

# Living With FLT3+ **Acute Myeloid Leukemia (AML)**

## A Guide For Patients Taking RYDAPT<sup>®</sup> (midostaurin)

RYDAPT is indicated in combination with standard daunorubicin and cytarabine induction and high-dose cytarabine consolidation chemotherapy, and for patients in complete response followed by RYDAPT single agent maintenance therapy, for adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive. Please see Important Safety Information at the back of this brochure and accompanying Prescribing Information.

# Introduction

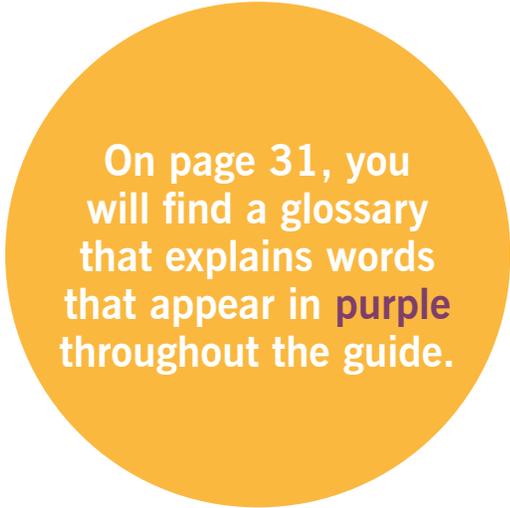
Living with **FLT3+ acute myeloid leukemia (AML)** can be physically and emotionally challenging, especially without extra support and care. It can feel like there is a lot to learn about an acute diagnosis like this, and your treatment plan.

This guide contains tips and support for living with FLT3+ AML to help you make informed decisions and better manage your care. Some pages will contain questions you may want to ask your doctor to help you learn more about each topic.

## How To Use This Guide

There are sections throughout this guide that you can use to keep track of your treatment, write down questions to ask your doctor, and record your notes. You may want to bring this guide with you to appointments to support your discussions with your doctor.

**If you have any questions about FLT3+ AML, taking RYDAPT, your overall treatment plan and goals, or any possible side effects, please talk with your doctor or nurse.**



On page 31, you will find a glossary that explains words that appear in **purple** throughout the guide.

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# Treatment With RYDAPT



# YOUR TREATMENT WITH RYDAPT

## What is RYDAPT?

Your doctor has prescribed RYDAPT to help treat your FLT3+ AML. RYDAPT is a medicine that is used together with standard daunorubicin and cytarabine **induction** and high-dose cytarabine **consolidation chemotherapy**, and for patients in complete response followed by RYDAPT single agent **maintenance therapy**, for adult patients with newly diagnosed AML who are FLT3 mutation-positive.

## What is the goal of treatment?

The goal of treatment for AML is to<sup>1</sup>:

- Remove leukemia cells
- Restore normal blood cell counts

## What is FLT3?

Refer to page 26 for more information.

## What is your daily dose of RYDAPT?

Write down your doctor's instructions here:

mg, or  capsules taken twice a day.

Additional instructions:


When in active treatment with RYDAPT, standard dose for AML is two 25-mg capsules twice a day. Individual doses may vary. Your doctor will advise the appropriate dose for you.

## Question for Your Doctor

Why do you think RYDAPT is the right treatment for me?

# TYPICAL FLT3+ AML TREATMENT PATH WITH RYDAPT<sup>1,2</sup>

For more information about FLT3+ AML and how RYDAPT may work, please refer to pages 25-27.



## Diagnosis

Diagnosis of FLT3+ AML is based on: Clinical evaluation, age, health status, comorbidities, and FLT3 mutation status

## INDUCTION High Intensity Chemotherapy with RYDAPT

**Induction** is the first phase of chemotherapy to treat AML. **The goal of this treatment phase is to achieve a complete response.** In order to do that you destroy the malignant cells.

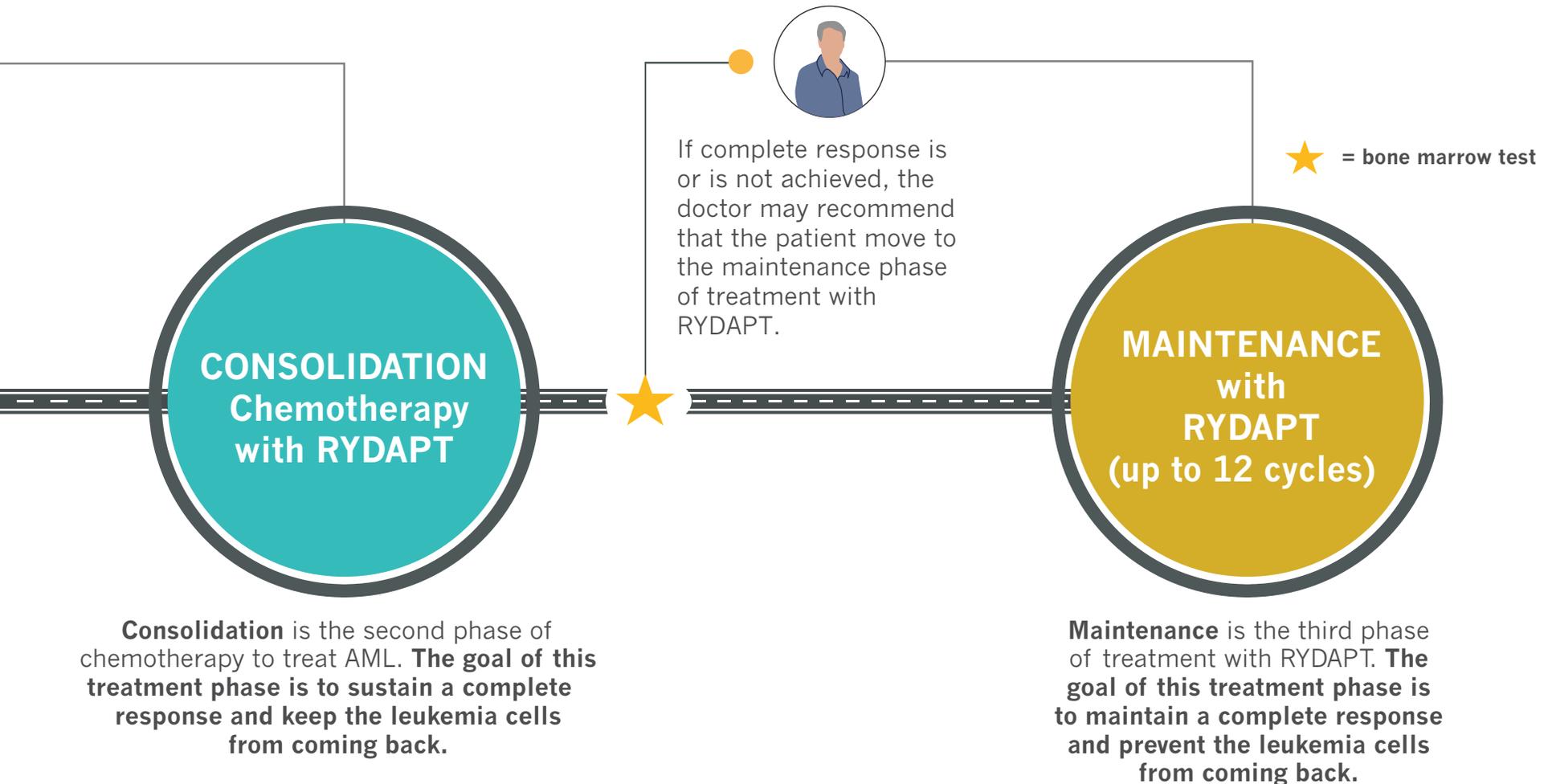


If complete response is or is not achieved, the doctor may recommend that the patient move to the consolidation phase of treatment with RYDAPT.

**Complete response** (also referred to as **complete remission**) is when your bone marrow contains less than 5% **blast** cells, your organs show no signs of AML, and the numbers of platelets and white blood cells in your blood are normal.



Each person's treatment will be different. Below are examples of a typical treatment path with RYDAPT for people with FLT3+ AML. You should not make any changes to your treatment without speaking to your doctor first.



**Stem cell transplant** is the goal of treatment that gives the best chance of curing AML. If certain conditions are met, the doctor may recommend that the patient receive a stem cell transplant at any time. (Rydapt stops.)

# HOW TO TAKE RYDAPT

## General instructions for taking RYDAPT include <sup>2</sup>:

-  • Take RYDAPT by mouth two times each day about 12 hours apart.\*
-  • RYDAPT should be taken with food.
-  • Swallow the capsules whole with a glass of water. Do not open, crush, or chew the capsules.
-  • If you miss a dose, wait and take the next dose of RYDAPT at the next scheduled time. Do not take an extra dose to make up for a missed dose.
-  • If you vomit after taking a dose, do not take an extra dose. Take your next dose at the scheduled time.
-  • If you take more capsules than you should, contact your doctor right away.

\*When in active treatment with RYDAPT, standard dose for AML is two 25-mg capsules twice a day. Individual doses may vary. Your doctor will advise the appropriate dose for you.

†For as long as your doctor prescribes RYDAPT.



## Sample Schedule for Taking RYDAPT†

Take RYDAPT at 07:00 with breakfast and a glass of water.

Take RYDAPT at 19:00 with dinner and a glass of water.

Take RYDAPT 2 times each day  
**12**  
hours apart

The illustration shows two scenes of a person taking capsules. The top scene is set against a blue sky with a sun and clouds, showing a hand holding two orange capsules and another hand holding a glass of water. A clock shows 7:00, and a plate of breakfast (toast, fruit, and eggs) is shown. The bottom scene is set against a dark blue night sky with a crescent moon and stars, showing a hand holding two orange capsules and another hand holding a glass of water. A clock shows 7:00, and a plate of dinner (vegetables, tomatoes, and meat) is shown. A circular badge on the left indicates 'Take RYDAPT 2 times each day 12 hours apart'.

## Tips for swallowing capsules

- **Drink a little water before swallowing the capsules.** This moistens the throat. Then drink the full glass of water to help wash it down.
- **Stand or sit up** while taking the capsules.
- **Eat something like apple puree (applesauce) or yogurt** when you take the capsules.<sup>3</sup>
- If you are bothered by any smell when opening the package, **ask someone else to open the packaging a few minutes ahead of time.** You can also mask any odor with something that smells good (e.g., lighting a candle or using a fragrance spray in the room).

# AVOID CERTAIN MEDICINES WHEN TAKING RYDAPT

Taking some medicines together can change the way one or both of the medicines act in the body. Talk to your doctor and/or pharmacist about any other medicines you are taking, have recently taken, or might take. Also tell them about medicines you bought without a prescription. Tell your doctor if you are pregnant, think you may be pregnant, or plan to become pregnant, or if you are breast-feeding or plan to breast-feed.

MEDICINE CLASS	EXAMPLES
<b>Antifungals</b>	ketoconazole
Certain <b>antivirals</b>	ritonavir
<b>Macrolide antibiotics</b>	clarithromycin
<b>Antidepressants</b>	nefazodone
Certain <b>anticonvulsants</b>	carbamazepine, phenytoin
Certain <b>antibiotics</b>	rifampicin
Certain <b>herbal medicines</b>	St John's wort
Certain <b>androgen receptor inhibitors</b>	enzalutamide

## **For women of childbearing potential:**

The doctor will ask you to take a pregnancy test before starting treatment with RYDAPT to make sure you are not pregnant. You must use an effective method of contraception while taking RYDAPT and for at least 4 months after stopping treatment. If you use a hormonal contraceptive, you must also use a barrier method, such as a condom or a diaphragm.



# POSSIBLE SIDE EFFECTS OF RYDAPT

As with all medicines, RYDAPT may cause side effects, although not everyone gets them. Similarly, side effects may be more severe in some patients than in others. Understanding which side effects are possible is important so that you can report them promptly to your health care team.

Some side effects of RYDAPT may be serious, such as low white blood cell count, infections, heart problems, and lung problems.\*<sup>2</sup> These are more likely to occur during the induction and consolidation phases of treatment.<sup>2</sup> During the maintenance phase of treatment, low white blood cell count is the most frequent serious side effect, which increases the patient's risk of infection.<sup>4</sup>

Please read the Patient Leaflet for signs of these serious side effects and tell your doctor right away if you have any of them.

The most common side effects of RYDAPT are<sup>2</sup>:

Induction and Consolidation		Maintenance
 Low white blood cell count	 Nausea	 Nausea
 Skin rash	 Vomiting	 High blood sugar
 Headache	 Bruising	 Vomiting
 Fever	 Abnormal laboratory values	 QT prolongation

\*This is not a complete list of side effects. For a complete list, see Important Safety Information on pages 34-35 and the accompanying Patient Leaflet and Prescribing Information.

## Questions for Your Doctor



What side effects should I watch for? Who should I call if I experience any side effects?

# HOW TO MANAGE SOME SIDE EFFECTS

If you have any side effects while taking RYDAPT, **tell your doctor right away**. Together, you can discuss things you can do to help manage some of these side effects. Your doctor may suggest making changes to your diet, taking other medicines, or other ways to help you manage some side effects without stopping treatment. **Here are some things you might try:**

Possible Side Effects*	Possible Management Tips
Headache <sup>5</sup> 	<ul style="list-style-type: none"><li>• Ask your doctor about pain relievers.</li><li>• Make sure you are getting enough sleep, eating well, and reducing stress.</li><li>• Ask your doctor about therapeutic medicine techniques (e.g., acupuncture, massage).</li></ul>
Nausea/ vomiting 	<ul style="list-style-type: none"><li>• Ask your doctor about medicine to prevent nausea and/or vomiting.<sup>2</sup></li><li>• Allow your food to cool down before you eat it. This may make it have less flavor.<sup>6</sup></li><li>• Try eating foods that are bland and easy to digest (e.g., broiled or baked chicken [without skin], pasta, crackers, oatmeal, white rice, toast, bananas, or plain yogurt). Avoid foods that are greasy, fried, or spicy.<sup>6</sup> <i>If you have any food sensitivities or allergies (e.g., a gluten allergy), check with your doctor about appropriate foods to help you manage nausea/vomiting.</i></li></ul>
Rash <sup>7</sup> 	<ul style="list-style-type: none"><li>• Ask your doctor if there is any treatment that may help.</li><li>• Avoid the sun. Use sunscreen and wear a broad-brimmed hat when going outside.</li><li>• Use lukewarm water and a mild soap for bathing.</li></ul>

\* This is not a complete list of side effects. For a complete list, see Important Safety Information on page 35 and the accompanying Patient Leaflet and Prescribing Information.



# PREVENTING INFECTIONS

People with AML sometimes have an increased chance of getting an infection. Here's why: White blood cells help the body fight germs and prevent infection.<sup>4,8</sup> AML can lower the number of healthy white blood cells, making it hard for the body to fight infection.<sup>9</sup> In addition, treatment causes the white blood cells to not work as well as they should.<sup>8</sup> Both of these can raise the chance of getting an infection.

## To protect yourself from getting an infection:



- **Wash your hands often with soap and water.** Wash before eating and when preparing food, before and after you use the bathroom, and after being in a public place.<sup>10,11</sup>



- **Try to stay away from germs.** Avoid people who you know are sick and try to stay away from large crowds of people.<sup>11</sup> Consider limiting your interactions with children, as they may be exposed to germs at school or other places. You might also try using a surgical mask.



- **Be extra careful when using scissors and knives.** You can also try an electric shaver instead of a razor.<sup>11</sup>

**Report any signs of infection to your doctor right away.**

## Question for Your Doctor





## Call your doctor right away if you see any signs or symptoms of an infection, such as<sup>8</sup>:

- Fever that is 100.5° F (38 °C) or higher
- Chills and sweats
- Cough or shortness of breath
- Sore throat
- Sores or white coating in mouth
- Nasal congestion
- Stiff neck
- Swelling or redness anywhere
- Frequent diarrhea or loose bowel movements
- Pain or burning when you urinate
- Unusual vaginal/penile discharge or irritation
- Pain or tenderness in the abdomen
- Sinus pain, ear pain, headache

## Be watchful for signs and symptoms of relapse

Symptoms of FLT3+ AML may look like those of the flu or other common illnesses. Symptoms may include<sup>4,9</sup>:

- Fever
- Bone pain
- Tiredness (Fatigue)
- Difficulty or labored breathing
- Infection
- Unusual bleeding, such as frequent nosebleeds

Tell your doctor, pharmacist or nurse right away if you get any of these symptoms during treatment with RYDAPT or if:

- You experience new or worsening symptoms such as fever, cough with or without mucous, chest pain, trouble breathing or shortness of breath, because these may be signs of infections or lung problems.
- You experience chest pain or discomfort, light headedness, fainting, dizziness, blue discoloration of your lips, hands or feet, shortness of breath, or swelling of your lower limbs (edema) or skin, because these may be signs of heart problems.

# REMEMBERING TO TAKE RYDAPT



Take RYDAPT at the same time as other daily activities you already do, like eating breakfast and dinner twice a day.<sup>12</sup>



Use reminders<sup>12</sup>: Set an alarm on your phone or watch to alert you every time you need to take RYDAPT. Mark each dose on a calendar as you take it, and make sure there are two marks at the end of each day. You can also try using an app on your smartphone to remind you to take your medicine on time.



Ask a family member or friend to remind you.<sup>12</sup>



Put your medicine in an appropriate safe place where you will see it when you need to take it, like where you keep your dishes.<sup>12</sup>

The following pages can be cut out and placed in a visible location (e.g., refrigerator or table). They include helpful tips, and space to write in the dates when you need to take RYDAPT. Having this information in a visible place may help you remember when to take RYDAPT.



**It may be difficult to remember when to take your medicine. Having a routine may help. Talk to your local patient organization about adherence reminders. For more tips on building a routine or other support, talk to your doctor.**



# YOUR TREATMENT AT-A-GLANCE\*

If you have questions about your treatment plan or phase, please talk to your doctor. More information is also provided on pages 6–7.

**If you are in the induction or consolidation phase of treatment, you will normally be in the hospital. Your treatment schedule may be similar to this.<sup>2</sup>**

During the induction and consolidation phases of treatment, take RYDAPT on days 8–21 of your treatment cycle.<sup>2</sup>

## Treatment schedule during induction and consolidation (day 8–21)

1 cycle = 28 days

Sample Treatment Cycle						
Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
← Chemotherapy →						
Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
RYDAPT	RYDAPT	RYDAPT	RYDAPT	RYDAPT	RYDAPT	RYDAPT
Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21
RYDAPT	RYDAPT	RYDAPT	RYDAPT	RYDAPT	RYDAPT	RYDAPT
Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28
← No AML Medication →						

**\*This treatment schedule may be different from the one your doctor recommended. Always take RYDAPT at the dose and schedule that your doctor recommends.**

## Questions for Your Doctor



When should I take RYDAPT? How long will I stay on this schedule?

# My RYDAPT Schedule: Induction and Consolidation\*

Use the space in the chart to write down which days you will need to take RYDAPT.

Treatment schedule during induction and consolidation (days 8–21, or 14 days with RYDAPT)

1 cycle = 28 days

Treatment Cycle						
Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21
Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28

Note: If/When you begin the maintenance phase of treatment, please use the chart on the next page.

\*This treatment schedule may be different than the one your doctor recommended. Always take RYDAPT at the dose and schedule your doctor recommends.

Reminders I will use to help me remember when to take RYDAPT (see page 16 for examples):





## My RYDAPT Schedule: Maintenance

During the maintenance phase of treatment, you will take RYDAPT twice a day, every day.\*2

This treatment schedule may be different than the one you followed during consolidation. Please complete the information below to record information about when you will take your medicine.

I WILL TAKE RYDAPT EVERY DAY AT:

AM

PM

AT THE SAME TIME AS (DAILY ACTIVITY)

*(e.g., walking the dog)*

AND

I WILL MAKE SURE I TAKE RYDAPT WITH

*(e.g., cereal, salad)*

AND

*(e.g., breakfast, dinner)*

REMINDERS I WILL USE (SEE PAGE 16 FOR EXAMPLES):

\*This treatment schedule may be different than the one your doctor recommended. Always take RYDAPT at the dose and schedule your doctor recommends.

# Managing Emotions and Finding Support



# TIPS FOR MANAGING EMOTIONS

Throughout your treatment path, you may experience a range of feelings such as sadness, fear, isolation/boredom, and stress/uncertainty. There are different ways you can overcome these challenges. **Here are some ideas:**

## SADNESS

-  Always share your feelings with your doctor, who may be able to help you find other ways to manage them.
-  Share your feelings with others if you are feeling sad or discouraged. Talking about it may help you find solutions.

## FEAR

-  Don't be afraid to ask for and accept help from your friends and family. Be clear about what you need (e.g., ask someone to cook a meal for you and your family or drive you to an appointment).
-  Try deep breathing exercises, writing your thoughts in a journal, using a coloring book, or taking a warm bath.

## ISOLATION/BOREDOM

-  Think about joining a support group of people who also have AML.
-  Try making time for your favorite hobbies and interests, such as listening to music or solving puzzles.

## STRESS/UNCERTAINTY

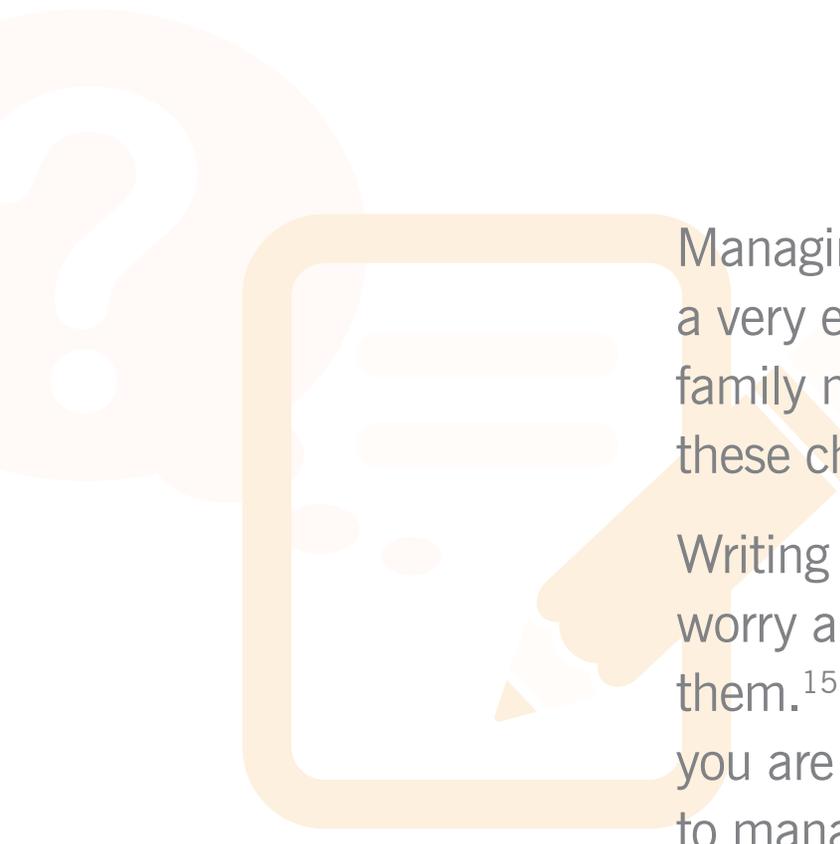
-  Focus on the things you can control, like taking your medicine and staying on your course of treatment.
-  When you feel tense or worried, stop what you are doing for a minute or two and relax.

## Question for Your Doctor



What are some local resources for support?

# LIVING WITH FLT3+ AML



Managing FLT3+ AML can be a real challenge. It can be a very emotional time not only for you, but also for your family members and/or friends. It is important to address these challenges and find extra support, when needed.

Writing down your feelings can help reduce stress and worry and help you make a plan for how to handle them.<sup>15</sup> Use the worksheet below to note the emotions you are experiencing as well as ways in which you will try to manage them.



What emotions am I experiencing?	What strategies will I use to manage my emotions?

# **Additional Information and Glossary**



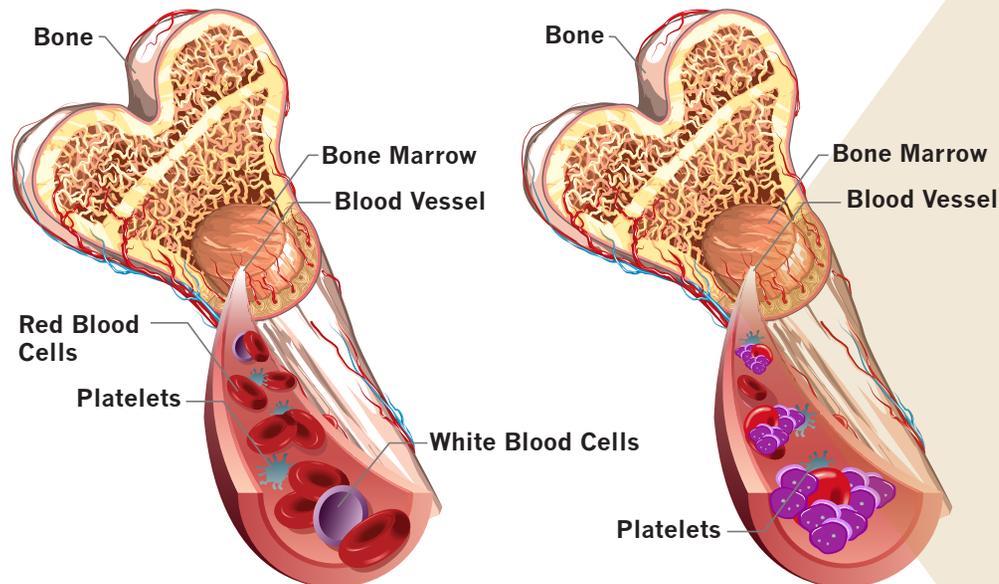
# AML OVERVIEW

## What is AML?

**Acute myeloid leukemia**, or **AML**, is a type of **leukemia** that affects the blood and **bone marrow**.<sup>9</sup> There are 8 different types of AML, called subtypes (e.g., **myeloblastic**, **promyelocytic**, **monocytic**). These subtypes are based on how developed the cancer cells are.<sup>9</sup> Most subtypes of AML are treated in the same way.

### Bone marrow and blood **without** AML

Normal bone marrow (the soft-spongy tissue in the center of bones) makes new cells that become different types of blood cells over time.



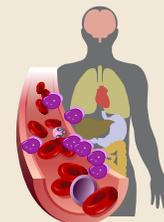
### Leukemic cells in bone marrow and blood **with** AML



AML starts in the bone marrow. The bone marrow makes cells called **myeloid cells** which include red blood cells, certain white blood cells, and platelet-making cells. In people with AML, these myeloid cells don't function normally and are called **myeloblasts**, or blasts.<sup>9</sup>



These **blasts** (leukemia cells), grow quickly and build up in the bone marrow and blood. They leave less room for healthy blood cells or platelets and have a negative effect on someone's health.<sup>9</sup>



Sometimes the leukemia cells can also spread outside of the blood to other parts of the body.<sup>9</sup> When this happens, the leukemia cells can keep other cells in the body from doing their jobs.

# HOW ARE AML AND FLT3 MUTATIONS DIAGNOSED?

## What is FLT3+ (pronounced “flit three”) AML?

- During AML diagnosis, one of the things lab tests look for is a change to genes in the AML cells. These changes are called mutations.
- One of the gene changes can happen in the gene called **FLT3**. Changes in the *FLT3* gene cause leukemia cells to grow.
- AML with the FLT3 mutation is sometimes called “FLT3-positive (+) AML.” FLT3+ AML tends to have poorer outcomes than AML without the FLT3 mutation.<sup>13</sup>
- There are different types of FLT3 changes: FLT3-ITD (FLT3 internal tandem duplication) is the most common mutation and FLT3-TKD (FLT3 tyrosine kinase domain) is another less common mutation. RYDAPT may work for both ITD and TKD.



- Blood and bone marrow tests are used to diagnose AML.<sup>3</sup>



- A laboratory test called a **PCR test** (polymerase chain reaction test) may also be done to determine if there are changes (mutations) in the genes, such as the FLT3 mutation.<sup>13</sup>

## What causes AML?

Researchers have found that AML is caused by changes in the **DNA** of bone marrow cells.<sup>11</sup> These changes may cause cancer cells to form.

Some risk factors that may increase the chance of getting AML include being male, smoking (especially after age 60), having received or taken treatment for cancer in the past, being exposed to the chemical benzene or to high levels of radiation, and having a history of a blood disorder (e.g., myelodysplastic syndrome [MDS]).<sup>9</sup>



About one out of three people with AML have a mutation in the **FLT3** gene.<sup>2</sup>

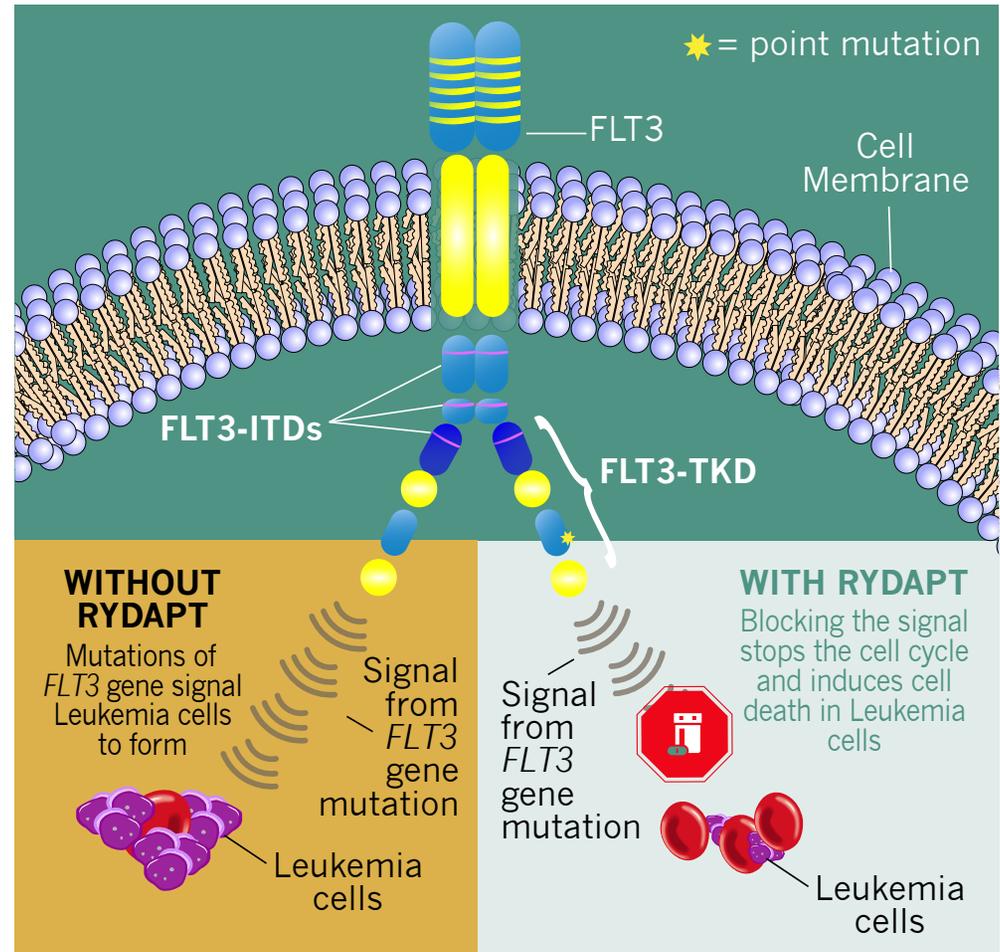
*FLT3* mutation testing is performed by the Laboratory of Personalized Molecular Medicine GmbH (Germany), a subsidiary of Invivoscribe Technologies, Inc.



# HOW RYDAPT MAY WORK

RYDAPT is a type of medicine called a “**protein kinase inhibitor**.” In most AML cells with a FLT3 mutation, proteins called tyrosine kinases send a signal that tells leukemia cells to grow.<sup>2</sup> RYDAPT may work by blocking these proteins and their signals.<sup>2</sup> By blocking these signals, RYDAPT may help cause the AML cells to stop working and destroy themselves.<sup>2</sup>

Please see Important Safety Information on page 35 and accompanying Prescribing Information.



## Question for Your Doctor



How does the FLT3 mutation affect my treatment plan?

# GETTING THE MOST FROM YOUR DOCTOR VISITS

Having good communication with your health care team is an important part of managing FLT3+ AML. Preparing for your appointments ahead of time, speaking openly, and asking questions may help you get the most out of your doctor visits.



## Tips to help you prepare for your visits:

- **Keep a log of symptoms and side effects** and bring it with you to your appointment.
- **Write down any questions** you have and prioritize them. The following cut-out page contains some questions you may find helpful when talking to your doctor.

## Tips you can use during your visits:

- **Let your doctor know** the things you would like to talk about at the beginning of the appointment.
- **Ask questions, share all concerns,** and **talk to your doctor** about your disease, treatment, emotional challenges, or other concerns.
- **Take notes** during the appointment to help you remember any information. Ask a friend, family member, or nurse to help if you need it.

## Tips you can use after your visits

- **Follow up** on any instructions from your doctor, such as making another appointment for follow-up tests or filling a prescription.
- **Share any notes or your experiences** from the visit with family members or friends who support you.

# QUESTIONS TO ASK YOUR DOCTOR



Having an open relationship with your doctor is an important part of your care. Make sure you ask (and get answers to) all of your questions, so that you are well informed about your disease and its management. Below is a list of sample questions to help you get the conversation started. **Please write down any additional questions for your doctor in the notes section at the back of the brochure, bring this list with you to your next appointment, and record your doctor's answers.**

Why do you think RYDAPT is the right treatment for me?

What side effects should I watch for?

Who should I call if I experience any side effects?

What can I do to manage my side effects?

How will an infection impact the effectiveness of my treatment?

When should I take RYDAPT?

How long will I stay on this schedule?

Which tests will I need to have?

When will I need to have them?

What are some local patient support groups?

What are some local resources that my caregiver can join for support?

How does the FLT3 mutation affect my treatment plan?

Are there foods or activities that I should avoid?

Is a stem cell transplant an option for me?

How does RYDAPT work differently from chemotherapy and/or other treatment options?

What type of support will I have when I leave the hospital?

What can I expect from treatment with RYDAPT?

How will having AML or taking RYDAPT affect my family planning?

What can I expect from treatment with RYDAPT?

How will treatment with RYDAPT affect me in the long term?

Is FLT3+ AML something that I can pass on to my children?



# HEALTH CARE TEAM CONTACT INFORMATION

Write down the contact information for your health care team here, and place it near your telephone or in another visible place for easy reference. Having this information in one place may be helpful to you and your family members or friends.

<b>Name</b>	
<b>Specialty</b>	
<b>Address</b>	
<b>Telephone Number</b>	

<b>Name</b>	
<b>Specialty</b>	
<b>Address</b>	
<b>Telephone Number</b>	

<b>Name</b>	
<b>Specialty</b>	
<b>Address</b>	
<b>Telephone Number</b>	



# GLOSSARY<sup>14</sup>



**Acute:** illness that worsens quickly and requires urgent care.

**Acute myeloid leukemia (AML):** disease that progresses quickly in which there are too many blood-forming cells in the blood and bone marrow that have not fully developed. These cells crowd out healthy cells.

**Antibiotic:** a drug used to treat infections caused by bacteria.

**Antiepileptic:** a drug used to treat epilepsy.

**Antifungal:** a drug that limits or prevents the growth of yeasts and other fungal organisms.

**Antiviral:** a drug that kills a virus or stops it from multiplying and reproducing.

**Blast:** a blood-forming cell of the bone marrow that has not fully developed.

**Bone marrow:** the soft, blood-forming tissue inside bones that contains developed and undeveloped blood cells, including white blood cells, red blood cells, and platelets.

**Complete response** (also referred to as **complete remission**): when your bone marrow contains less than 5% blast cells, your organs show no signs of AML, and the numbers of platelets and white blood cells in your blood are normal.

**Consolidation chemotherapy:** the second phase of chemotherapy to treat AML. The goal of this treatment phase is to destroy any remaining leukemia cells.

**DNA (deoxyribonucleic acid):** the molecules inside cells that carry genetic information and pass it from one generation of cells to the next. DNA determines the cell type and its functions.<sup>17</sup>

**FLT3:** FMS-like tyrosine kinase 3

**FLT3 gene:** a gene that instructs cells to make a protein (FLT3) that controls the growth, division, and survival of cells.

**Induction chemotherapy:** the first phase of chemotherapy to treat AML. The goal of this treatment phase is to destroy as many leukemia cells as possible.

**Leukemia:** a cancer of blood cells.

**Macrolide antibiotics:** a type of antibiotic used to treat common bacterial infections.

**Maintenance therapy:** the third phase of treatment for AML. The goal of this treatment phase is to keep leukemia cells from coming back.

**Monocytic AML:** a subtype of AML that affects monocytes (a type of white blood cell).

**Mutation:** a change in the DNA.

**Myeloblastic AML:** a subtype of AML that affects myeloblasts.

**Myeloblast:** a blood-forming cell of the bone marrow that has not fully developed.

**Myeloid cells:** red blood cells, certain white blood cells, and platelet-making cells.

**Platelets:** disc-shaped elements in the blood that join together for blood clotting.

**PCR (polymerase chain reaction) test:** a test that expands trace amounts of DNA so that a specific type of the DNA can be determined or studied (e.g., genes with the FLT3 mutation)

**Promyelocytic AML:** a subtype of AML that affects promyelocytes, which are a type of blood-forming cells in the bone marrow that are not fully developed.

**Protein kinase inhibitor:** a therapy that targets genes and blocks abnormal cell function, sometimes used to treat certain types of cancer.

**Red blood cell:** a type of blood cell that carries oxygen.

**Stem cell transplant:** the use of stem cells (undeveloped cells that have the potential to develop into a variety of cell types) as a treatment for cancer. Before the transplant, the patient receives chemotherapy to destroy diseased cells. Then the stem cells are returned to the patient, where they can form new blood cells to replace those destroyed by the treatment.

**White blood cells:** cells in the blood that fight infections. There are several different types of white blood cells.





**Important  
Safety Information**



## RYDAPT®

**Important note:** Before prescribing, consult full prescribing information of RYDAPT.

**Presentation:** Soft capsules containing 25 mg of midostaurin.

**Indications:** Rydapt® is indicated • in combination with standard daunorubicin and cytarabine induction and high-dose cytarabine consolidation chemotherapy, and for adult patients in complete response followed by Rydapt single agent maintenance therapy, for patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive • as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM AHN), or mast cell leukaemia (MCL).

### Dosage and administration:

**AML Adults:** Recommended dose is 50 mg orally twice daily. Rydapt is dosed on days 8 to 21 of induction and consolidation chemotherapy, and then for patients in complete response twice daily as a single agent maintenance until relapse for 12 cycles of 28 days each.

**Advanced SM Adults:** Recommended dose is 100 mg twice daily.

**Dose modifications:** Management of adverse drug reactions (ADRs) may require treatment interruption, dose reduction or treatment discontinuation

**Special populations:** • **Renal impairment:** Mild or moderate: no dose adjustment required. Severe or end stage renal disease: No data. • **Hepatic impairment:** Mild or moderate: no dose adjustment required. Severe: No data. • **Geriatrics (≥65 years):** No dose adjustment required. Patients aged ≥60 years: Rydapt should be used only in patients eligible to receive intensive induction chemotherapy with adequate performance status and without significant comorbidities. • **Pediatrics:** Safety and efficacy have not been established.

**Contraindications:** Patients with hypersensitivity to midostaurin or to any of the excipients. Concomitant administration of potent CYP3A4 inducers.

**Warnings and precautions:** • **Neutropenia and infections:** Rydapt can cause severe neutropenia. Consider treatment interruption or discontinuation. Monitor White Blood Cells counts regularly and especially at treatment initiation. Delay starting monotherapy with Rydapt until active serious infections have resolved. Observe and promptly manage symptoms of serious infection in patients receiving Rydapt. • **Cardiac dysfunction:** Transient decreases in Left Ventricular Ejection Fraction and Congestive Heart Failure were observed in patients treated with Rydapt in Advanced SM studies. Use Rydapt with caution in patients at risk and monitor patients by assessing LVEF when clinically indicated (at baseline and during treatment). An increased frequency of QTc prolongation was observed in Rydapt-treated patients, without an identified mechanistic explanation. Use Rydapt with caution in patients at risk and consider interval QT assessment by ECG when taken concurrently with medicines that can prolong QT interval. • **Pulmonary toxicity:** Interstitial Lung Disease (ILD) and pneumonitis have been reported during treatment with Rydapt. Monitor patients for severe pulmonary symptoms of ILD or pneumonitis and discontinue Rydapt if patients experience Grade 3 symptoms. • **Embryo-fetal toxicity and lactation:** Rydapt can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during treatment and for at least 4 months after stopping treatment with Rydapt. Women using systemically acting hormonal contraceptives should add a barrier method. Advise nursing women to discontinue breastfeeding during treatment and for at least 4 months after stopping treatment with Rydapt. • **Severe hepatic impairment:** Caution is warranted in patients with severe hepatic impairment and patients should be monitored for toxicity. • **Severe renal impairment:** Caution is warranted in patients with severe renal impairment and patients should be monitored for toxicity. • **Interactions:** Caution is required when concomitantly prescribing with strong inhibitors of CYP3A4. • **Excipients:** Rydapt contains macrogolglycerol hydroxystearate, which may cause stomach discomfort and diarrhoea. Rydapt contains ethanol anhydrous which may be harmful in patients with alcohol related problems, epilepsy or liver problems or during pregnancy or breast feeding.

### Pregnancy, lactation, females of reproductive potential:

**Pregnancy:** Rydapt can cause fetal harm. Pregnant women should be advised of the potential risk. Rydapt is not recommended during pregnancy and in women of childbearing potential not using contraception.

**Lactation:** Breast-feeding should be discontinued during treatment with Rydapt and for at least 4 months after stopping treatment.

**Females of reproductive potential:** • **Pregnancy testing:** A pregnancy test is recommended prior to starting treatment. • **Contraception:** Sexually active females of reproductive potential should use effective contraception during treatment with Rydapt and for at least 4 months after stopping treatment. Women using systemically acting hormonal contraceptives should add a barrier method of contraception.

**Infertility:** May impair fertility.

### Adverse drug reactions:

#### AML:

**Very common (≥10%):** Device related infections, febrile neutropenia, petechiae, lymphopenia, hypersensitivity, insomnia, headache, hypotension, epistaxis, laryngeal pain, dyspnoea, nausea, vomiting, stomatitis, abdominal pain upper, haemorrhoids, hyperhidrosis, exfoliative dermatitis, back pain, arthralgia, pyrexia, hyperglycaemia, activated partial thromboplastin time prolonged, absolute neutrophils decreased, haemoglobin decreased, aspartate aminotransferase (AST) increased, alanine aminotransferase (ALT) increased, hypokalaemia, hypernatraemia.

**Common (1 to 10%):** Upper respiratory tract infection, hyperuricaemia, syncope, tremor, eyelid oedema, hypertension, sinus tachycardia, pericardial effusion, nasopharyngitis, pleural effusion, acute respiratory distress syndrome, anorectal discomfort, abdominal discomfort, dry skin, keratitis, neck pain, bone pain, pain in extremities, catheter-related thrombosis, weight increased, hypercalcaemia.

**Uncommon (0.1 to 1%):** Neutropenic sepsis

#### Advanced SM:

**Very common (≥10%):** Nausea, vomiting, diarrhea, constipation, peripheral edema, fatigue, pyrexia, urinary tract infection, upper respiratory tract infection, headache, dizziness, dyspnea, cough, pleural effusion, epistaxis, glucose increased, absolute neutrophils decreased, absolute lymphocyte decreased, lipase increased, aspartate aminotransferase (AST) increased, alanine aminotransferase (ALT) increased, total bilirubin increased, amylase increased.

**Common (1 to 10%):** Hypersensitivity, febrile neutropenia, dyspepsia, gastrointestinal hemorrhage, asthenia, chills, edema, pneumonia, sepsis, bronchitis, oral herpes, cystitis, sinusitis, erysipelas, herpes zoster, contusion, fall, weight increased, disturbance in attention, tremor, vertigo, oropharyngeal pain, hypotension, hematoma.

**Uncommon (0.1 to 1%):** Anaphylactic shock.

**Interactions:** • Caution when co-administration of strong CYP3A4 inhibitors including, but not limited to, ketoconazole, ritonavir, clarithromycin and nefazodone as strong CYP3A4 inhibitors may significantly increase exposure to midostaurin especially when (re-)starting midostaurin treatment. Consider alternative therapeutic agent or monitor patient closely for toxicity. Clinical relevance limited. • Co-administration of strong CYP3A4 inducers including, but not limited to carbamazepine, rifampin, enzalutamide, phenytoin or St. John's Wort may significantly decrease exposure to midostaurin. Concomitant use of Rydapt with strong CYP3A4 inducers is contraindicated. • The PK of midazolam (sensitive CYP3A4 substrate) was not affected following three dosing days of midostaurin in healthy subjects. • Midostaurin and its active metabolites may inhibit P-glycoprotein (P-gp), BCRP, OATP1B1, CYP1A2, CYP2C8, CYP2C9, CYP2D6, CYP2E1 and CYP3A4/5; may induce CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19 and CYP3A4/5. Medicinal products with a narrow therapeutic range that are substrates of transporters or CYPs should be used with caution when administered concomitantly with midostaurin, and may need dose adjustment to maintain optimal exposure. Midostaurin may inhibit BSEP.

**Packs and prices:** Country-specific.

**Legal classification:** Country-specific.

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Please see accompanying Prescribing Information.