About Rydapt® (midostaurin) in newly diagnosed FLT3-mutated acute myeloid leukemia (AML) and three types of systemic mastocytosis (SM)

	AML	Advanced SM
Indication	For the treatment of adult patients with newly diagnosed AML who are FMS-like tyrosine kinase 3 mutation-positive (FLT3+), as detected by an FDA-approved test,* in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy. Rydapt is not indicated as a single-agent induction therapy for the treatment of patients with AML.[1]	For the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN) and mast cell leukemia.[1]
How Rydapt works	Rydapt inhibits multiple kinases, including FLT3,† which help regulate many essential cell processes, thereby interrupting cancer cells' ability to grow and multiply.[2‡] FLT3 is a receptor tyrosine kinase, a type of cell-surface receptor, which plays a role in the proliferation, or increase, in the number of certain blood cells.[3] About 30% of adults with AML have a FLT3 gene mutation,[4] which is the most common and associated with poor prognosis.[5,6]	Rydapt inhibits multiple kinases, including KIT,[1] which help regulate essential cell processes, interrupting cancer cells' ability to grow and multiply.[7‡] The uncontrolled proliferation of mast cells in advanced SM is caused in many people by a KIT gene mutation, with the most common mutation, KIT D816V, occurring in approximately 90% of people with SM.[8]
Dosing and adminstration	The recommended dose of Rydapt is 50 mg orally twice daily with food on days 8 to 21 of each cycle of induction with cytarabine and duanorubicin and on days 8 to 21 of each cycle of consolidation with high dose cytarabine. For a description of the experience with single-agent treatment beyond induction and consolidation, healthcare professionals should refer to the Clinical Studies section of the Prescribing Information (14.1).[1]	The recommended dose of Rydapt is 100 mg orally twice daily with food. Continue treatment until disease progression or unacceptable toxicity occurs.[1]

*In order to identify FLT3+ AML patients, Novartis collaborated with Invivoscribe Technologies, Inc. on the development of LeukoStrat® CDx FLT3 Mutation Assay, a companion molecular diagnostic test. LeukoStrat® CDx FLT3 Mutation Assay is the first molecular companion diagnostic in AML and identifies both FLT3 internal tandem duplication (ITD) and tyrosine kinase domain (TKD) mutations and is performed by The Laboratory for Personalized Molecular Medicine, a subsidiary of Invivoscribe Technologies, Inc.

†Rydapt also inhibits the activity of the kinases KIT (wild type and D816V mutant), PDGFRα/ß, VEGFR2, as well as members of the serine/threonine kinase PKC family.

‡Clinical benefit unknown.

About acute myeloid leukemia (AML)

- AML is an aggressive cancer of the blood and bone marrow.[9] It prevents blood cells from maturing, causing an accumulation of "blasts" which do not allow room for normal blood cells.[9]
- Mutations in specific genes are found in many cases of AML, and mutation testing is recommended as part of the diagnostic process.[10]

About advanced systemic mastocytosis (SM)

- In advanced SM, the uncontrolled growth and accumulation of mast cells leads to organ damage and dysfunction.[7]

See safety information on reverse side.

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Important Safety Information

Patients who are allergic to midostaurin or any of the ingredients in Rydapt should not take Rydapt. If a patient taking Rydapt develops signs of an allergic reaction, they should seek medical help immediately. Signs of an allergic reaction include trouble breathing, flushing, chest pain, throat tightness, and swelling of lips, mouth or throat.

Rydapt should be not be used during pregnancy since Rydapt may harm an unborn baby. Pregnancy testing should be conducted for women who might become pregnant. Effective birth control should be used during treatment and for at least four months after stopping Rydapt. If a patient becomes pregnant or thinks she may be, the patient should tell their doctor right away. Women should not breastfeed during treatment with Rydapt and for at least four months after the final dose. Men taking Rydapt who have female partners that are able to become pregnant should use effective birth control during his treatment with Rydapt and for at least four months after the last Rydapt dose. Rydapt may cause fertility problems in women and men, which may affect their ability to have children.

Rydapt may cause lung problems that may lead to death. Patients on Rydapt who develop a new or worsening cough, shortness of breath, or chest discomfort should get medical help right away. These may be signs of serious lung problems.

Common sides effects reported during Rydapt treatment for AML included low level of white blood cells with fever (febrile neutropenia); nausea; redness, pain or ulcers inside the mouth (mucositis); vomiting; headache; bruising; muscle or bone pain; nose bleeds; device-related infection; high blood sugar levels (hyperglycemia) and upper respiratory infections.

Common side effects reported during treatment for ASM, SM-AHN or mast cell leukemia included nausea; vomiting; diarrhea; swelling of the hands, feet or ankles; muscle or bone pain; stomach-area pain; tiredness; upper respiratory infection; constipation; fever; headache and trouble breathing.

If side effects including nausea, vomiting, and diarrhea occur, get worse or do not go away during treatment with Rydapt, patients should contact their doctor. Depending on the side effect and/or severity of the side effect that occur, their doctor may decrease their dose, temporarily stop, or completely stop treatment with Rydapt.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Rydapt may affect how these medicines work or these other medicines may affect how Rydapt works.

The full prescribing information for Rydapt can be found at:
https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/rydapt.pdf.

References

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