Azacitidine for Acute Myeloid Leukaemia (AML)

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity
Azacitidine is a chemotherapy drug, which is used for the treatment of adult patients who are not eligible for a stem cell transplant, with acute myeloid leukaemia (AML), high-risk myelodysplastic syndrome (MDS) or chronic myelomonocytic leukaemia (CMML).

This booklet was compiled by Saloua Najjam, and Shirley Aston, a former Nurse Advisor at Leukaemia Care and has since been updated by our Patient Information Writer, Isabelle Leach. This booklet has been peer reviewed by Nurse Advisor Fiona Heath and medical advisors Professor David Bowen and Dr Steve Knapper. We are also grateful to leukaemia patients Sue Chambers, Anne Taylor and Nigel Lilburn for their valuable contributions as patient reviewers.

For more information, please talk to your consultant, haematologist, clinical nurse specialist or hospital pharmacist.

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 0808 801 0444.

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@leukaemiacare.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.leukaemiacare.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.leukaemiacare.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.

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.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 azacitidine?

Azacitidine is an antimetabolite drug that interferes with the formation of DNA, with the result of preventing the reproduction of cells in the body, particularly cancer cells which are multiplying at a greater rate than normal cells.

The patent for Vidaza (a branded version of azacitidine) which was developed by Celgene Europe B.V. in 2008, expired in 2018, making way for the application for authorisation of a number of generic products. Celgene Europe B.V. agreed to make all their scientific data available to other companies to facilitate this.

Celgene Europe B.V.’s own generic version of azacitidine, called Azacitidine Celgene, received approval by the European Medicines Agency (EMA) on 14th August 2019. Three other generics of azacitidine are under consideration by the EMA.

If you wish to have further information on AML, MDS or CMML, please view our collection of patient information booklets that are available on our website at www.leukaemiacare.org.uk
Who receives azacitidine?

Azacitidine is approved for the treatment of adult patients under the age of 65 years who are not eligible for a bone marrow stem cell transplant (SCT) with the following specific types of AML or AML-related conditions:

- AML with 20% to 30% marrow blasts in the bone marrow
- Intermediate- to high-risk myelodysplastic syndromes (MDS)
- Chronic myelomonocytic leukaemia (CMML) with 10% to 19% marrow blasts that is of ‘dysplastic disease subtype.’

In acute myeloid leukaemia (AML), there is an uncontrolled production of abnormal myeloblasts or leukaemia cells. As these cells accumulate in the bone marrow, they can prevent the production of healthy red blood cells, platelets and white blood cells.

Myelodysplastic syndromes (MDS) is the collective name for a group of cancers where bone marrow cells of varying types reproduce excessively and have dysplastic changes. In addition, MDS are characterised by a poorly functioning bone marrow and a likelihood for developing into AML.

With MDS, the bone marrow does not make enough normal blood cells. The blood cells made are not fully developed and unable to work correctly. These blood cells include red blood cells which supply oxygen to the body’s tissues, the white blood cells which fight infection and the platelets which help the blood to clot.

CMML is a form of blood cancer in which the bone marrow makes too many monocyte white blood cells. To make a diagnosis of CMML, the absolute monocyte count should be greater than 1x10⁹/L, accounting for more than 10% of white blood cells. The term chronic refers to the fact that it progresses slowly.

If you are older than 65 years and not eligible for a SCT and have been recently diagnosed with AML with more than 30% blasts, your doctor will be able to discuss other treatment options available.

In addition to the approved indications above, azacitidine can be used in the context of clinical trials, and where special funding arrangements have sought to use it (for example, for patients who have relapsed after chemotherapy or after a stem cell transplant).
How is azacitidine administered?

Azacitidine should be started and monitored under the supervision of a doctor experienced in the use of chemotherapeutic agents. Patients should receive anti-emetic drugs to prevent nausea and vomiting.

Before starting treatment with azacitidine, 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.
- Bone marrow biopsy to check how many cancer cells there are in your bone marrow. In a bone marrow biopsy, a sample of bone marrow is collected from the chest or hip bone, generally under local anaesthesia, using a bone marrow surgical instrument. The sample is then examined for abnormal cells.

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.

Azacitidine Celgene is available as a 25mg/ml powder to be suspended ready for injection. The recommended dose is 75mg/m² of body surface area, once a day for seven days, followed by a rest period of 21 days (totalling a treatment cycle of 28 days). It is administrated subcutaneously, under the skin of the upper arm, thigh or stomach. Sometimes it will be given on seven consecutive days, but most haematology day units will administer it on weekdays only (i.e. skipping the weekend; sometimes referred to as ‘5+2+2’).

Treatment should be given for at least six cycles and then for as long as it is of benefit to you. This
will depend on the leukaemia or MDS type you have. You should talk to your consultant or nurse if you have any queries about the length of treatment you are receiving.

You will have blood tests before each cycle of treatment to monitor your blood cell counts, liver and kidneys. If your blood counts become too low or the kidney tests are not satisfactory, your next treatment cycle may be delayed or your dose of azacitidine may be adjusted.

As it can be administered subcutaneously, you can usually receive azacitidine as an outpatient, meaning you will be able to go home after each treatment session.

Occasionally your doctor may adjust your dose of azacitidine or may delay your treatment for a short while. This may be because of the effects of the azacitidine on your body or on the cancer itself.
What are the side effects of azacitidine?

Everyone will experience different side effects with azacitidine. 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.

Common side effects

- **Nausea and vomiting, abdominal pain, diarrhoea or constipation.** You should be given anti-sickness medication before your treatment to help nausea and vomiting, but if not please tell your doctor or nurse as anti-emetics will help. You can manage the symptoms of diarrhoea or constipation with anti-diarrhoea drugs, laxatives and/or stool softeners as appropriate.

Tips for managing diarrhoea:

1. Drink plenty of water, but avoid alcohol and coffee.
2. Eat small, frequent meals and take your time to eat.
3. Eat fewer fibrous foods, such as cereals, raw fruits and raw vegetables.
4. Avoid greasy, fatty food.
5. Avoid spicy food.

- **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, you may need a blood transfusion.

- **Increased risk of infection due to low levels of the white blood cells which fight infection.** Common types of infections are chest infections and pneumonia. 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 37.8°C or above, contact your nurse or doctor straightaway as it is important to treat it as soon as possible.

You can try the following methods to try and minimise the risk of infection:

1. Hand washing.
2. Avoidance of people who are ill.
3. Perform regular temperature checks using a thermometer.
4. Place high importance on personal hygiene.

5. If you have a central line (also known as a Hickman line), keep the area around it clean and dry.

6. Clean your teeth every day and check for sores in your mouth or other signs of infection.

7. If you get injured and have a scrape or cut, make sure you clean it well.

8. Let your doctor or hospital team know if you have a sore bottom, or whether it bleeds.

- **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.

- **Headaches or dizziness.** Pain killers can be prescribed for the headaches if necessary.

- **Aching or pain in joints or muscles.** If you experience this, please discuss it with your doctor who can prescribe the appropriate pain killers.

- **Shortness of breath.**

- **Inflammation of the skin or veins at the injection site.** Redness, irritation and pain may occur around the injection site. The administration site of the injections will be changed regularly. This can often be improved using aloe vera or anti-inflammatory gels (such as ibuprofen gel) – your medical team will be able to advise on this.

- **Insomnia.**

- **Inflammation of the nose and/or throat.**

- **Loss of appetite or weight loss.**

- **Pins and needles, or a tingling feeling in your fingers and toes.**

**Uncommon side effects**

- **Hypertension or hypotension** (high or low blood pressure, respectively).

- **Heart problems.** Azacitidine can affect the way your heart works,
What are the side effects of azacitidine? (cont.)

including an irregular heartbeat. Tell your doctor or nurse straightaway if you experience chest pains, breathlessness or dizziness.

- **Bone marrow failure.**
- **Allergic reactions.** Symptoms you might get are difficulty breathing, swelling of the lips, itching or rash.
- **Bruising or bleeding due to low platelet levels, the type of blood cell which helps to stop bleeding.** You may experience bleeding from the mouth or gums and blood in your stools due to bleeding from the stomach or haemorrhoids. Let your doctor know if you have any unexplained bleeding. You may need a platelet transfusion.
- **Bleeding into the brain may make you drowsy, tired out or faint.** Please tell your doctor or nurse if you experience these symptoms.
- **Lung or heart problems tend to occur if you have existing lung or heart conditions.** Tell your doctor or nurse straightaway if you develop a cough or a wheeze or if you feel breathless.
- **Changes in kidney function.** Your kidney function will be monitored by your routine blood tests. Please tell your doctor or nurse if you notice blood in your urine.
- **Changes in liver function.** This will be picked up by your routine blood tests.
- **Hair loss.** Your hair may thin and you may lose your hair. However, hair loss is almost always temporary and your hair will grow back after chemotherapy ends.
- **Dehydration.**
- **Confusion and anxiety.**
- **Indigestion.**
- **Changes to your skin.** This can include skin ulcers, large, plum-coloured, raised, painful patches on your skin or cold sores.

**Fertility, pregnancy and breastfeeding**

There is no data on the effect of azacitidine on human fertility.
Adverse effects on male fertility have been shown in animals. Patients should be advised to use effective contraception while receiving treatment, and up to three months after treatment. Patients should also seek advice from their doctor on the need for sperm storage or egg freezing prior to starting treatment.

There are no studies of the use of azacitidine in pregnant women, but studies in animals have shown harmful effects. It is advised that azacitidine should not be used during pregnancy, especially during the first trimester.

It is not known whether azacitidine is transferred to breast milk. However, as a precaution, women who are taking azacitidine should not breastfeed.
What happens if azacitidine doesn’t work?

If following your treatment with azacitidine, your AML, MDS or CMML has not gone into remission or you have relapsed after achieving remission, your consultant is the best person to discuss what other treatments are available, and help you decide the next course of action. Knowledge of your type of disorder, your physical condition and any new treatments which may help you will guide your consultant’s recommendations.

Options that may be available to you could include:

**Conventional care regimens such as:**
- Subcutaneous low-dose cytarabine 20mg twice daily for ten days per 28-day cycle.

**Best supportive care:** This may include blood product transfusions and antibiotics with granulocyte colony-stimulating factor for infections.

**If you are relatively young and healthy, you may be offered:**
- A stem cell transplant for those patients who can withstand high-dose chemotherapy required to prepare your bone marrow for the transplant.
- Novel and experimental agents may be helpful for patients with primary refractory and high-risk MDS.
- Clinical trials can become a valid option for many patients, especially for those with refractory AML or MDS.

Leukaemia Care offers nationwide support groups for people affected by a diagnosis of a blood or lymphatic cancer. Visit [www.leukaemiacare.org.uk](http://www.leukaemiacare.org.uk), or call [08088 010 444](tel:08088%20010%20444), to find out more and to find a group near you.
### Acute Myeloid Leukaemia (AML)
A rapid and aggressive cancer of the myeloid cells in the bone marrow.

### 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
A large Y-shaped protein produced by B-cell lymphocytes in response to a specific antigen, such as 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 DNA synthesis, and therefore preventing growth or reproduction of cells.

### Body Surface Area (BSA)
Measured or calculated surface area of a human body. There are tables of average BSAs for men, women and children of different ages. BSA is expressed as $m^2$, height in cm and weight in kg.

### 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.
Glossary (cont.)

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<td><strong>Bone Marrow Biopsy</strong></td>
<td>A collection of a sample of bone marrow from the hip bone, generally under local anaesthesia. A bone marrow surgical instrument with a cylindrical blade, called a trephine, is used to remove a one to two-centimetre core of bone marrow in one piece.</td>
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<tr>
<td><strong>Bone Marrow Failure</strong></td>
<td>The term used when the bone marrow is unable keep up with the body’s need for white blood cells and red blood cells and platelets.</td>
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<td><strong>Chemotherapy</strong></td>
<td>Drugs that work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.</td>
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| **Complete Remission** | Complete remission has occurred when:  
  - Blood cell counts have returned to normal  
  - Less than 5% of abnormal, leukaemia cells are still present |
| **DNA (Deoxyribonucleic Acid)** | A 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. |
| **Electrocardiogram (ECG)** | A test that records the electrical signals in your heart to detect any heart problems and monitor the heart's status. |
| **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** | A 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.

Generic Drug
A copy of the brand-named drug that has exactly the same dosage, intended use, effects, side effects, route of administration, risks, safety, and strength as the original drug.

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

Granulocyte-Macrophage Colony-Stimulating Factor
A growth factor required to stimulate the growth of living cells.

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 (develops quickly) or chronic (develops slowly).

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

Lymphoid
Related to lymphocytes.

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.

Patent
A government authority or license conferring the right for a set period, especially the sole right to exclude others from making,
using, or selling an invention. Pharmaceutical companies are normally granted a ten-year patent to recover the money spent on developing a drug.

Platelets
A type of blood cell which helps to stop bleeding.

Red Blood Cells
Small blood cells that contain haemoglobin and carry oxygen and other substances to all tissues of the body.

Refractory Condition
A 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 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 make these stem cells reproduce uncontrollably, as in cancer, is thought to be linked to chromosome abnormalities.

Stem Cell Transplants
A transplant of stem cells derived from part of the same individual or a donor.

White Blood Cells
A type of cell 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).
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 helpline for any medical queries relating to your diagnosis.

Helpline: 08088 010 444
www.leukaemiacare.org.uk
support@leukaemiacare.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.leukaemiacare.org.uk](http://www.leukaemiacare.org.uk)
support@leukaemiacare.org.uk

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Leukaemia Care is registered as a charity in England and Wales (no.1183890) and Scotland (no. SCO49802).  
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