
HiDAC for Acute Myeloid Leukaemia (AML)

**A Guide for
Patients**

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

High dose cytarabine (referred to as HiDAC) is mainly used to treat patients with acute myeloid leukaemia (AML). It may also be used to treat other types of leukaemia, or lymphoma.

This booklet was originally compiled by Saloua Najjam, PhD and peer reviewed by our Nurse Advisor Fiona Heath and Dr Steve Knapper. This booklet has then been updated by our Patient Information Writer, Isabelle Leach. We are also grateful for the valuable contributions of Louise Moreton and Tracy Richardson as patient reviewers.

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 8:30am – 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@leukaemicare.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.

Patient and carer conferences

Our nationwide conferences provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support.

Website

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

Patient magazine

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

What is HiDAC?

HiDAC is the abbreviation for high-dose cytarabine. Cytarabine (also called cytosine arabinoside or Ara-C) is an antimetabolite chemotherapy drug that prevents the growth or reproduction of leukaemia cells by interfering with the information of their DNA.

The doses of cytarabine given to patients are determined according to their body surface area (BSA), which takes into account the patient's height and weight. Three dose regimens of cytarabine are generally described:

- **HiDAC:** 2000 to 3000mg/m² of BSA, twice daily over three or five days.
- **Intermediate-dose cytarabine (IDAC):** 1000 to 2000mg/m², twice daily over three or six days.
- **Low-dose cytarabine (LDAC):** a regimen of either 20mg twice daily for 10 days given subcutaneously (a total dose of 400mg), or a similar dosage given as 20mg/m² for 10 days (a total dose of 200mg/m²) which is about the same.

The dosing strategy of cytarabine is determined according to the patient's age and medical fitness and the genetic risk factors of their acute myeloid leukaemia (AML).

In the intensive treatment of AML, cytarabine is usually administered with other chemotherapies such as an anthracycline drug (sometimes with the addition of a 'targeted drug') as part of induction chemotherapy. In this setting cytarabine may be given as twice daily injections (usually for 10 days) or as a seven-day continuous infusion, along with several doses of anthracycline chemotherapy. This is usually referred to as the DA regimen.

The phrase HiDAC (high dose cytarabine) is usually used to refer to the administration of high doses of cytarabine as a single agent (monotherapy) as part of consolidation treatment. This is where disease remission has already been achieved following induction therapy. Complete remission at a cellular level is defined as less than 5%

of leukaemia cells in the bone marrow and recovery of blood cell counts to normal.

The regimen for HiDAC is for consolidation of remission, and is normally given over five days. This is repeated about every four weeks, usually for a total of two cycles.

HiDAC is particularly suited to patients less than 60 years old as they can withstand the challenges of the doses of this treatment. Patients older than 60 years may not tolerate the side effects and there is an increased rate of early death while on treatment due to their age and other illnesses. If suitable for intensive chemotherapy then these patients are usually given consolidation therapy with intermediate dose Ara-C (IDAC).

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 HiDAC administered?

Before starting treatment with cytarabine, the following clinical assessments will be carried out:

- Measurement of your weight and height.
- Full blood count, liver function tests, and urea/electrolyte levels as a measure of kidney function. These tests will be performed before each treatment cycle.
- A pregnancy test will be carried out on all female patients of child-bearing age two weeks before starting treatment.
- Electrocardiogram (ECG) to check that your heart is working normally.

You will then need to read and sign a consent form summarising the receipt of verbal and written information in relation to your disease, treatment and potential side effects.

Cytarabine 20mg/ml and 100mg/ml are available to be diluted into solutions containing the appropriate dose prescribed. HiDAC is administered as a rapid

intravenous infusion as patients tolerate higher doses better than when given as a slow intravenous injection.

You generally receive treatment with cytarabine in hospital and you may have to stay in until your blood counts recover. However, if you are feeling well you may be able to go home for periods and be monitored closely as an outpatient until your blood counts recover. This usually takes about four weeks, but this can be different for everyone.

Most HiDAC regimens are given over five days on a one-day off, one-day on basis (for example, two doses of 3000mg/m² on days one, three and five). That is a total of six injections and a total dose of 18g/m², which equals around 30g to 36g in most average sized patients. In some cases, you may receive a steroid or anti-emetics beforehand.

Frequency of treatment cycles will depend on your response to the cytarabine and any side effects.

If you are visiting a doctor for something else, or the dentist, it is important to make it clear to them that you are receiving chemotherapy. Your treatment can impact on how you are treated for other conditions.

What are the side effects of HiDAC?

Everyone will experience different side effects with cytarabine. The most common side effects are shown below. It is important to report side effects to your doctor or nurse so that they can be managed and treated effectively.

Side effects from cytarabine are dose-dependent. Therefore, they tend to be most common with HiDAC compared with IDAC and LDAC.

Common side effects

- Nausea, vomiting, anorexia and abdominal pain. The severity of these symptoms vary from patient to patient. You will be given anti-sickness medication along with your chemotherapy to help with this.
- Anaemia due to low red blood cell levels. This may make you feel tired and breathless. Let your doctor know if these symptoms become a problem, as you may need a blood transfusion.
- Increased risk of infection due to low levels of the white blood cells which fight infection. If you have any signs of infection, such as fever, shivering, breathlessness, a sore throat, cough, needing to pass urine often, diarrhoea or a temperature of 37.8°C or above, contact your nurse or doctor straight away as it is important to treat it as soon as possible.
- Bruising or mild bleeding due to low platelet levels which are a type of blood cell which help to stop bleeding. Let your doctor know if you have any unexplained bruising or bleeding such as nosebleeds, bloodspots or rashes on the skin, or bleeding gums. You may need a platelet transfusion.
- Reversible conjunctivitis due to bleeding or infection of the cornea (clear, protective outer layer of the eye). Your eyes may become sticky or sore. You will receive steroid eye drops to help prevent this. Do not wear contact lenses while you are having treatment with cytarabine.
- Fatigue. You may feel tired and lacking in energy. It is

often worse towards the end of treatment and for some weeks after treatment has finished. Take rests when necessary. Gentle exercise such as walking can help.

- Changes in kidney function, urinary retention and increases in uric acid levels. Your kidney function will be monitored by your routine blood tests. Drinking plenty of fluids will help prevent you becoming dehydrated.
- Reversible changes to liver enzyme levels.
- Sore, dry mouth or small mouth ulcers. Drinking plenty of fluids and cleaning your teeth regularly and gently with a soft toothbrush can help to reduce the risk of this happening.
- Hair loss. Your hair may thin and you may lose hair from your head. However, hair loss is almost always temporary and your hair will grow back after chemotherapy ends.
- Skin changes, including dry patches and rashes. Creams

and moisturisers can be used to provide some relief.

- Difficultly urinating.

Uncommon side effects

- Shortness of breath.
- Pneumonia.
- Central nervous system (brain and spinal cord) harmful effects. You may feel drowsy, confused, dizzy or unsteady. Rarely, cytarabine treatment can cause seizures. Tell your nurse or doctor straight away if you notice any of these symptoms.
- Inflammation of the veins or skin at the injection site.
- Skin ulceration, itching and burning pain of palms and soles.
- Cytarabine syndrome is an allergic reaction which manifests itself by fever, skin rash, nausea, muscle and bone pain and conjunctivitis. It usually occurs six to 12 hours after administration of cytarabine. Giving the patient

What are the side effects of HiDAC? (cont.)

treatment with steroids has been shown to be helpful in treating or preventing this syndrome. This will not affect everyone and will disappear soon after the cytarabine infusions stop.

- There is a risk of developing blood clots in your deep veins. This is known as deep vein thrombosis (DVT). You can receive blood thinners to help prevent this.

Patients who are receiving HiDAC should be specifically monitored for the following side effects because of their serious consequences:

- Neuropathy is a disease of one or more nerves in the body, characterised by numbness or weakness. Adjusting the dose of cytarabine can avoid irreversible damage to the nerves.
- Lung toxicity with inflammation of lung tissue and fluid in the lungs. You may develop wheezing, a cough, or breathlessness.
- Cardiomyopathy, which is

disease of the heart muscle.

- CNS toxicity is likely to be worse if HiDAC is given in combination with radiation therapy or in patients who have previously received intrathecal chemotherapy.

Fertility, pregnancy and breastfeeding

There have not been any studies of the effect of cytarabine on patient fertility. However, from clinical experience, absence of menstruation (including early menopause) and lack of sperm in semen may occur in patients taking cytarabine. In general, these side effects appear to be related to the dose and length of therapy, and may be irreversible.

Cytarabine can cause chromosome damage in the sperm, and men undergoing cytarabine treatment should be advised to use a reliable contraceptive method. Also, it can cause abnormalities to an unborn baby if it is exposed during pregnancy. It should, therefore, not be used in pregnant women (especially during the first

trimester), or in those who may become pregnant.

Men and women should be advised to use effective contraception during and up to six months after treatment.

It is not known whether cytarabine is transferred to breast milk. However, as a precaution, women who are taking cytarabine should not breastfeed.

Glossary

Acute Myeloid Leukaemia (AML)

The rapid and aggressive cancer of the myeloid cells in the bone marrow.

Allogeneic Stem Cell Transplant (allo-SCT)

The transplant of stem cells from a matching donor.

Amino Acids

Organic molecules which are the building blocks for making proteins.

Anaemia

A 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

An antibiotic derived from the bacteria *Streptomyces peucetius* and found to be an effective anticancer drug.

Antibody

The large Y-shaped protein produced by B-cell lymphocytes in response to a specific antigen,

such as a bacteria, virus or a foreign substance in the blood. The antibodies neutralise the bacteria and viruses.

Antigen

A toxin or other foreign substance which induces an immune response in the body, especially the production of antibodies.

Antimetabolite

A drug that interferes with the enzymes necessary for DNA synthesis, and therefore preventing growth or reproduction of cells.

Bone Marrow

The soft blood-forming tissue that fills the cavities of bones and contains fat, immature and mature blood cells, including white blood cells, red blood cells and platelets.

Bone Marrow Failure

The term used when the bone marrow is unable to keep up with the body's need for white and red blood cells and platelets.

Bone Marrow Relapse

Bone marrow relapse is defined

as the presence of greater than 25% of leukaemia cells in a bone marrow aspirate following the first complete remission.

Central Nervous System (CNS)

Part of the nervous system which includes the brain and spinal cord.

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.

Chromosomes

Thread-like structures which carry the genes, and are located in the nuclei of every cell in the body. There are 46 chromosomes (23 pairs) in humans.

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 (Phase)

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

DNA (Deoxyribonucleic Acid)

The thread-like chain of amino acids found in the nucleus of each cell in the body which carries genetic instructions used in the growth, development and functioning of the individual's cells.

Electrolytes

Salts and minerals in the blood that help conduct electrical impulses in the body. They include sodium, potassium, chloride and bicarbonate among others.

Eosinophil

The type of white blood cell which has a protective immunity role against parasites and allergens.

Fatigue

Tiredness and weakness rendering the patient unable to work or perform usual activities.

FLT3 (FMS-like tyrosine kinase 3)

A mutation in a gene called FLT3

Glossary (cont.)

which is responsible for AML leukaemia.

Genes

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

Induction (Phase)

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

Intrathecal Therapy

An injection of chemotherapy into the cerebrospinal fluid that surrounds and protects the brain and spinal cord.

Leukaemia

A group of cancers that usually begin in the bone marrow and result in high numbers of abnormal 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 (develops quickly) or chronic (develops slowly).

Minimal Residual Disease (MRD)

A measure of the presence of leukaemia at a molecular level rather than at a cell level. It is measured using molecular techniques such as flow cytometry and polymerase chain reaction analysis.

Monocyte

A white blood cell that attacks invading organisms and helps combat infections.

Myeloid

Relates to bone marrow.

Neutrophils

White blood cells involved in fighting inflammation and infection specifically bacterial infections.

Platelets

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

Radiation Treatment

Cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumours.

Red Blood Cells

The blood cell that carries oxygen. Red cells contain haemoglobin, which permits them to transport oxygen to body cells and collect carbon dioxide for disposal.

Refractory Condition

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

Relapse Condition

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.

Stem Cell

The most basic cell in the body that has the ability to develop into any of the body's specialised cell types, from muscle cells to brain cells. However, what makes these stem cells reproduce uncontrollably, as in cancer, is thought to be linked to chromosome abnormalities.

Steroids (also called Corticosteroids)

Man-made versions of the

hormones normally produced by the adrenal glands, two small glands above the kidneys. Steroids reduce inflammation (redness and swelling) and the activity of the immune system.

Targeted Therapy

Drugs that specifically interrupt the leukaemia cells from growing in the body. These drugs do not simultaneously harm healthy cells the way conventional chemotherapy drugs do.

Toxicity

Harmful effect.

Tyrosine Kinase

An 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.

Uric Acid

The product of the metabolic breakdown of purine nucleotides which are the chemical building blocks of DNA. Uric acid is a normal component of urine.

Glossary (cont.)

White Blood Cells

White blood cells are one of the types of cells found in the blood and bone marrow, along with red blood cells and platelets. White blood cells create an immune response against both infectious disease and foreign invaders. Granulocyte white blood cells include the neutrophils (protect against bacterial infections and inflammation), eosinophils (protect against parasites and allergens) and basophils (create the inflammatory reactions during an immune response). Other white blood cells include the lymphocytes (recognise bacteria, viruses and toxins, to which they produce antibodies) and monocytes (clear infection products from the body).

For more definitions of terms that you may come across during your blood cancer journey, you can download our booklet A to Z of Leukaemia from our website at www.leukaemiacare.org.uk

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 169 5155
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

Leukaemia Care,
One Birch Court,
Blackpole East,
Worcester,
WR3 8SG

Leukaemia Care is registered as a charity in England and Wales (no.1183890) and Scotland (no. SC049802).
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Registered office address: One Birch Court, Blackpole East, Worcester, WR3 8SG

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