POLICY NUMBER UM_1315	SUBJECT Rydapt™ (midostaurin)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATE REVIEWED 05/04/17, 05/07/18, 07/05/19	APPROVAL DATE July 10, 2019	EFFECTIVE DATE July 10, 2019	REVISION DATES (latest version listed last) 07/10/19	
PRIMARY BUSINESS OWNER: APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Oncology	

I. PURPOSE

To define and describe the accepted indications for Rydapt (midostaurin) usage in the treatment of cancer.

II. DEFINITIONS

Rydapt (midostaurin): is an inhibitor of multiple receptor tyrosine kinases and has the ability to inhibit FLT3 receptor signaling and cell proliferation. Midostaurin induces apoptosis in leukemic cells that express FLT3 mutant kinases (ITD and TKD) or overexpress wild type FLT3 and PDGF receptors. Mast cell apoptosis and inhibition of KIT signaling, cell proliferation, and histamine release were also demonstrated.

Rydapt (midostaurin) is FDA approved in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by a FDA approved test. It is also indicated for aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia

Rydapt (midostaurin) is available in 25 mg capsules.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Rydapt (midostaurin) may be considered medically necessary when any of the following selection criteria is met:

1. **Acute Myelogenous Leukemia (AML)**
    a. The member has documented FLT3 mutation-positive (both ITD and TKD mutations) AML and Rydapt (midostaurin) is being used for any of the following conditions:
        i. For treatment induction and re-induction in combination with standard cytarabine and daunorubicin induction and cytarabine chemotherapy OR
        ii. For post-remission therapy in combination with cytarabine following complete response to previous intensive therapy OR

iii. For relapsed/refractory disease as a component of repeating the initial successful induction regimen if late relapse (≥12 months).

2. **Systemic Mastocytosis**

   a. The member has aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL) and Rydapt (midostaurin) is being used as a single agent.

Exclusion Criteria: Rydapt (midostaurin) is not considered medically necessary when any of the following selection criteria is met:

1. Rydapt (midostaurin) is being used after disease progression with the same regimen.
2. Member has AML related to prior chemotherapy or RT for another cancer.
3. Prior use of cytotoxic therapy including azacitidine or decitabine.
4. Dosing exceeds single dose limit of Rydapt (midostaurin) 100 mg.
5. Treatment exceeds the maximum limit of 240 (25 mg) tablets/month.
6. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Rydapt (midostaurin) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:**

   a. **AML:** 50 mg orally twice daily (12-hour intervals) with food on days 8 to 21 of each cycle of induction with cytarabine and daunorubicin, and on days 8 to 21 of each cycle of consolidation with high-does cytarabine.

   b. **ASM, SM-AHN, and MCL**: 100 mg orally twice daily with food. Continue treatment until disease progression or unacceptable toxicity occurs.

2. **Dosage Adjustments:**

   a. Systemic mastocytosis, without mast cell leukemia, absolute neutrophil count (ANC) less than 1 x 10(9)/L caused by midostaurin: Interrupt therapy until ANC 1 x 10(9)/L or greater, then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily; discontinue therapy if low ANC persists for more than 21 days and midostaurin is suspected as the cause.

   b. Systemic mastocytosis, ANC less than 0.5 x 10(9)/L caused by midostaurin in patients with baseline ANC 0.5 to 1.5 x 10(9)/L: Interrupt therapy until ANC 1 x 10(9)/L or greater, then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily; discontinue therapy if low ANC persists for more than 21 days and midostaurin is suspected as the cause.

   c. Systemic mastocytosis, without mast cell leukemia, platelet count less than 50 x 10(9)/L caused by midostaurin: Interrupt therapy until platelet count 50 x 10(9)/L or greater, then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily; discontinue therapy if low platelet count persists for more than 21 days and midostaurin is suspected as the cause.

d. Systemic mastocytosis, platelet count less than 25 x 10(9)/L caused by midostaurin, in patients with baseline platelet count of 25 to 75 x 10(9)/L: Interrupt therapy until platelet count 50 x 10(9)/L or greater, then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily; discontinue therapy if low platelet count persists for more than 21 days and midostaurin is suspected as the cause.

e. Systemic mastocytosis, without mast cell leukemia, Hb less than 8 g/L caused by midostaurin: Interrupt therapy until Hb 8 g/L or greater, then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily; discontinue therapy if low Hb persists for more than 21 days and midostaurin is suspected as the cause.

f. Systemic mastocytosis, life-threatening anemia caused by midostaurin in patients with baseline Hb of 8 to 10 g/L: Interrupt therapy until Hb 8 g/L or greater, then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily; discontinue therapy if low Hb persists for more than 21 days and midostaurin is suspected as the cause.

g. Systemic mastocytosis, Grade 3 or 4 nausea and/or vomiting despite optimal antiemetic therapy: Interrupt therapy for 3 days (6 doses), then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily.

h. Systemic mastocytosis, other Grade 3 or 4 non-hematological toxicities: Interrupt therapy until resolution to Grade 2 or lower, then resume at 50 mg twice daily; if tolerated, increase to 100 mg twice daily.

3. **Monitoring**

a. Disease response or stabilization may indicate efficacy.

b. FLT3 mutation: Prior to initiation, with an FDA-approved companion diagnostic test available at http://www.fda/gov/CompanionDiagnostics.

c. Pregnancy status (women of reproductive potential): Within 7 days prior to initiation of therapy.

d. CBC: At least weekly for the first 4 weeks, every other week for the next 8 weeks, and monthly thereafter during therapy ; include a differential.

e. Toxicities, including nausea, vomiting, and other non-hematologic toxicities: At least weekly for the first 4 weeks, every other week for the next 8 weeks, and monthly thereafter during therapy.

f. Pulmonary symptoms of interstitial lung disease or pneumonitis

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Rydapt PI prescribing information. Novartis Pharmaceuticals Corporation. East Hanover, New Jersey 2018.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.