MidAC (Mitoxantrone and Cytarabine) for Acute Myeloid Leukaemia (AML)

A Guide for Patients
Introduction

Mitoxantrone and Cytarabine (AraC, Cytosine arabinoside) are two licensed drugs that can be used together as a combination therapy (named MidAC) in the treatment of acute myeloid leukaemia (AML).

For more information, or if you are unsure about anything, please talk to your consultant, haematologist, clinical nurse specialist (CNS) or hospital pharmacist.

This booklet was compiled by one of our medical writers Saloua Najjam, PhD. (Haematology) and peer reviewed by one of our medical professionals. We are also grateful to Ian Micklewright and his valuable contribution as a patient 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 - 10.00pm on weekdays and 9.00am - 12.30pm on Saturdays. If you need someone to talk to, call 08088 010 444

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, over the phone on 08088 010 444 or via LiveChat.

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/

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, as well as speak to one of our care advisers on our online support service, LiveChat (9am-5pm weekdays).

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 free quarterly magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe go to www.leukaemiacare.org.uk/communication-preferences/
What is MidAC?

MidAC is the combination therapy of Mitoxantrone and Cytarabine.

Mitoxantrone
Mitoxantrone is a chemotherapy drug. It belongs to the group of drugs called Anthracyclines and is used in cancer chemotherapy with the aim of destroying cancer (Leukaemia) cells.

Cytarabine
Cytarabine belongs to the group of drugs called Antimetabolites. It is a molecule that interferes with DNA replication which reduces the growth and spread of cancer cells in the body. This is known as antineoplastic activity. It also has antiviral and immunosuppressant activities, meaning that it reduces the strength of your body’s immune system.

For more information about cytarabine as a treatment for patients with AML, you can order our booklets on HidAC (high dose cytarabine) and low dose cytarabine by calling the helpline on 08088 010 444 or emailing support@leukaemiacare.org.uk
Who receives MidAC?

The two drugs Mitoxantrone and/or Cytarabine are licensed for the treatment of malignant diseases.

Mitoxantrone
Mitoxantrone is used, as a monotherapy (used alone) or in combination with other drugs, in the treatment of patients with:

- Acute myeloid leukaemia (AML) in adults
- Metastatic breast cancer
- Non-Hodgkin’s lymphoma
- Blast crisis in chronic myeloid leukaemia
- Advanced castrate resistant prostate cancer
- Highly active relapsing multiple sclerosis

Cytarabine
Cytarabine is mainly used in the induction of remission of AML, given in either a low, medium or high dose. Cytarabine can be used alone (monotherapy) or in combination with other antineoplastic drugs (drugs that kill cancer cells) to treat other illnesses such as:

- Other acute leukaemias of adults and children
- Lymphomatous meningitis

MidAC
MidAC is not a standardised licensed drug but Mitoxantrone/Cytarabine combination therapy is a part of a clinical trial.

The doses of Mitoxantrone and Cytarabine as well as the number of days to administrate them are defined by your consultant based on the best results from clinical trial studies. This combination therapy is used for induction (first phase of treatment of cancer) and for consolidation (therapy that is given after cancer has disappeared to kill any cancer cells that may be left in the body).

When your diagnosis with AML is confirmed by your consultant, they will explain to you in more detail the use of MidAC as pre- or post-remission induction chemotherapy.
Before starting MidAC combination therapy, your doctor run a few pre-assessments:

- To confirm your diagnosis.
- To record your weight and height.
- To run a full blood count (FBC).
- For female patients, a pregnancy test will be carried out to rule out any childbearing potential before each new chemotherapy course.
- To record your heart’s rhythm, using an electrocardiogram (ECG) test to check that your heart is working normally.
- To explain the potential risk of infertility related to this treatment.
- To consider a dental check.

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

**Mitoxantrone**

Mitoxantrone should be given to patients by intravenous infusion only. This means that the drug is sent directly into your vein using a needle or a tube.

**Cytarabine**

Cytarabine is a drug that can be given to patients as a solution for:

- Intravenous administration (infusion or injection) directly into a vein.
- Subcutaneous administration which is a injection under the skin.
- Intrathecal administration – this method is used for lymphomatous meningitis and involves an injection into the spinal canal, or into the subarachnoid space (a cavity in the brain) which allows the drug to reach the cerebrospinal fluid (CSF).
**MidAC combination therapy**

For AML patients, both Mitoxantrone and Cytarabine are given straight into the vein through a needle or tube. This is called an intravenous infusion.

During your treatment, investigations will be run for a full blood count (FBC), liver Function Tests (LFTs) and a measure of kidney function (U&Es). This is to check if any doses of Mitoxantrone and/or Cytarabine need adjusting.

When you are taking Cytarabine in this combination therapy, the usual dose used is low. However, if the high dose of Cytarabine is used, your doctor will measure GFR (glomerular filtration rate) level to consider dose change. Also, any sign of liver damage (hepatic impairment) will be considered by your doctor for lowering the dosage of both Cytarabine and Mitoxantrone.

While administrating MidAC, your clinical nurse will avoid causing any extravasation which is when chemotherapy leaks outside the vein. However, if you experience any signs or symptoms of extravasation (burning, pain, pruritus, erythema, swelling, blue discolouration, or ulceration), the administration of the drug should be stopped immediately.

During treatment, the cardiac function of patients will be monitored regularly because cardiotoxicity that could happen at any time during Mitoxantrone therapy with the risk of cumulative dose.

As Mitoxantrone is an immunosuppressive agent, this means that it partially or completely decreases your immune system’s ability to fight off infection. As a result of this, your doctor will advise that systemic infections are treated while taking or just prior to commencing therapy with Mitoxantrone. Systematic infections are those that effect multiple organs or your body as a whole.
However, live virus vaccines should not be administered during therapy.

Mitoxantrone should not be administrated to pregnant women. Breastfeeding should be avoided as Mitoxantrone can be detected in breast-milk, which could have potential adverse reactions in infants from this drug. Women could experience the absence of menstrual periods, known as amenorrhoea, which could be temporary or persistant. Therefore, some consideration to the preservation of eggs should be made before starting therapy.

Moreover, men receiving this drug should protect their partner through contraceptive measures during and at least six months after therapy. They may also want to consider freezing sperm as a precaution if they are considering starting a family in the future.

The course of Cytarabine

After intravenous administration of the drug, blood levels fall to unmeasurable levels within 15 minutes in most patients. Some patients have showed circulating drug as early as five minutes after injection. Cytarabine is metabolised primarily by the liver and perhaps by the kidney to produce arabinofuranosyl uracil. There is only about 6% of the active form which is excreted in urine within 12 to 24 hours.

The course of Mitoxantrone

Mitoxantrone is broken down in the body and passes through as bile and urine. You will be advised by your clinical nurse that you may notice a blue-green colouration to the urine for 24 hours after the drug administration.
What are the side effects of MidAC?

The side effects that you might experience with Mitoxantrone/ Cytarabine combination therapy correspond to the side effects derived from Mitoxantrone or Cytarabine.

This treatment can have serious or possibly life-threatening side effects so it is very important that you report side effects straight away. However, it is important to note that, with this combination therapy, there is only a 2% risk of death.

Chemotherapy is the most commonly prescribed anti-cancer treatment but while you are having it, you are vulnerable to infections. Symptoms of infection like fever, shivering, discomfort when you pass urine, sweats, sore throat, diarrhoea, coughing or breathlessness should be reported to your doctor or nurse immediately so that they can be treated.

Everyone will experience different side effects from this induction chemotherapy. Although you may experience them occasionally, it is important to report them so your nurse is able to monitor them and, where possible, have them treated. You will have a routine blood test to monitor the effects of the chemotherapy.

There are four types of side effect that this treatment may cause:

**Very common side effects**
- Infection.
- **Blood and lymphatic system disorders** - Anaemia, neutropenia and leukopenia.
- **Gastrointestinal disorders** - Nausea and vomiting.
- **Skin and subcutaneous tissue disorders** - Alopecia (partial or complete hair loss).
- **Nervous system disorders** - Cerebral disorder, cerebellar disorder and somnolence.
- **Eye disorders** - Corneal disorder.
- **Respiratory, thoracic and mediastinal disorders** - Acute
respiratory distress syndrome, pulmonary oedema.

**Common side effects**

- **Blood and lymphatic system disorders** - A decrease in number of granulocytes (granulocytopenia) and platelets (thrombocytopenia).

- **Metabolism and nutrition disorders** - Anorexia or loss of appetite.

- **Nervous system disorders** - Lethargy, characterised by tiredness and lack of energy.

- **Cardiac disorders** - Congestive heart failure and myocardial infarction (including fatal events).

- **Respiratory, thoracic and mediastinal disorders** - Shortness of breath.

- **Gastrointestinal disorders** - Constipation, diarrhoea, inflamed and sore mouth.

- **General disorders** - Administration site conditions like fatigue and fever.

- **Skin and subcutaneous tissue disorders** - Skin exfoliation.

**Uncommon side effects**

- **Infections and infestations** - Urinary tract infection, upper respiratory tract infection and sepsis.

- **Benign and malignant neoplasms** - Abnormal cell growth, also known as tumours, can lead to conditions such as myelodysplastic syndrome (MDS) can develop through the interference of the drugs in a patient’s DNA.

- **Blood and lymphatic system disorders** - Myelosuppression, bone marrow failure and white blood cell count abnormal.

- **Immune system disorders** - Anaphylaxis/anaphylactic reactions.

- **Metabolism and nutrition disorders** - Weight fluctuations and tumour lysis syndrome.

- **Nervous system disorders** - Anxiety, confusion, headache and paraesthesia.
What are the side effects of MidAC? (cont.)

- **Eye disorders** - Discolouration of the white of the eye.

- **Cardiac disorders** - Arrhythmia, sinus bradycardia and abnormal electrocardiogram (ECG) results.

- **Vascular disorders** - Contusion, haemorrhage and hypotension.

- **Gastrointestinal disorders** - Abdominal pain, gastrointestinal haemorrhage, mucosal inflammation and pancreatitis.

- **Hepatobiliary disorders** - Toxicity of the liver and elevated aspartate aminotransferase levels.

- **Skin and subcutaneous tissue disorders** - Red patches of the skin, nail disorders, rash, skin discolouration and tissue necrosis (after extravasation).

- **Renal and urinary disorders** - Elevated serum creatinine, elevated blood urea nitrogen levels, nephropathy toxic and urine discolouration.

- **Breast disorders** - Absence of menstrual periods.

- **General disorders and administration site conditions** - Accumulation of fluid under the skin (Oedema), extravasation and salty metallic taste sensation (Dysgeusia).

**Rare side effects**

- **Infections** - Pneumonia.

- **Cardiac disorders** - Cardiomyopathy.
What happens if MidAC doesn’t work for me?

If MidAC as a consolidation therapy does not give the expected results, your doctor may suggest stem cell transplantation.

Overall, following the outcome of your treatment with MidAC, your consultant is the best person to discuss with and to decide on the next step to take.

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.

Tell us what you think!

If you would like to give us some feedback about this patient information booklet, please hover over the code to the right using your phone or tablet’s camera. Click the link as it appears and this will take you to a short web form to fill in.

Suitable for Android, iPhone 7 and above.
**Glossary**

**Acute myeloid leukaemia (AML)**
A blood cancer which affects the myeloid cells, which include red cells, platelets and some white blood cells.

**Anaemia**
A medical condition in which the red blood cell count or haemoglobin is less than normal.

**Antineoplastic**
A type of drug that inhibits or prevents the growth and spread of tumours or malignant cells.

**Cerebrospinal fluid (CSF)**
A clear, colourless body fluid found around the brain and spinal cord.

**Clinical trial**
A medical research study involving patients with the aim of improving treatments and their side effects. You will always be informed if your treatment is part of a trial.

**Chemotherapy**
A type of cancer treatment that uses one or more drugs with powerful chemical to kill growing cancer cells.

**Deoxyribonucleic Acid (DNA)**
A molecule that carries the genetic instructions used in the growth development, functioning and production of all living organisms.

**Leukaemia**
A cancer of the blood with many different subtypes. Some forms are acute (develop quickly) and others are chronic (develop slowly). Leukaemia is an excess number of abnormal cells in the blood, usually white blood cells, which stop the bone marrow working properly.

**Relapse**
The return of a disease or the signs and symptoms of a disease after a period of improvement.

**Remission**
A period of time when illness is less severe or is not effecting someone.

**Remission induction**
Initial treatment with anticancer drugs to decrease the signs or symptoms of cancer or make the disappear.
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.leukaemiaicare.org.uk
care@leukaemiaicare.org.uk

Bloodwise

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

020 7504 2200
www.bloodwise.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
support@leukaemiacare.org.uk

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