

CARING FOR SOMEONE WITH FLT3+ ACUTE MYELOID LEUKEMIA (AML)

A Guide For Caregivers of People Taking RYDAPT[®] (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

As a caregiver for someone with FLT3-positive acute myeloid leukemia (FLT3+ AML), you are an important member of his/her health care team. Not only are you helping your family member or friend to manage FLT3+ AML, you are also helping him/her get the support he/she needs. This can be stressful, and even overwhelming at times. It can feel like there is a lot to learn about an acute diagnosis like this, the treatment plan, and how to best support your family member or friend.

On page 21 you will find more information on AML and FLT3.

On page 29, you will find a glossary that explains words that appear in purple throughout the guide.

This guide contains general tips for supporting someone with FLT3+ AML. You will find information about how to help your family member or friend make informed decisions and better manage his/her care. Some pages will contain questions that you and your family member or friend may want to ask the doctor. You may also want to bring this guide with you to appointments to support discussions with the doctor.

Remember, it is important that your family member or friend talks to the doctor about any questions or concerns he/she may have about topics such as treatment goals or possible side effects of RYDAPT.

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Caring for Someone with FLT3+ AML

UNDERSTANDING TREATMENT WITH RYDAPT



What is RYDAPT?

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 have the FLT3 mutation.

What is the goal of treatment?

The goal of treatment for FLT3+ AML is to⁶:

- Remove leukemia cells
- Restore normal blood cell counts

What is FLT3?

Refer to page 26 for more information.

What is AML?

Refer to page 25 for more information

What is the daily dose of RYDAPT for your family member or friend?

Write down the 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 the patient.



Question for the doctor

Why do you think RYDAPT is the right treatment for my friend/family member?

TYPICAL FLT3+ AML TREATMENT PATH WITH RYDAPT^{1,2}

For more information about AML and how RYDAPT may work, please refer to pages 25-26.



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 the bone marrow contains less than 5% **blast** cells, the organs show no signs of AML, and the numbers of platelets and white blood cells in the blood are normal.

PATIENT CHALLENGES

During induction, patients are typically in the hospital. At this time, patients may feel social, financial, and emotional stresses of being in the hospital and away from the comfort of their own home. Patients may also feel overwhelmed and fearful about their diagnosis and what to expect with treatment, and may experience side effects from treatment.

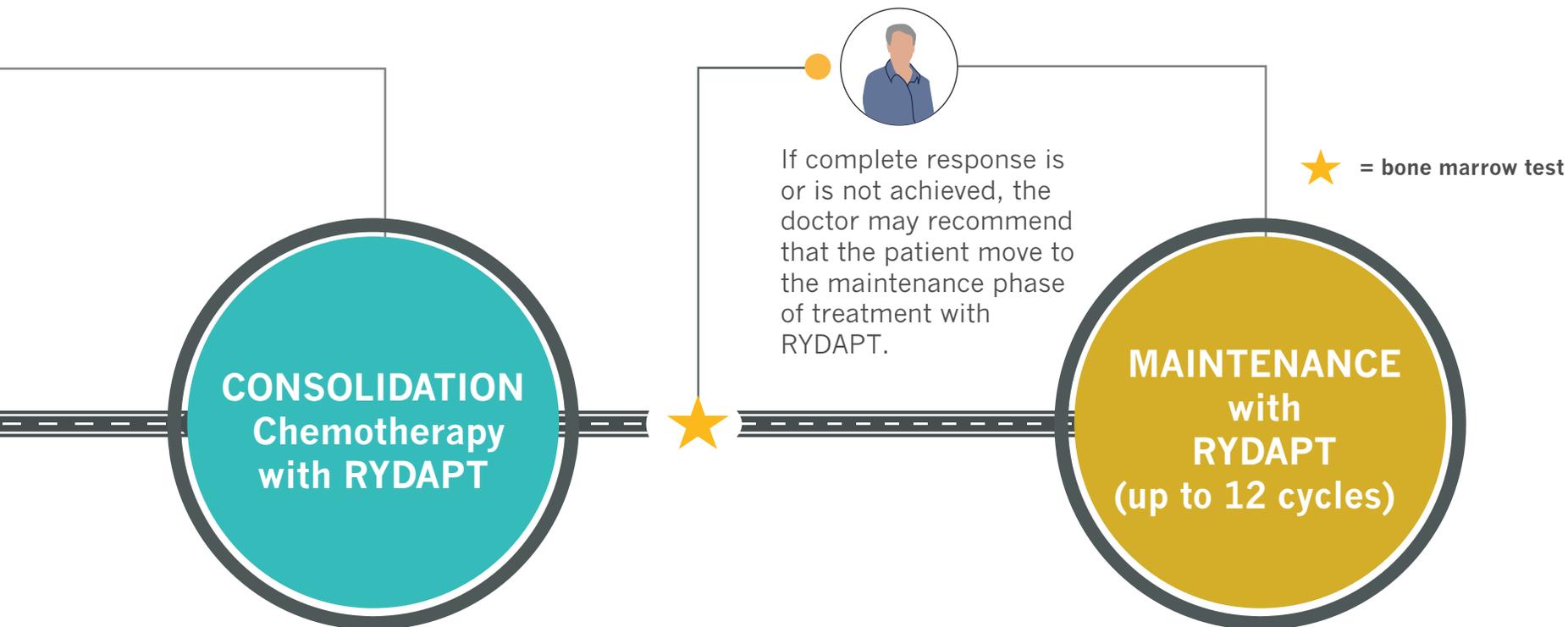
Questions for the doctor



Where is my family member/friend along this FLT3+ AML treatment path?
What will be the next step of my family member's/friend's treatment path?



Below are examples of a typical treatment path with RYDAPT for someone with FLT3+ AML, and the common challenges patients may face during their treatment.¹ This can help you understand and plan for what to expect from your family member's or friend's treatment with RYDAPT. Each person's treatment and the challenges he/she faces will differ. For more information about treatment with RYDAPT, please refer to pages 8 to 11.



Consolidation is the second phase of chemotherapy to treat AML. **The goal of this treatment phase is to sustain a complete response and keep the leukemia cells from coming back.**

PATIENT CHALLENGES

During consolidation, patients may be discharged from the hospital. Initially, patients are relieved to return home. However, they may feel anxious or worried without full-time access to their health care team, or have difficulty transitioning back to life at home.

Maintenance is the third phase of treatment with RYDAPT. **The goal of this treatment phase is to maintain a complete response and prevent the leukemia cells from coming back.**

PATIENT CHALLENGES

During maintenance, patients are relieved to have reached remission, but may still worry about relapse and long-term side effects. A cold or fever can trigger worry about relapse. Patients may also have difficulty returning to work or getting used to “a new normal” in remission.



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

You can support your family member or friend with FLT3+ AML by making sure he/she is taking RYDAPT correctly. General instructions for taking RYDAPT include²:



- The patient should take RYDAPT two times each day about 12 hours apart.*



- The patient should take RYDAPT with food.



- The patient should swallow the capsules whole with water. The capsules should not be opened, crushed, or chewed.



- If the patient misses a dose, he/she should wait and take the next dose of RYDAPT at the next scheduled time. He/she should not take an extra dose to make up for a missed dose.



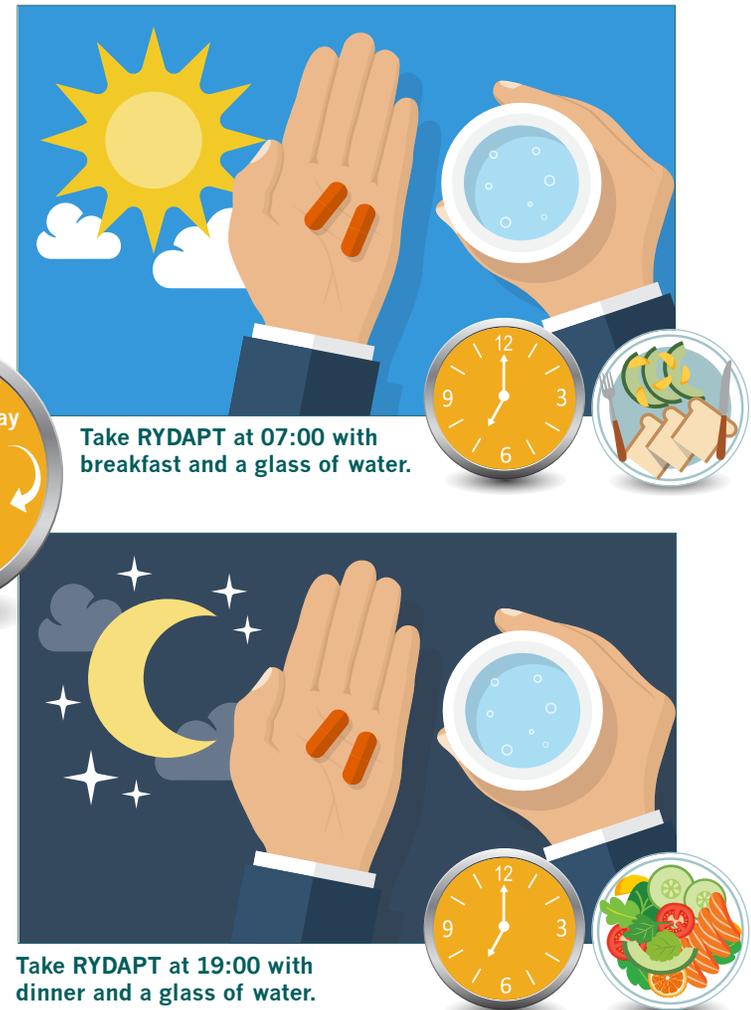
- If the patient vomits after taking a dose, he/she should not take an extra dose. He/she should take the next dose at the scheduled time.



- If the patient takes more capsules than he/she should, you or the patient should contact his/her 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. Ask the doctor what the appropriate dosage is for your family member/friend.

Sample Schedule for Taking RYDAPT





Medicines the patient should avoid when taking RYDAPT

Taking some medicines together can change the way one or both of the medicines act in the body. Encourage your family member or friend to talk to his/her doctor and/or pharmacist about any other medicines or supplements he/she is taking, has recently taken, or might take. Your family member or friend should tell the doctor if she is pregnant, thinks she may become pregnant, or plans to become pregnant, or if she is breast-feeding or plans to breast-feed.

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

Help your family member or friend take RYDAPT exactly as his/her doctor instructed. If the patient takes RYDAPT exactly as prescribed, he/she will have the best chance of treatment working. If you have any questions about how your family member or friend should take RYDAPT, talk to the doctor together.

Tips for swallowing capsules

If your family member or friend is having trouble swallowing the capsules or managing the smell of RYDAPT,

you can suggest that he/she—

- **Drink some water** before swallowing the capsules to moisten his/her throat. Then drink the full glass of water to help wash it down.³
- **Stand or sit up** while taking the capsules.³
- **Eat something like apple puree (applesauce) or yogurt** when he/she is taking the capsules.³
- If your family member or friend is bothered by any smell when opening the package, **offer 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)

WHAT ARE THE POSSIBLE SIDE EFFECTS OF RYDAPT?

As with all medicines, RYDAPT may cause side effects, although your friend or family member may not get them. Understanding the possible side effects will allow you to help recognize side effects so that they can be reported to the health care team.

Some side effects of RYDAPT may be serious, such as low white blood cell count, infections, heart problems, and lung problems.*² These are more likely to occur during the induction and consolidation phases of treatment.² 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.⁴ Please read the Patient Leaflet for signs of these serious side effects and tell your doctor right away if your family member or friend has any of them.

The doctor will ask your family member or friend to take a pregnancy test before starting treatment with RYDAPT to make sure she is not pregnant.

Your family member or friend must use an effective method of contraception while taking RYDAPT and for at least 4 months after stopping treatment. If your family member or friend uses a hormonal

contraceptive, she must also use barrier method, such as a condom or a diaphragm.

The most common side effects of RYDAPT are²:

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 32-33 and the accompanying Patient Leaflet and Prescribing Information.

HOW TO MANAGE SOME SIDE EFFECTS OF RYDAPT



If your family member or friend has any side effects while taking RYDAPT, make sure he/she tells the doctor right away. Together, you and your family member/friend can talk to the doctor about things that can be done to help manage some of these side effects. The doctor may suggest making dietary changes, taking other medicines, or other strategies to help manage any side effects. **Here are some things to try:**

Possible Side Effects	Possible Management Tips to Discuss with Your Family Member's or Friend's Doctor
Headache ⁵ 	<ul style="list-style-type: none"> • Ask the doctor about pain relievers. • Make sure your family member or friend is getting enough sleep, eating well, and reducing stress. • Suggest that your family member or friend ask the doctor about complementary medicine techniques (e.g., acupuncture, massage).
Nausea/vomiting 	<ul style="list-style-type: none"> • Ask the doctor about medicine to prevent nausea and/or vomiting.² • Have your family member or friend 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.⁶ <i>If your family member or friend has any food sensitivities or allergies (e.g., a gluten allergy), check with the doctor about appropriate foods to help manage nausea/vomiting.</i> • Have your family member or friend allow your food to cool down before you eat it. This may make it have less flavor.⁶
Rash ⁷ 	<ul style="list-style-type: none"> • Ask your family member's or friend's doctor if there is any treatment that can help. • Encourage your family member or friend to avoid the sun. This includes wearing sunscreen and a broad-brimmed hat while outside. • Suggest lukewarm water and a mild soap for bathing.

* This is not a complete list of side effects. For a complete list, see Important Safety Information on page 32 and the accompanying Patient Leaflet and approved Prescribing Information.



Question for the doctor

What can we do to manage side effects?

PREVENTING INFECTIONS

White blood cells help the body fight germs and prevent infection.^{4,8} AML lowers the number of healthy white blood cells, making it hard for the body to fight infection.⁹ In addition, many treatments, including treatment with RYDAPT, cause the white blood cells to not work as well as they should.⁸ Both of these raise the chance of getting an infection.

How to spot signs and symptoms of relapse

Symptoms of FLT3+ AML may be similar to those of the flu or other common illnesses. Symptoms may include^{4,9}:

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

Call the doctor right away if your family member or friend has any signs or symptoms of an infection, such as⁸:

- **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 he/she urinates**
- **Unusual vaginal/penile discharge or irritation**
- **Pain or tenderness in the abdomen**
- **Sinus pain, ear pain, headache**

Tell your family member or friend's doctor, pharmacist or nurse right away if he/she gets any of these symptoms during treatment with RYDAPT or if:

- he/she experiences 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
- he/she experiences chest pain or discomfort, light headedness, fainting, dizziness, blue discoloration of his/her lips, hands or feet, shortness of breath, or swelling of his/her lower limbs (oedema) or skin, because these may be signs of heart problems



Your family member or friend should follow these tips to prevent getting an infection:



- **Wash hands often with soap and water.** He/She should wash before eating and when preparing food, before and after using the bathroom, and after being in a public place.¹⁰



- **Try to stay away from germs.** He/She should avoid people who are sick and try to stay away from large crowds of people.¹¹ He/She should consider limiting interactions with children, as they may be exposed to germs at school or other places. He/She might also try using a surgical mask.



- **Avoid cuts and nicks using scissors or knives.** He/She could try using an electric shaver instead of a razor.¹¹



- **Carry an alcohol-based hand sanitizer** to clean hands when he/she is out of the house.¹²



- **Take appropriate steps around pets.** He/she should always wash his/her hands after touching pets or their food. He/she should not clean up droppings/feces from pets. He/she should ask someone else to clean bird cages, litter boxes, fish or turtle tanks, etc., and make sure to keep up with routine veterinary care for pets.¹²

Report any signs of infection to your family member's or friend's doctor right away.

Because you are in close contact with your family member or friend, you should also follow these tips to help prevent getting an infection. **If you do get sick,** consider asking someone else to help care for your family member or friend so you can minimize the risk of passing along your germs. If that isn't possible, extra care, including use of a facemasks and gloves, will help protect your family member or friend from a potentially serious complication.

Questions for the doctor



How might an infection affect my family member/friend overall?

Do you have any other tips for me to help my family member/friend avoid infections?

THE RYDAPT TREATMENT SCHEDULE*:

Induction and Consolidation

During the induction and consolidation phase of treatment, your family member or friend will have chemotherapy for the first 7 days of a 28-day cycle. Then, he/she will take RYDAPT on days 8 through 21². He/She will not have chemotherapy or RYDAPT for the final 7 days of the cycle. Use the space below to write down which days your family member or friend will need to take RYDAPT:

***This treatment schedule may be different from the one the doctor recommended to your family member or friend. He/She should always take RYDAPT at the dose and schedule that his/her doctor recommends.**

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 →						

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

1 cycle = 28 days

Question for the doctor



Do you have any suggestions for how I can help my family member/friend build a routine with RYDAPT?



Maintenance

During the maintenance phase of treatment, RYDAPT is taken twice daily every day, approximately 12 hours apart.² Work together with your family member or friend to complete the information below about his/her medication schedule.

***This treatment schedule may be different from the one the doctor recommended to your family member or friend. He/she should always take RYDAPT at the dose and schedule that his/her doctor recommends.**

**MY FAMILY MEMBER OR
FRIEND WILL TAKE
RYDAPT EVERY DAY AT:**

AM

PM

AT THE SAME TIME AS (DAILY ACTIVITY)

(e.g., walking the dog)

AND

WE'LL MAKE SURE RYDAPT IS TAKEN WITH

(e.g., breakfast, dinner)

AND

(e.g., cereal, salad)

REMINDERS WE CAN USE TO CREATE A ROUTINE:

HELPING YOUR FAMILY MEMBER OR FRIEND BUILD A ROUTINE FOR TAKING RYDAPT



Your family member or friend should take RYDAPT twice a day, at the same time every day, with a meal and a large glass of water so it becomes a familiar routine.¹³



Help your family member or friend set a reminder on an electronic device, such as a watch, mobile phone, tablet, computer, or alarm clock.¹³ You can also try using an app on your smartphone to help remind your family member or friend to take their medicine on time.



Ask your family member or friend if he/she would like a reminder from you.¹³



Keep a calendar together so that you and your family member or friend can track each time he/she takes RYDAPT.¹³



Brainstorm with your family member or friend about where to put his/her medicine so it will be seen when it is time to take it (e.g., near the plates in your kitchen).¹³



It may be difficult for your family member or friend to remember when to take the medicine when he/she transitions from the hospital to being at home. Having a routine may help.

PROVIDING CARE AND SUPPORT



Types of **SUPPORT** you can provide

As a caregiver, you may feel like you have little control over your family member's or friend's condition. It can be helpful to ask your family member or friend what type of support would be helpful. Keep in mind that caregiving is a team effort and you are not responsible for everything.

Some ways you can offer help may include:

- Offering encouragement and listening to your family member's or friend's emotional needs. Even just listening can be helpful, and lets your family member or friend know that you are there for him/her.
- Helping with practical and organizational needs, such as:
 - Rides to doctor visits and monitoring appointments.
 - Collecting information from doctor's appointments and handling medical paperwork.
 - Researching support groups or counselors.
 - Organizing medical bills and helping to manage finances while your family member or friend is in the hospital.
 - Obtaining any information or paperwork regarding medical leave from your family member's or friend's employer
- Helping your family member or friend build a medication routine with RYDAPT.
- Helping respond to other people's questions when your family member or friend is not up to it.
- Offer help with developing a healthy lifestyle, such as:
 - Tips on how to eat a well balanced diet.
 - Tips on how to prevent infection.
 - Tips on how to manage any accidents that occur at home.

PROVIDING CARE AND SUPPORT



Tips for COMMUNICATING with your family member or friend

An important part of caregiving is being able to understand your family member's or friend's needs. One way you can do this is to actively listen. Focus your attention on what your family member or friend says and rephrase it in your own words. This tells him/her that you heard and understood, and allows you to clarify if you misunderstood. Active listening means¹⁴:

- Avoiding being judgmental about what is said; you don't have to agree, just acknowledge
- Looking for feelings or intentions beyond the words

Some examples of active listening are:

- Your family member or friend may say, *"I feel like I never talk to my doctor anymore."* You might respond, *"I hear your concern about not being in the hospital anymore."*
- Your family member or friend may say, *"I feel like I was just at the lab yesterday!"* You might respond, *"I understand that managing multiple appointments can be difficult."*



Helping your family member or friend with DECISIONS

It's important to let the person *receiving* the care make decisions about the care whenever possible. Your family member or friend, however, may shift some or all of this decision making to you over time. Try to get a sense of his/her beliefs and priorities before this happens so that you can make choices that respect their opinions, even if they differ from your own.

Start by listening to your family member's or friend's wants and needs. You can help by speaking up for his/her needs, helping him/her get needed information, and serving as a sounding board throughout the decision-making process.

Some choices you may be involved with include:

- Treatment goals and other medical decisions
- Financial and/or employment decisions
- How to get support from family members



Tips for managing TRANSITIONS

While most people are relieved to leave the hospital, both you and your family member or friend may feel some stress without round-the-clock medical support or contact with your health care team. You can help ease the transition by:

- Ensuring you have a written list of who to call for urgent help at any time, day or night
- Getting clear instructions on what requires an immediate call to the doctor's office and/or an emergency room visit
- Having clear direction for following the treatment plan, and setting up a routine to achieve it
- Knowing what the next appointment is for and when it needs to be, and then helping set it up
- Creating a specific place to keep hospital discharge orders, medical contact information, prescriptions, testing orders, and other paperwork



Tips for COMMUNICATING with the health care team

Caregivers are often placed in the role of advocating for their family member or friend during appointments with the health care team. Some ways you can help include:

- Helping your family member or friend write down a list of questions for his/her doctor prior to appointments
- Tracking any changes you notice in your family member's or friend's symptoms, mood, etc.
- Taking notes during the appointment
- Speaking up and asking questions if your family member or friend is comfortable with you actively participating in appointments

**Caring for
Yourself**

TAKING CARE OF YOURSELF



Tips for managing your EMOTIONS

Caregivers may feel overwhelmed by all that a family member's or friend's diagnosis may bring, such as difficult emotions, increased responsibilities, and a lot of new information to learn. The constant stress that comes with dealing with cancer can build up over time, making you feel tense, lose sleep, or feel down.¹⁵

- **Make sure you have someone to talk to.** If you don't feel you can share your fears, anger, concerns, or other emotions with your family member or friend, find a friend, counselor or support group. You might consider asking your family member's or friend's doctor if there are any local support groups for caregivers.
- **Notice what you're feeling.** Be mindful of the emotions you are experiencing. It can be helpful to write them down in a journal, and talk to a doctor if you have concerns or need additional support.

Take care of your WELLNESS

It's natural for caregivers to put their own feelings and needs aside and devote all their attention and care to their family member or friend. Taking time for yourself is not selfish, it's self-nurturing! You always need time to recharge your body and mind to avoid burnout. Balance is about finding ways to take a break from caregiving to refresh your spirit.¹⁶

Dedicating some of your energy to taking care of yourself can help you become a more effective caregiver.

- **Take short breaks.** You might try listening to music, walking or stretching, writing in a journal, watching a favorite television show, or meditating.
- **Plan activities with friends and family.** You might try meeting friends for lunch, seeing a movie, getting tickets to a sporting event or the theatre, playing a sport, or taking an exercise class.
- **Take a moment.** Even if you can't go away for a weekend or even read a book without getting distracted by worry, take small steps. For example, try deep breathing: (1) close your eyes; (2) take a slow, deep breath in and hold it for 5 seconds; (3) slowly exhale; (4) repeat these steps four more times. You might also consider looking online or at your local library for more detailed tips for practicing mindfulness.
- **Take good care of yourself.** Eat a healthy diet and get plenty of rest.
- **Do not try to do it all.** Try to find a balance between your caregiving and your own daily life. Build a support network of friends and family and ask for help when you need it.

ASKING FOR HELP



It is important to ask for help when you need it. Try writing down some specific things you need help with, and when someone asks what they can do to help you out, give them an item on your list.

Find additional support by connecting with other caregivers either online or in person through a local or national network. Next time you are at an appointment with your family member or friend, ask the doctor or nurse for suggestions of local support groups for caregivers.



Question for the doctor

What are some resources I can look into for support?

GETTING MORE SUPPORT



Things I need help with	Who I could ask for help
e.g., Walking the dog on the day of an appointment	e.g., Neighbor

Appendix



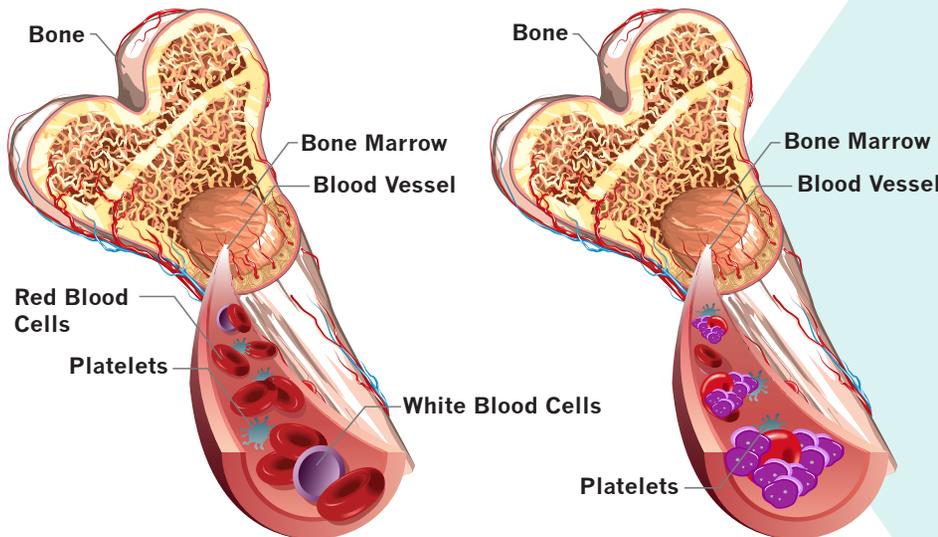
FLT3+ AML OVERVIEW

What is AML?

Acute myeloid leukemia, or **AML**, is a type of **leukemia** that affects the blood and **bone marrow**.⁹ 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.⁹ 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.



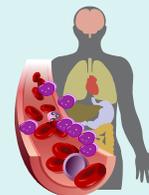
Leukemic cells in bone marrow and blood **with** AML



In people with AML, the bone marrow makes **white blood cells** that don't function normally, called **myeloblasts**.⁹



Sometimes in AML, the bone marrow also makes **red blood cells** and **platelets** that are not normal (leukemia cells).⁹ These leukemia cells, also called **blasts**, 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.⁹



Sometimes the leukemia cells can also spread outside of the blood to other parts of the body.⁹

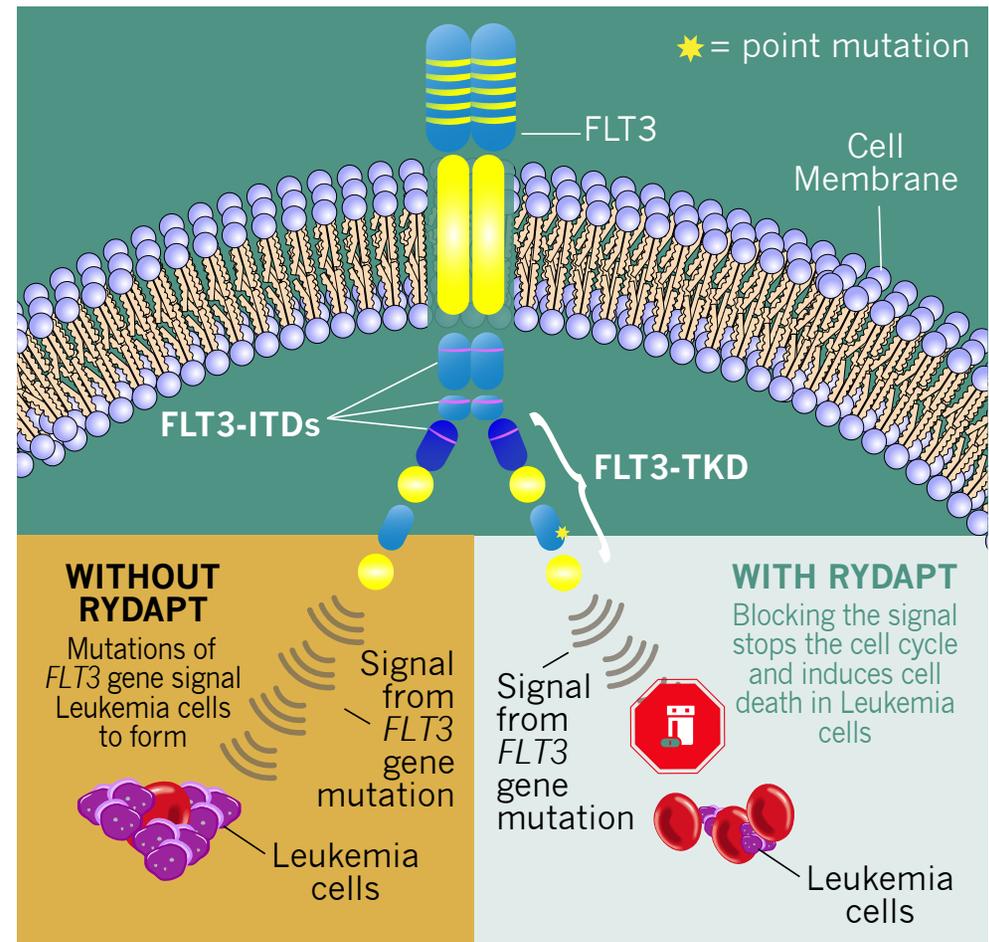
HOW RYDAPT MAY WORK

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. RYDAPT may work by blocking these proteins and their signals.² By blocking these signals, RYDAPT may help cause the AML cells to stop working and destroy themselves.²

Please see Important Safety Information on pages 32-33 and accompanying Prescribing Information.

What is *FLT3*? (pronounced “flit three”)

- 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. About one out of three people with AML have a **mutation** in this gene.¹⁷
- AML with the *FLT3* mutation is sometimes called “*FLT3*-positive AML.” *FLT3*+ AML tends to have poorer outcomes than AML without the *FLT3* mutation.¹⁷
- There are two 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.



Question for the doctor



QUESTIONS TO ASK THE HEALTH CARE TEAM

Encouraging your family member or friend to have an open relationship with his/her health care team is an important part of care. Below is a list of the questions from this brochure to help you both get the conversation started. **Please write down any additional questions for the doctor in the notes section at the back of the brochure, bring the list to the next appointment, and record the doctor's answers.**

Why do you think RYDAPT is the right treatment for my family member/friend?

Is a stem cell transplant an option for my family member/friend?

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

How does having the FLT3 mutation affect my family member's/friend's treatment path?

Where is my family member/friend along the FLT3+ AML treatment path? What will be the next step of my family member's/friend's treatment path?

What type of support will my family member/friend have when he/she is discharged from the hospital?

Are there foods or activities that my family member/friend should avoid?

What side effects should we watch for? What should I do if my family member/friend experiences any side effects?

What can we do to manage side effects?

How might an infection affect my family member/friend overall?

Do you have any other tips for me to help my family member/friend avoid infections?

Which tests will my family member/friend need to have? When will he/she need to have them?

What's the schedule for taking RYDAPT? What if a dose is missed?

Do you have any suggestions for how I can help my family member/friend build a routine with RYDAPT?

How will having AML or taking RYDAPT affect my family member's/friend's family planning?

How will treatment with RYDAPT affect my family member/friend in the long term?

Is FLT3+ AML something that my family member or friend can pass on to his/her children?

What are some local caregiver support groups?

HEALTH CARE TEAM CONTACT INFORMATION

Write down the contact information for your family member's or friend's health care team, and place it near your telephone or in another visible place for easy reference.

Name	
Specialty	
Address	
Telephone Number	

Name	
Specialty	
Address	
Telephone Number	

Name	
Specialty	
Address	
Telephone Number	

GLOSSARY¹⁸



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 the bone marrow contains less than 5% blast cells, the organs show no signs of AML, and the numbers of platelets and white blood cells in the 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.¹⁹

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.

