

# Living With and Caring for Someone With **Advanced Systemic Mastocytosis (advanced SM)**

**A Guide For Patients  
Taking RYDAPT<sup>®</sup> (midostaurin)  
and Their Caregivers**

RYDAPT is indicated for the treatment of adult patients with advanced systemic mastocytosis (advanced SM). Please see Important Safety Information at the back of this brochure and accompanying Prescribing Information.

# Introduction

Living with or caring for someone with **advanced systemic mastocytosis (advanced SM)** can be overwhelming. Reaching the diagnosis may have been a frustrating process and trying to find information for a rare condition like this and its treatment may be challenging.

This guide contains tips about living with advanced SM to help you or your family member or friend make informed decisions and better manage your or his/her care. Some pages will suggest questions to ask the doctor to help you or your family member or friend 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 or your family member or friend's treatment, write down questions to ask the doctor, and record your notes. You may want to bring this guide with you to appointments to support discussions with the doctor.

**If you have or your family member or friend has any questions about advanced SM, taking RYDAPT, the overall treatment plan and goals, or any possible side effects, please talk with a member of the health care team.**

Keywords in the guide appear in **bold purple text**. On page 29, you will find a glossary that defines each keyword.

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# Treatment With RYDAPT

Caring for someone with advanced SM? This section provides an overview of treatment with RYDAPT, including how your friend or family member should take RYDAPT, information on side effects, and tips for how to take RYDAPT as prescribed by the doctor. Read this section to better understand what your friend or family member can expect during treatment with RYDAPT.



# TREATMENT WITH RYDAPT

## Why am I taking RYDAPT?

Your doctor has prescribed RYDAPT to help treat your advanced SM by targeting the build up of mast cells.<sup>1</sup>

## What is the goal of treatment?

The goals of treatment for advanced SM are to:

- Control the growth of **mast cells**<sup>2</sup> (a type of white blood cell) that are building up in the bone marrow and other organs/tissues in the body.<sup>3</sup>
- Recover the organs/tissues that have been damaged by the buildup of mast cells.

## What is advanced SM?

Refer to page 27 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:

The recommended starting dose for RYDAPT is four 25-mg capsules twice a day, for a daily total of 200-mg.<sup>1</sup> Individual doses may vary. The doctor will advise the appropriate dose for you.

## Question for the Doctor



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

# HOW TO TAKE RYDAPT

## General instructions for taking RYDAPT include<sup>1</sup>:

-  • Take RYDAPT by mouth two times each day about 12 hours apart.\*
-  • RYDAPT should be taken with food to help prevent nausea. (Your doctor may also prescribe anti-nausea medicine.)
-  • 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 scheduled 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 scheduled dose at the next scheduled time.
-  • If you take more capsules than you should, contact your doctor right away.

\* The recommended starting dose for RYDAPT is four 25-mg capsules twice a day, for a daily total of 200-mg.<sup>1</sup> Individual doses may vary. Your doctor will advise the appropriate dose for you.

\*\* For as long as your doctor prescribes RYDAPT.

## Question for Your Doctor





## Sample Schedule for Taking RYDAPT \*



Take RYDAPT at 10:00 with a morning snack and a glass of water.



Take RYDAPT at 22:00 with a glass of water.



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



## Tips for swallowing capsules<sup>5</sup>

- **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.
- 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>              | e.g., ketoconazole, itraconazole |
| Certain <b>antivirals</b>       | e.g., ritonavir                  |
| <b>Macrolide antibiotics</b>    | e.g., clarithromycin             |
| <b>Antidepressants</b>          | nefazodone                       |
| Certain <b>antiepileptics</b>   | e.g., carbamazepine              |
| Certain <b>antibiotics</b>      | e.g., rifampin                   |
| Certain <b>herbal medicines</b> | e.g., St John's wort             |

Women: 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.

Men: If you have sexual intercourse with a woman who could become pregnant or who is already pregnant, you should use a condom while taking RYDAPT and for at least 4 months after stopping treatment. Talk to your doctor if you have questions regarding appropriate methods of contraception.



# 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>1</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.

## Some of the most common side effects of RYDAPT are<sup>1</sup>:



Nausea



Fatigue



Vomiting



Increased blood sugar levels



Diarrhea



Increased liver enzymes levels



Swelling in feet, legs, ankles, and/or hands

\* This is not a complete list of side effects. For a complete list, see Important Safety Information on pages 37–38 and the accompanying Patient Leaflet and approved Prescribing Information. It is important that you call your doctor right away to report any side effects.

## Questions for Your Doctor



What side effects should I watch for? Is there anything that I can do to prepare ahead of time? 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 talk 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 side effects without stopping treatment. **Here are some things you might try\*:**

|  |  |
|--|--|
| <p><b>Nausea/vomiting<sup>6</sup></b></p>                                 | <ul style="list-style-type: none"> <li>• Ask your doctor about medicine to prevent nausea and/or vomiting.<sup>2</sup></li> <li>• You can also talk to your doctor about the best time to take RYDAPT to help avoid nausea (e.g., bedtime).</li> <li>• Allow your food to cool down before you eat it. This may make it have less flavor.</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.**</li> </ul> |
| <p><b>Tiredness<sup>7</sup></b></p>                                       | <ul style="list-style-type: none"> <li>• Try to fit in light exercise, such as walking. Be sure to talk to your doctor before starting any exercise plan.</li> <li>• Pace activities throughout the day.</li> <li>• Get at least 8 hours of sleep each night. Try to take short naps during the day.</li> <li>• Eat a balanced diet.</li> </ul>  |
| <p><b>Diarrhea<sup>8</sup></b></p>                                       | <ul style="list-style-type: none"> <li>• Ask your doctor about anti-diarrhea medications.</li> <li>• Drink fluids, such as water, tea, and sports drinks daily to stay hydrated.</li> <li>• Eat small meals throughout the day. Eat foods in protein/carbohydrate combinations that are easy to digest, such as chicken with pasta or fish with rice.**</li> <li>• Cut back on fried, spicy, or greasy foods.</li> </ul>   |
| <p><b>Swelling in feet, legs, ankles, and/or hands<sup>9</sup></b></p>  | <ul style="list-style-type: none"> <li>• Do not stand for long periods of time. When seated, elevate your feet.</li> <li>• Eat a well-balanced diet and reduce your salt intake.</li> <li>• Avoid tight fitting clothing and shoes.</li> </ul>   |

\* This is not a complete list of side effects. For a complete list, see Important Safety Information on page 37 and the accompanying Prescribing Information.

\*\* If you have any food sensitivities or allergies (e.g., a gluten allergy), check with your doctor about appropriate foods to help you manage your side effect(s).

## Question for Your Doctor





# PREVENTING INFECTIONS

Treatment with RYDAPT can sometimes increase the chance of getting an infection. Here's why: White blood cells help the body fight germs and prevent infection. Treatment may cause the white blood cells not to work as well as they should, which 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</sup>



- **Try to stay away from germs.** Avoid people who you know are sick and try to stay away from large crowds. 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.<sup>10</sup>



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



- **Carry an alcohol-based hand sanitizer** to clean your hands when you are out of the house.<sup>11</sup>



- **Take appropriate steps around pets or animals.** Always wash your hands after touching pets or their food. Do not clean up droppings/feces from pets. 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.<sup>11</sup>

**As a caregiver,** you can also help prevent infection for your family member or friend by washing your hands often and being watchful for signs of infections. If you are sick, ask others to step in and help with caregiving so that you do not expose your family member or friend to germs.

**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>11</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

Signs and symptoms of advanced SM vary depending on which part of the body is affected by the condition. Symptoms may include<sup>3</sup>:

- Low red blood cell count and bleeding disorders
- Gastrointestinal symptoms such as abdominal pain, diarrhea, nausea, and/or vomiting
- Itching, hives, and/or flushing of the skin
- **Anaphylactoid reactions**
- Enlarged liver, spleen, and lymph nodes

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, or 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 (oedema) or skin, because these may be signs of heart problems.

# REMEMBERING TO TAKE RYDAPT

It may be difficult to remember when to take your medicine, especially if you are already trying to remember to take other medicines. Having a routine may help. Here are some tips that help you remember to take your medicine:



Take RYDAPT at the same time as other daily activities you already do, like eating breakfast and dinner each 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 page can be cut out and placed in a visible location (e.g., refrigerator or table). It includes space to write in when you need to take RYDAPT. Having this information in a visible place may help you remember when to take RYDAPT.



For more tips on building a routine or other support, talk to your doctor or local patient organization.



# MY RYDAPT SCHEDULE FOR ADVANCED SM

You will take RYDAPT twice a day, every day. Please fill in the boxes on the chart 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 14 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

# MANAGING EMOTIONS WHILE LIVING WITH ADVANCED SM



PATIENT

Living with advanced SM can have a big impact on your daily life. You may experience a range of feelings such as sadness, fear/uncertainty, isolation, and/or frustration. Many things may cause these feelings, such as concerns about the future, feeling alone with this disease, or the lack of information about advanced SM. Physical symptoms of the disease may also cause distress. These feelings may be overwhelming at times, but there are different ways that you can try to manage them. **Here are some ideas:**



## SADNESS

- Always share your feelings with the doctor, who may be able to help you find ways to manage them.
- Share your feelings of sadness with family members or friends. Talking honestly with others about how you are feeling may relieve the sadness and help you to feel supported. Sharing has been found to decrease the amount of time that people experience the emotion.<sup>13</sup> As you share, you or the person you share with may also come up with some creative solutions or strategies for easing any distressing emotions you are experiencing (such as journaling or taking a walk).



## FEAR/UNCERTAINTY

- Talk to your doctor about your fears and concerns as he/she may be able to help you feel more comfortable. Also ask questions. If you know what to expect, you can try to prepare for it.
- Use relaxation strategies, like deep breathing or mindfulness exercises, as a way to lessen your fears or worries.<sup>14,15,16</sup> Mindfulness refers to the practice of being in the present moment. Try being aware of your experiences, thoughts, and feelings without judging them. Ask your doctor for more information and tips on how to do these types of exercises. You can also find guidance and suggestions on relaxation strategies online.
- Focus on the things you can control to help you deal with uncertainty, like taking your medicine and staying on your course of treatment.



## Question for Your Doctor

What are some local resources for support?

# MANAGING EMOTIONS WHILE LIVING WITH ADVANCED SM (CONTINUED)

## ISOLATION



- Keep your friends and family close by staying connected in person, via social media, or with video calls.



- Join a support group of people who also have advanced SM, or are caregivers of people with advanced SM. Advanced SM is a rare condition, so if a support group is not available in your area, talk to your doctor about other options for support.

## FRUSTRATION

- Try distracting yourself and keeping your mind off of what is frustrating you with a productive and healthy activity, such as doing a hobby.
- If you feel frustrated, try taking a moment to close your eyes and take a few deep breaths, focusing on your inhaled and exhaled.
- In some cases, frustration may be caused by not feeling in control. Taking an action may help you to feel more in control. For example, by taking your medicine exactly as your doctor prescribed every day, you may feel more empowered and that you are being proactive about your health. Or the action you take could be a physical activity, which may provide an outlet for and alleviate frustration, both physically and emotionally. Be sure to discuss any physical activity with your doctor beforehand.



Managing and living with advanced SM can be a real challenge. It may be stressful and bring up different emotions. Writing down your feelings can help you make a plan for how to handle them.<sup>17</sup> Use the worksheet on the opposite page to note the emotions you are experiencing as well as the ways you will try to manage them. Remember to bring this worksheet with you to your doctor's appointments, and share your feelings with your doctor. That way, he/she can help you determine the best management strategies and what works or doesn't work for you in different situations.



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

# FINDING CARE AND SUPPORT WHILE LIVING WITH ADVANCED SM



PATIENT

## 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 he/she can do to help you, give him/her an item from your list.

| 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           |
|  |                          |
|  |                          |
|  |                          |
|  |                          |

## Finding Support

Remember that you are not alone as you manage advanced SM. You can find additional support by connecting with others who are going through a similar experience through online or in-person support groups. Next time you are at an appointment, ask the doctor or nurse for suggestions of local support groups for people with advanced SM or their caregivers.

# PROVIDING CARE AND SUPPORT AS A CAREGIVER



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. It lets him/her know that you are there for support, and it can decrease the amount of time where he/she feels negative emotions.<sup>13</sup>
- 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.
  - 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.

# PROVIDING CARE AND SUPPORT AS A CAREGIVER (CONTINUED)



## 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 means<sup>18</sup>:

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

An example of active listening is:

- Your family member or friend may say, *"I feel like I was just at the lab yesterday!"* You might respond, *"Managing multiple appointments can certainly be difficult."*



## Helping your family member or friend with DECISIONS

It's important to let the person receiving the care make decisions about their care whenever possible. However, your family member or friend 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 his/her 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 decisions you may be involved with include:

- Treatment goals and other medical decisions
- Financial and/or employment decisions



**Tips for  
COMMUNICATING  
with the  
health care team  
(i.e., role as an  
advocate)**

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

# TAKING CARE OF YOURSELF AS A CAREGIVER



Caregivers may feel overwhelmed by all that a family member's or friend's diagnosis may bring, such as difficult emotions, increased responsibilities, and lack of information about advanced SM. The stress that comes with being a caregiver can build up over time, making you feel tense, lose sleep, or feel down.<sup>19</sup>

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

The icon for the section header, showing a teal silhouette of a head with three curved lines representing breath or thought coming out of the mouth.

**Taking care  
of your  
WELL-BEING**

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.<sup>20</sup>

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

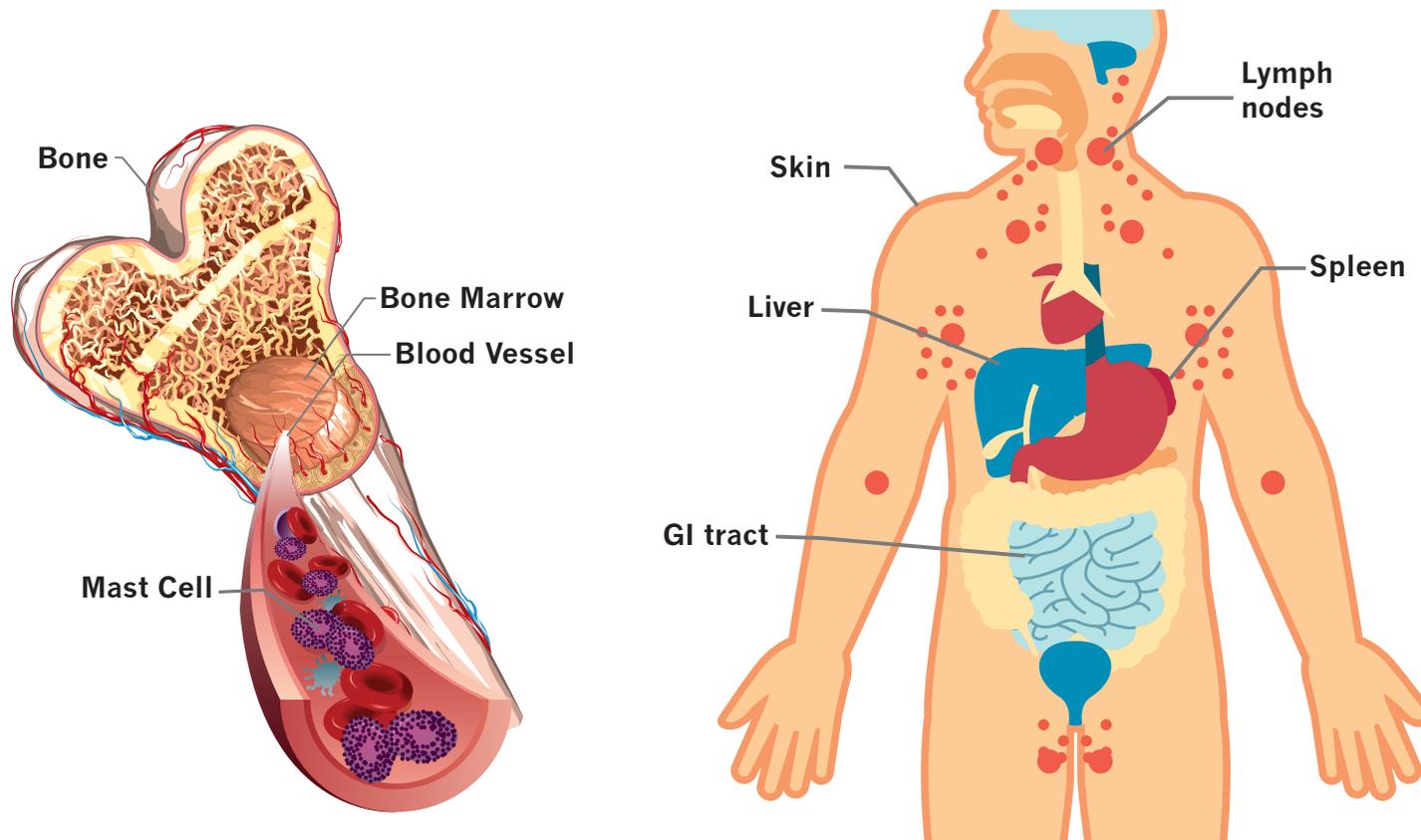
- **Take short breaks.** You might try listening to music, walking or stretching, writing in a journal, watching a favorite television show, or meditating.
- **Plan activities with friends and family.** You might try meeting friends for lunch, seeing a movie, getting tickets to a sporting event or the theatre, playing a sport, or taking an exercise class.
- **Take a moment for yourself.** Even if you can't run an errand or 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 tips on practicing mindfulness, which is another way to help you relax. This means focusing on living in the moment and being aware of your experience, thoughts, and feelings without judging any of them.<sup>15,16</sup>
- **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.

# **Additional Information and Glossary**



# WHAT IS ADVANCED SM?

Advanced systemic mastocytosis (advanced SM) is a condition where there is a buildup of **mast cells** in the bone marrow and other organs/tissues in the body. Mast cells are a type of **white blood cell** that are found in the skin, **bone marrow**, lymph nodes, liver, **spleen**, and gastrointestinal (GI) tract.<sup>21</sup> Depending on where the mast cells grow, symptoms can develop, such as abdominal pain, diarrhea, or enlarged spleen or liver.<sup>3</sup> Depending on the type of advanced SM you have, the mast cells may cause the organs/tissues to stop working correctly.<sup>21</sup>



# HOW IS ADVANCED SM DIAGNOSED?

## What are the different types of advanced SM?

advanced SM has 3 different subtypes<sup>3</sup>:

- ▶ Aggressive systemic mastocytosis (ASM)
- ▶ Systemic mastocytosis with an associated hematologic neoplasm (SM-AHN)
- ▶ Mast cell leukemia (MCL)



**RYDAPT may work for all three subtypes of advanced SM.**

## To diagnose advanced SM, your doctor will do<sup>3</sup>:

-  • A bone marrow biopsy to take a sample of your solid bone tissue. This sample would show an abnormally high number of mast cells.
-  • Blood tests to check blood cell levels, liver enzymes, and serum tryptase levels.
-  • Laboratory and medical evaluations to look at how your organs, such as your liver and spleen, are functioning.

## What causes advanced SM?

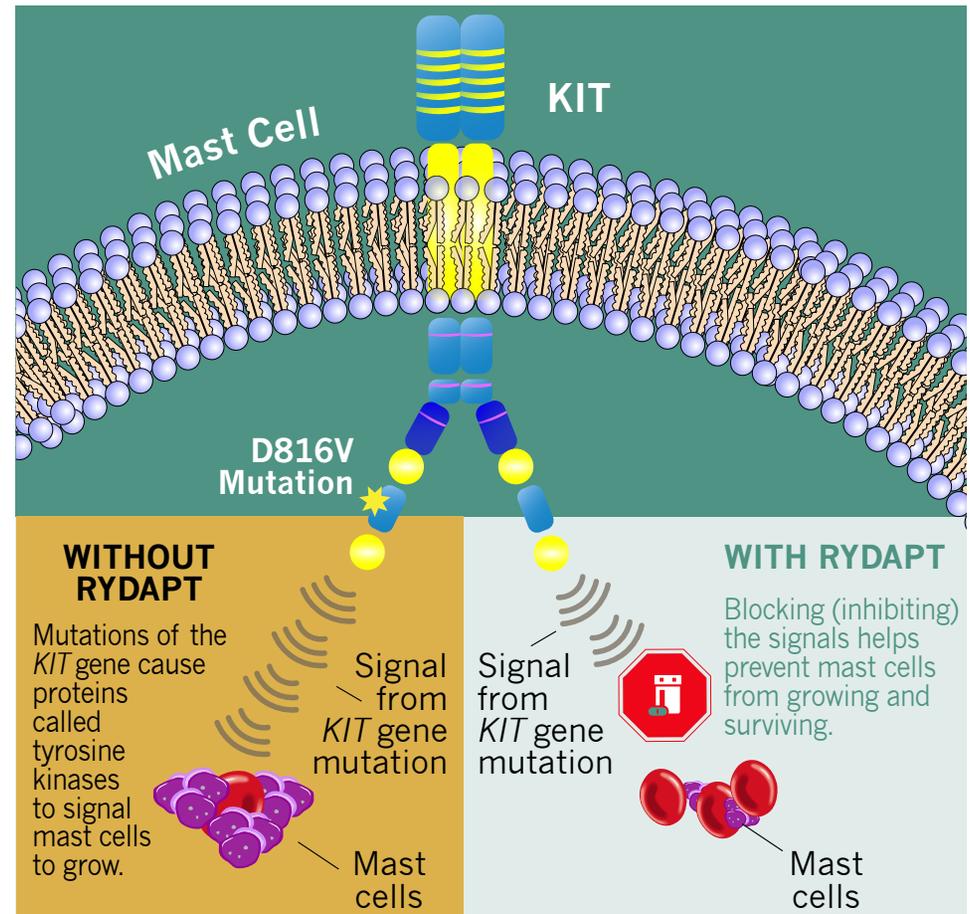
Researchers have found that advanced SM is caused by changes in the genes (**mutations**), specifically in the *KIT* gene. The ***KIT* gene** is responsible for the growth and buildup of mast cells in tissues.<sup>3</sup> The most common mutation of the *KIT* gene is called D816V and is found in approximately 90% of adults with Advanced SM.<sup>22</sup>



# HOW RYDAPT MAY WORK

RYDAPT is a type of medicine called a “**protein kinase inhibitor**.” In most cases of advanced SM, cells have a mutation in the *KIT* gene. This mutation causes proteins called tyrosine kinases to send a signal that tells mast cells to grow.<sup>1</sup> RYDAPT may work by blocking these proteins and their signals.<sup>1</sup> By blocking these signals, RYDAPT may help prevent mast cells from growing and surviving.<sup>1</sup>

Please see Important Safety Information on page 37 and accompanying Prescribing Information.



# GETTING THE MOST FROM YOUR DOCTOR VISITS

The relationship you have and how you communicate with your health care team are important parts of treatment for and managing advanced SM. The journey to reach your diagnosis may have been frustrating. Remember, though, that your doctor wants to support you and give you the information you need. Preparing for appointments ahead of time, speaking openly, and asking questions may help you get the most out of doctor visits.



## Tips to help you prepare for doctor visits:

- **Keep a log of symptoms and side effects** and bring it with you to the 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 HEALTH CARE TEAM



Communicating openly and honestly with your doctor is an important part of your care and treatment for advanced SM. 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?

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

What side effects should I watch for? Is there anything that I can do to prepare ahead of time?  
Who should I call if I experience any side effects?

What can I do to manage my side effects?

Which tests will I need to have? When will I need to have them?

Will an infection have any effect on how my treatment works?

What are some local resources for support?

What can I expect from treatment with RYDAPT?

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



# HEALTH CARE TEAM CONTACT INFORMATION

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

|                         |  |
|-------------------------|--|
| <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>23</sup>



**Anaphylactoid reaction:** A reaction similar to anaphylaxis that produces hives and itching or in severe cases shock, but is not due to an allergy.

**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.

***KIT* gene:** a gene that helps control cell growth, division, and survival and the development of certain cells, such as mast cells.<sup>3</sup>

**Mast cells:** a type of white blood cell that is found in the skin, bone marrow, lymph nodes, liver, spleen, and gastrointestinal tract.<sup>21</sup>

**Mutation:** a change in deoxyribonucleic acid, DNA.

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

**Serum tryptase:** An enzyme that is released by mast cells when they are activated as part of an immune response.<sup>24</sup>

**Spleen:** An organ that makes lymphocytes (a type of white blood cell), filters the blood, stores blood cells, and destroys old blood cells.

**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.

## References:

1. Rydapt [Core Data Sheet]. Novartis Pharma AG. March 2017.
2. Valent P. Mastocytosis: a paradigmatic example of a rare disease with complex biology and pathology. *Am Journal Cancer Res.* 2013;3(2):159.
3. National Institute of Health: Genetic and Rare Diseases Information Center. Systemic mastocytosis. <https://rarediseases.info.nih.gov/diseases/8616/systemic-mastocytosis>. Accessed April 19, 2017.
4. Arock M, Akin C, Hermine O. Current treatment options in patients with mastocytosis: status in 2015 and future. *European Journal of Haematology.* 2015;94(6):474-490.
5. NHS Choices. Problems swallowing pills. <http://www.nhs.uk/conditions/swallowing-pills/Pages/swallowing-pills.aspx>. Accessed April 3, 2017.
6. Macmillan Cancer Support. Managing nausea and vomiting. <http://www.macmillan.org.uk/information-and-support/coping/side-effects-and-symptoms/other-side-effects/nausea-and-vomiting.html#290074>. Accessed April 3, 2017.
7. American Cancer Society. Managing Cancer-related Fatigue. <https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/fatigue/managing-cancer-related-fatigue.html>. Accessed June 21, 2017.
8. National Cancer Institute. Diarrhea. <https://www.cancer.gov/publications/patient-education/diarrhea.pdf>. Accessed April 19, 2017.
9. ChemoCare. Swelling. <http://chemocare.com/chemotherapy/side-effects/swelling.aspx>. Accessed April 19, 2017.
10. American Cancer Society. Preventing infections in people with cancer. <https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/infections/infections-in-people-with-cancer/signs.html>. Accessed April 19, 2017.
11. Macmillan Cancer Support. Avoiding infection. <http://www.macmillan.org.uk/information-and-support/coping/side-effects-and-symptoms/other-side-effects/avoiding-infection.html>. Accessed April 19, 2017.
12. National Library of Medicine. Medline Plus®. Taking medicine at home – create a routine <https://medlineplus.gov/ency/patientinstructions/000613.htm>. Accessed November 10, 2016.
13. Brans K, et al. The relation between social sharing and the duration of emotional experience. *Cogn Emot.* 2013;27(6):1023-41.
14. Benson H, Greenwood MM, Klemchuk H. The relaxation response: psychophysiological aspects and clinical applications. *Int J Psychiatry Med.* 1975;6(1-2):87-98.
15. van den Hurk DG, Schellekens MP, Molema J, Speckens AE, van der Drift MA. Mindfulness-Based Stress Reduction for lung cancer patients and their partners: Results of a mixed methods pilot study. *Palliat Med.* 2015;29(7):652-60.
16. Lengacher CA, et al. Randomized controlled trial of mindfulness-based stress reduction (MBSR) for survivors of breast cancer. *Psychooncology.* 2009;18(12):1261-72.
17. Graf MC, Gaudiano BA, Geller PA. Written emotional disclosure: A controlled study of the benefits of expressive writing homework in outpatient psychotherapy. *Psychother Res.* 2008;18(4):389-399.
18. Conflict Research Consortium. University of Colorado. Active Listening. International Online Training Program On Intractable Conflict. Available at: <http://www.colorado.edu/conflict/peace/treatment/activel.htm>. Published 1998. Accessed December 1, 2016.
19. National Cancer Institute. Caring for the Caregiver. <http://www.cancer.gov/cancertopics/coping/caring-for-the-caregiver.pdf>. Accessed February 7, 2017.
20. Cancer Council Australia, Clinical Oncological Society of Australia. Submission: Towards a National Carer Strategy. [https://www.cancer.org.au/content/pdf/CancerControlPolicy/Submissions/CCA\\_COSA\\_final\\_submission\\_Towards\\_a\\_National\\_Carer\\_Strategy\\_submission.pdf](https://www.cancer.org.au/content/pdf/CancerControlPolicy/Submissions/CCA_COSA_final_submission_Towards_a_National_Carer_Strategy_submission.pdf). Accessed April 3, 2017.
21. Hermine O, Lortholary O, Leventhal PS, et al. Case-control cohort study of patients' perceptions of disability in mastocytosis. *PLoS one.* 2008 May 28; 3(5):e2266.
22. Gotlib J, et al. Efficacy and Safety of Midostaurin in Advanced Systemic Mastocytosis. *N Engl J Med.* 2016; 374:2530-41.
23. National Cancer Institute. NCI dictionary of cancer terms. <https://www.cancer.gov/publications/dictionaries/cancer-terms>. Accessed March 30, 2017.
24. American Association for Clinical Chemistry: Lab Tests Online. Tryptase. <https://labtestsonline.org/understanding/analytes/tryptase/tab/sample/>. Accessed June 21, 2017.