Investigational or Not Medically Necessary Uses

I. The safety and efficacy of midostaurin (Rydapt) has not been sufficiently established in the following settings:
   A. Pediatric leukemia
   B. Rectal cancer
   C. Acute myeloid leukemia in absence of FLT3 mutation

References

1. Rydapt [Prescribing Information]. East Hanover, NJ. Novartis Pharmaceuticals Corporation. 2017.
2. Gotlib J., Kluin-Nelemans HC, George TI, et al. Efficacy and safety of midostaurin in advanced systemic mastocytosis. N Engl J Med. 2016. June 30;374(26): 2530-2541.
3. NCCN Clinical Practice Guidelines in Oncology. Acute Myeloid Leukemia. Version 2.2020. Updated September 2019. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx
4. Stone RM, Mandrekar SJ, Sandfor BL, et al. Midostaurin plus chemotherapy for acute myeloid leukemia with a FLT3 mutation. N Engl J Med. 2017. Aug 3;377(5): 454-464.

Policy Implementation/Update:

Date Created	July 2017
Date Effective	August 2017
Last Updated	November 2019
Last Reviewed	November 2019

Action and Summary of Changes	Date
Prior authorization criteria transitioned to policy. Age requirement added. Clarification of appropriate line of therapy required for approval. Renewal allowance removed for AML and extended to six months for SM.	11/2019