
Midostaurin for Acute Myeloid Leukaemia (AML)

**A Guide for
Patients**

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Midostaurin is a multi-targeted protein kinase inhibitor. Midostaurin has been approved for the treatment of adult patients with AML.

If you need specific advice or have any questions about this treatment, please speak to your haematologist or clinical nurse specialist.

This booklet was put together by our Patient Information Writer, Isabelle Leach and peer reviewed by Dr Manos Nikolousis and Dr Steve Knapper. We are also

grateful to a leukaemia patient, Julie Quigley, for her valuable contribution as a reviewer.

If you would like any information on the sources used for this booklet, please email communications@leukaemiacare.org.uk for a list of references.

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About Leukaemia Care

Leukaemia Care is a national charity dedicated to ensuring that people affected by blood cancer have access to the right information, advice and support.

Our services

Helpline

Our helpline is available 9:00am – 5:00pm Monday – Friday and 7:00pm – 10:00pm on Thursdays and Fridays. If you need someone to talk to, call **08088 010 444**.

Alternatively, you can send a message via WhatsApp on **07500068065** on weekdays 9:00am – 5:00pm.

Nurse service

We have two trained nurses on hand to answer your questions and offer advice and support, whether it be through emailing **nurse@leukaemicare.org.uk** or over the phone on **08088 010 444**.

Patient Information Booklets

We have a number of patient information booklets like this available to anyone who

has been affected by a blood cancer. A full list of titles – both disease specific and general information titles – can be found on our website at **www.leukaemicare.org.uk/support-and-information/help-and-resources/information-booklets/**

Support Groups

Our nationwide support groups are a chance to meet and talk to other people who are going through a similar experience. For more information about a support group local to your area, go to **www.leukaemicare.org.uk/support-and-information/support-for-you/find-a-support-group/**

Buddy Support

We offer one-to-one phone support with volunteers who have had blood cancer themselves or been affected by it in some

way. You can speak to someone who knows what you are going through. For more information on how to get a buddy call **08088 010 444** or email **support@leukaemiacare.org.uk**

Online Forum

Our online forum, **www.healthunlocked.com/leukaemia-care**, is a place for people to ask questions anonymously or to join in the discussion with other people in a similar situation.

Webinars

Our webinars provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support. For information on upcoming webinars, go to **www.leukaemiacare.org.uk/support-and-information/support-for-you/onlinewebinars/**

Website

You can access up-to-date information on our website, **www.leukaemiacare.org.uk**.

Campaigning and Advocacy

Leukaemia Care is involved in campaigning for patient well-being, NHS funding and drug and treatment availability. If you would like an update on any of the work we are currently doing or want to know how to get involved, email **advocacy@leukaemiacare.org.uk**

Patient magazine

Our magazine includes inspirational patient and carer stories as well as informative articles by medical professionals: **www.leukaemiacare.org.uk/communication-preferences/**

What is midostaurin?

Midostaurin (Rydapt, Novartis Europharm Limited) is a multi-targeted protein kinase inhibitor. Protein kinase inhibitors block the various protein kinase enzymes that are involved with cell growth, and prevent the growth of the leukaemia cells. More specifically, midostaurin inhibits the signals from the FMS-like tyrosine 3 (FLT3) receptor, blocking the cell cycle and promoting the death of the leukaemia cells that have the FLT3 mutation.

Mutations in the FLT3 gene occur in around 30% of adult patients with AML and indicate a poor prognosis. In patients with a FLT3 mutation, the complete remission rates with first-line induction chemotherapy (daunorubicin and cytarabine) are similar to those of patients who do not have a FLT3 mutation.

Relapse can be seen at any point following AML therapy, irrespective of whether a patient has a FLT3 mutation or not. The risk of relapse is higher in patients with FLT3-ITD mutations than in those who don't have a FLT3 mutation - and FLT3+ positive patients are particularly prone to early relapses. Relapse

is the term for when a patient initially responds to treatment, but after six months or more, the response stops. This is also sometimes called a recurrence.

In September 2017, midostaurin was approved by the European Medicine Agency (EMA) for the treatment of adult patients with newly-diagnosed AML who are FLT3 mutation-positive when it is given in combination with daunorubicin and cytarabine. In the study on which the EMA based their approval, patients who received daunorubicin and cytarabine with midostaurin had an average duration of survival of 74.7 months compared with 25.6 months for those who received just daunorubicin and cytarabine. Midostaurin has been shown to improve the side effects of chemotherapy.

In May 2018, the National Institute for Health and Care Excellence (NICE) recommended the use of midostaurin in combination with daunorubicin and cytarabine as induction therapy for AML, and in combination with high-dose cytarabine as consolidation therapy to destroy any remaining cancer cells.

Who receives midostaurin?

Midostaurin is indicated for adult patients with newly-diagnosed AML who have the FLT3 mutation.

Midostaurin is also approved for the treatment of some patients with a completely different haematological condition called advanced systemic mastocytosis.

Midostaurin is only indicated for adult patients because the safety and efficacy of midostaurin in children and adolescents below 18 years has yet to be established.

When used for the treatment of AML, midostaurin is only indicated for newly-diagnosed patients with the FLT3 mutation who are able to withstand an intensive chemotherapy regime. There is little experience of the use of midostaurin in patients with AML aged 60-70 years, and none in patients over 70 years. For patients aged 60 years or older, midostaurin should be used only in patients who can tolerate intensive induction therapy to achieve remission of the AML, and patients who do not have any other serious illnesses.

Midostaurin is also being investigated in combination with chemotherapies such as

gemtuzumab ozogamicin, high-dose cytarabine or venetoclax.

If you wish to have further information on AML, please view our collection of patient information booklets that are available on our website at www.leukaemiacare.org.uk

How is midostaurin administered?

Midostaurin is mostly used in combination with other chemotherapies. It is approved for use with daunorubicin and cytarabine as induction treatment for AML adult patients with newly diagnosed AML and a FLT3 mutation. In AML patients with a complete response, midostaurin is administered with high-dose cytarabine as consolidation chemotherapy, and as a single agent for maintenance therapy.

The daily dose of midostaurin is normally determined by your haematologist according to the stage of your AML and your symptoms. However, the usual daily dose of midostaurin for most patients with AML is 50mg (two capsules) twice daily (12 hours apart).

Depending on the response to midostaurin, the daily dose may be lowered, or the treatment temporarily interrupted.

You should follow the steps below when taking midostaurin:

- Take midostaurin at the same time each day to help you

to remember to take your treatment.

- Midostaurin should be taken with food.
- It should be taken twice a day at about 12-hour intervals (for example, at breakfast and with your evening meal).
- Capsules should be swallowed whole with a glass of water. Do not open, crush or chew them to make sure you get the full dose and avoid any unpleasant taste of the capsule content.
- If taken with chemotherapy, it is very important to follow your doctor's instructions on how to take midostaurin.
- If you bring up the capsules after you swallow them, do not take any more capsules and wait until your next scheduled dose.

What are the side effects of midostaurin?

You may get some side effects when you first start taking midostaurin. They are usually mild or moderate, and will generally disappear after a few weeks of treatment. Some people have very few side effects, whereas other people experience more. Midostaurin is still working even if you don't have any side effects. Your haematologist can prescribe medicines to help with particular side effects if they become troublesome.

Common side effects

Common side effects for midostaurin are:

- Nausea and vomiting (both are less common if you take midostaurin with food)
- Diarrhoea
- Headache
- Fever
- Nose bleeds, bleeding gums, or petechiae (reddish purple, flat, pinhead spots under the skin)
- Exfoliative dermatitis which is redness and peeling of the skin

over large areas of the body

It is important to contact your haematologist if you have any of the following side effects as you may need treatment:

- Raised temperature (over 38°C/100.4°F) depending on the advice given by your consultant
- Bruising or bleeding that you can't explain such as nose bleeds, bleeding gums, blood spots, rashes (your levels of platelets may be low)
- Eye pain, dry or watery eyes (you may have changes in vision)
- Feeling very tired or short of breath (you may have anaemia)

What happens if midostaurin doesn't work?

Your haematologist will closely monitor how well midostaurin is working for you by taking regular blood tests.

If midostaurin, which is a first-generation protein kinase inhibitor, is not working or has stopped working for you, your haematologist will decide which is the next best treatment option. Midostaurin could be replaced with a second-generation

protein kinase inhibitor such as gilteritinib which tends to achieve better complete remission in patients with relapsed AML.

Alternatively, a different chemotherapy combination which includes gemtuzumab, ozogamicin or cladribine could be used.

Leukaemia Care offers nationwide support groups for people affected by a diagnosis of a blood or lymphatic cancer. Visit www.leukaemiacare.org.uk, or call **08088 010 444**, to find out more and to find a group near you.

Glossary

Acute Leukaemia

Leukaemia which progresses rapidly and is generally aggressive. There are two main types: acute lymphoblastic leukaemia and acute myeloid leukaemia.

Acute Lymphoblastic Leukaemia (ALL)

Leukaemia in which lymphocytes start multiplying uncontrollably in the bone marrow, resulting in high numbers of abnormal, immature lymphocytes. Lymphocytes are a type of white blood cell involved in the immune response.

Acute Myeloid Leukaemia (AML)

Rapid and aggressive cancer of the myeloid cells in the bone marrow.

Anaemia

Condition where the number of red blood cells are reduced. Red blood cells contain haemoglobin and transport oxygen to body cells. This may be due to a lack of iron, leukaemia, or sickle cell disease.

Anthracycline

Antibiotic derived from the bacteria *Streptomyces peucetius* which was found to be an effective anticancer drug.

Blood Cancer

Cancer of blood cells from the bone marrow or lymphatic system. There are three main types of blood cancer:

- Leukaemia begins in the bone marrow and is classified according to the type of blood cell it affects (either myeloid or lymphoid) and whether it grows quickly (acute) or slowly (chronic).
- Lymphomas start in the lymphocyte white blood cells within the lymphatic system.
- Myeloma is a cancer of the plasma cells and starts in the bone marrow. Plasma cells are a type of white blood cell that makes antibodies.

Blood Cells

Cells present in the blood and bone marrow which include red blood cells, white blood cells and

Glossary (cont.)

platelets. These three types of blood cell make up 45% of the blood volume, with the remaining 55% being plasma, the liquid component of blood.

Chemotherapy

Drugs that work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

Complete Remission

Complete remission has occurred when:

- Blood cell counts have returned to normal
- Less than 5% of abnormal, leukaemia cells are still present in the bone marrow

Consolidation Treatment

Treatment following remission intended to kill any cancer cells that may be left in the body.

Cytarabine

Antimetabolite drug which works by disrupting the DNA of cancer cells, thereby slowing or stopping their growth.

First-line Treatment

First treatment given for a disease. It is generally the treatment accepted by the medical profession as the best initial treatment for a given type and stage of cancer.

FLT3 (FMS-like tyrosine kinase 3) Mutation

Mutation in a gene called FLT3 which is seen in about one-third of patients with acute myeloid leukaemia.

Genes

Genes are made up of DNA which stores the genetic information required to make human proteins.

Immunotherapy

Treatment that uses the body's own immune system to fight the cancer.

Induction Treatment

First treatment after diagnosis intended to kill the majority of the leukaemia cells and stimulate remission.

Leukaemia

A group of cancers that usually

begin in the bone marrow and result in high numbers of abnormal blood cells. These cells are not fully developed and are called blasts or leukaemia cells. Depending on the type of blood cell involved, there are different types of leukaemia with varying characteristics, such as being acute (develop quickly) or chronic (develop slowly).

Lymphocytes

Type of white blood cell that is vitally important to the immune response. There are three types of lymphocytes: B-cells, T-cells and natural killer (NK)-cells. B-cells produce antibodies that seek out invading organisms. T-cells destroy the organisms that have been labelled by the B-cells, as well as internal cells that have become cancerous. NK-cells attack cancer cells and viruses.

Lymphoid

Relates to lymphocyte white blood cells.

Maintenance Treatment

Treatment given to prevent cancer from coming back after it has

disappeared following the first-line treatment.

Mutation (Gene)

Permanent alteration in the DNA sequence of a gene, so that it differs from what is found in most people.

Myeloid

Relates to bone marrow. The myeloid compartment of the bone marrow produces red cells, platelets and some types of white blood cells including neutrophils and monocytes.

Petechiae

Red or purple, flat, pinhead spots under the skin

Platelets

One of the types of blood cells which help to stop bleeding.

Prognosis

Indication of how well a patient is expected to respond to treatment based on their individual characteristics at the time of diagnosis or other timepoint in the disease.

Glossary (cont.)

Protein Kinase Inhibitor

Protein kinase inhibitors block the protein kinase enzymes that are involved with cell growth, thereby preventing the growth of the cancer cells.

Purpura

Small purplish-red bruises which may be seen in the skin in certain conditions. Purpura occurs when small blood vessels burst, causing blood to pool just under the skin.

Refractory

Condition for which treatment does not result in a remission. However, the condition may be stable.

Relapse

Relapse occurs when a patient initially responds to treatment, but after six months or more, the response stops. This is also sometimes called a recurrence.

Second-line Treatment

Treatment other than the type used the first time (first-line treatment).

Targeted Therapy

Drugs that specifically interrupt the leukaemia cells from growing in the body. However, these drugs do not also harm the body's healthy cells the way conventional drugs do.

Tyrosine Kinase

Enzyme which can switch 'on' and 'off' many of the functions of the body's cells. Cells have receptors for tyrosine kinases present in their membranes enabling tyrosine kinases to play a major role in the activation of the cells' processes.

Tyrosine Kinase Inhibitors

Drugs that inhibit the tyrosine kinase enzymes which control the function of a cell. Tyrosine kinase inhibitors can switch 'off' tyrosine kinase enzymes that are permanently active due to a mutation.

Tyrosine Kinase Receptors

Receptors present in the membranes of all of the body's cells which can be activated by a tyrosine kinase enzyme.

Useful contacts and further support

There are a number of helpful sources to support you during your diagnosis, treatment and beyond, including:

- Your haematologist and healthcare team
- Your family and friends
- Your psychologist (ask your haematologist or CNS for a referral)
- Reliable online sources, such as Leukaemia Care
- Charitable organisations

There are a number of organisations, including ourselves, who provide expert advice and information.

Leukaemia Care

We are a charity dedicated to supporting anyone affected by the diagnosis of any blood cancer.

We provide emotional support through a range of support services including a helpline, patient and carer conferences, support group, informative website, one-to-one buddy service and high-quality patient information. We also have a nurse on our help line for any medical queries relating to your diagnosis.

Helpline: **08088 010 444**
www.leukaemicare.org.uk
support@leukaemicare.org.uk

Blood Cancer UK

Blood Cancer UK is the leading charity into the research of blood cancers. They offer support to patients, their family and friends through patient services.

0808 2080 888
www.bloodcancer.org.uk

Cancer Research UK

Cancer Research UK is a leading charity dedicated to cancer research.

0808 800 4040
www.cancerresearchuk.org

Macmillan

Macmillan provides free practical, medical and financial support for people facing cancer.

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

Maggie's offers free practical, emotional and social support to people with cancer and their families and friends.

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

Leukaemia Care is a national charity dedicated to providing information, advice and support to anyone affected by a blood cancer.

Around 34,000 new cases of blood cancer are diagnosed in the UK each year. We are here to support you, whether you're a patient, carer or family member.

Want to talk?

Helpline: **08088 010 444**

(free from landlines and all major mobile networks)

Office Line: **01905 755977**

www.leukaemicare.org.uk

support@leukaemicare.org.uk

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Leukaemia Care is registered as a charity in England and Wales (no.1183890) and Scotland (no. SC049802).
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