

APPROVED PATIENT INFORMATION LEAFLET

Scheduling status: S4

MAVENCLAD 10 mg tablets

Cladribine

Contains sugar (sorbitol 64,04 mg)

Read all of this leaflet carefully before you start taking MAVENCLAD

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- MAVENCLAD has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What MAVENCLAD is and what it is used for
2. What you need to know before you take MAVENCLAD
3. How to take MAVENCLAD
4. Possible side effects
5. How to store MAVENCLAD
6. Contents of the pack and other information

1. What MAVENCLAD is and what it is used for

MAVENCLAD contains the active cladribine, a cytotoxic (cell killing) substance that works mostly on lymphocytes, cells of the immune system that are involved in inflammation.

MAVENCLAD is a medicine used to treat multiple sclerosis (MS) in adults.

Multiple Sclerosis is a disease in which inflammation destroys the protective sheath around the nerves.

Treatment with MAVENCLAD has been shown to reduce flare-ups of symptoms and to slow down progression of disability.

2. What you need to know before you take MAVENCLAD

Do not take MAVENCLAD:

- if you are allergic to cladribine or any of the other ingredients of MAVENCLAD (listed in section 6).
- if you are HIV positive, meaning you are infected with the human immunodeficiency virus (HIV).
- if you have active tuberculosis or liver inflammation (hepatitis).
- if you have a weakened immune system due to medical conditions or because you are taking other medicines that weaken your immune system or reduce the production of blood cells in your bone marrow. These include:
 - cyclosporin, cyclophosphamide and azathioprine (used to suppress the immune system, for example after organ transplantation)
 - methotrexate (used to treat conditions such as psoriasis or rheumatoid arthritis)
 - long-term corticosteroids (used to reduce inflammation, for example in asthma). See also “Other medicines and MAVENCLAD”.
- If you have active cancer.
- if you have moderate or severe kidney problems.
- if you are pregnant or breastfeeding (see Pregnancy and breastfeeding).

Do not take MAVENCLAD and talk to your doctor or pharmacist if you are unsure if any of the above applies to you.

Warnings and precautions

Special care should be taken with MAVENCLAD

Talk to your doctor or pharmacist before taking MAVENCLAD.

MAVENCLAD should be prescribed by a doctor experienced in the management of multiple sclerosis.

Blood tests

You will have blood tests before you start treatment to check that you can take MAVENCLAD.

The doctor will also do blood tests during and after treatment to check that you can continue to take MAVENCLAD, and that you are not developing any complications from the treatment.

Infections

You will be tested to see if you have any infections before you start MAVENCLAD treatment.

It is important to talk to your doctor if you think you have an infection. Symptoms of infections can include: fever, aching, painful muscles, headache, generally feeling unwell or loss of appetite. Your doctor may delay treatment, or interrupt it, until the infection clears up.

Shingles

If necessary, you will be vaccinated against shingles before you start treatment. You will need to wait between 4 and 6 weeks for the vaccination to take effect. **Tell your doctor immediately if you get symptoms of shingles**, a common complication of MAVENCLAD, which may need specific treatment.

Progressive multifocal leukoencephalopathy (PML)

If you believe your MS is getting worse or if you notice any new symptoms, for example changes in mood or behaviour, memory lapses, speech and communication difficulties, talk to your doctor as soon as possible. These may be the symptoms of a rare brain disorder caused by infection and called progressive multifocal leukoencephalopathy (PML). PML is a serious condition that may lead to severe disability or death.

Although PML has not been observed with MAVENCLAD, as a precaution, you may have a head MRI (magnetic resonance imaging) before you start treatment.

Cancer

Single events of cancer have been observed in patients who had received cladribine in clinical studies. Talk to your doctor if you have previously had cancer. Your doctor will decide the best treatment options for you. As a precautionary measure, you should follow standard cancer screening recommendations, as advised by your doctor.

Contraception

Men and women must use effective contraception during MAVENCLAD treatment and for at least 6 months after the last dose. This is important because MAVENCLAD can seriously harm your baby.

Blood transfusions

If you require blood transfusions, tell the doctor that you are taking MAVENCLAD. You may have to have the blood irradiated to prevent complications.

Changing treatments

If you change from other MS treatments to MAVENCLAD, your doctor will check that your blood cell counts (lymphocytes) are normal before you start treatment.

If you change from MAVENCLAD to other MS treatments, talk to your doctor. There can be overlaps in the effect on your immune system.

Liver problems

MAVENCLAD may cause liver problems. Talk to your doctor before taking MAVENCLAD if you have or have ever had liver problems. Tell your doctor immediately if you develop one or more of the following symptoms: feeling sick (nausea), vomiting, stomach pain, tiredness (fatigue), loss of appetite, yellow skin or eyes (jaundice) or dark urine. These could be symptoms of serious liver problems.

Children and adolescents

Use of MAVENCLAD is not recommended in patients below the age of 18 years, because it has not been investigated in this age group.

Other medicines and MAVENCLAD

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not start MAVENCLAD together with medicines that weaken your immune system or reduce the production of blood cells by your bone marrow. These include:

- ciclosporin, cyclophosphamide and azathioprine (used to suppress the immune system, for example after organ transplantation)
- methotrexate (used to treat conditions such as psoriasis or rheumatoid arthritis)

- long-term corticosteroids (used to reduce inflammation, for example in asthma). Short-term corticosteroids can be used when advised by your doctor.

Do not use MAVENCLAD together with other medicines for Multiple Sclerosis unless specifically advised by your doctor. Such medicines include alemtuzumab, daclizumab, dimethyl fumarate, fingolimod, glatiramer acetate, interferon beta, natalizumab or teriflunomide.

Do not take MAVENCLAD at the same time as any other medicine. Leave a gap of at least 3 hours between taking MAVENCLAD and other medicines taken by mouth. MAVENCLAD contains hydroxypropylbetadex that may interact with other medicines in your stomach.

Talk to your doctor if you are or have been treated with:

- medicines that may affect your blood cells (for example carbamazepine, used to treat epilepsy). Your doctor may need to supervise you more closely.
- certain types of vaccines (live and live attenuated vaccines). If you have been vaccinated within the last 4 to 6 weeks, MAVENCLAD therapy must be delayed. You must not receive such vaccines during MAVENCLAD treatment. Your immune system must have recovered before you can be vaccinated, and blood tests will check this.
- dilazep, nifedipine, nimodipine, reserpine, cilostazol or sulindac (used to treat the heart, high blood pressure, vascular conditions or inflammation), or eltrombopag (used to treat conditions associated with bleeding). Your doctor will tell you what to do if you have to take these medicines.
- rifampicin (used to treat certain types of infection), St. John's wort (used to treat depression) or corticosteroids (used to suppress inflammation). Your doctor will tell you what to do if you have to take these medicines.

Talk to your doctor if you take hormonal contraceptives (e.g. “the pill”). You need a second method of contraception during MAVENCLAD treatment and for at least 4 weeks after the last dose.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

Do not take MAVENCLAD if you are pregnant or trying to become pregnant. This is important because MAVENCLAD may seriously harm your baby.

You must use **effective methods of contraception** to avoid becoming pregnant during MAVENCLAD treatment and for 6 months after taking the last dose.

Talk to your doctor if you take hormonal contraceptives (e.g. “the pill”). You need a second method of contraception during MAVENCLAD treatment and for at least 4 weeks after the last dose. If you get pregnant more than 6 months after the last dose in year 1, no safety risk is expected but this will mean that you cannot receive treatment with MAVENCLAD while you are pregnant.

If you are male, you must use effective methods of contraception to prevent your partner from getting pregnant, whilst you are treated with MAVENCLAD and for 6 months after the last dose.

Your doctor will give you guidance on appropriate methods of contraception.

Do not take MAVENCLAD, if you are breastfeeding. If your doctor believes that MAVENCLAD is essential for you, your doctor will advise you to stop breastfeeding.

Driving and using machines

MAVENCLAD does not affect your ability to drive or use machines.

MAVENCLAD contains sorbitol.

Sorbitol is a source of fructose. If your doctor has told you that you (or your child) have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you (or your child) take or receive MAVENCLAD.

3. How to take MAVENCLAD

Do not share medicines prescribed for you with any other person.

Always take MAVENCLAD exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Treatment courses

You will be given MAVENCLAD as **two treatment courses over 2 years**.

Each treatment course consists of **2 treatment weeks**, which are one month apart at the beginning of each treatment year.

A **treatment week** consists of **4 or 5 days on which you receive 1 or 2 tablets daily**.

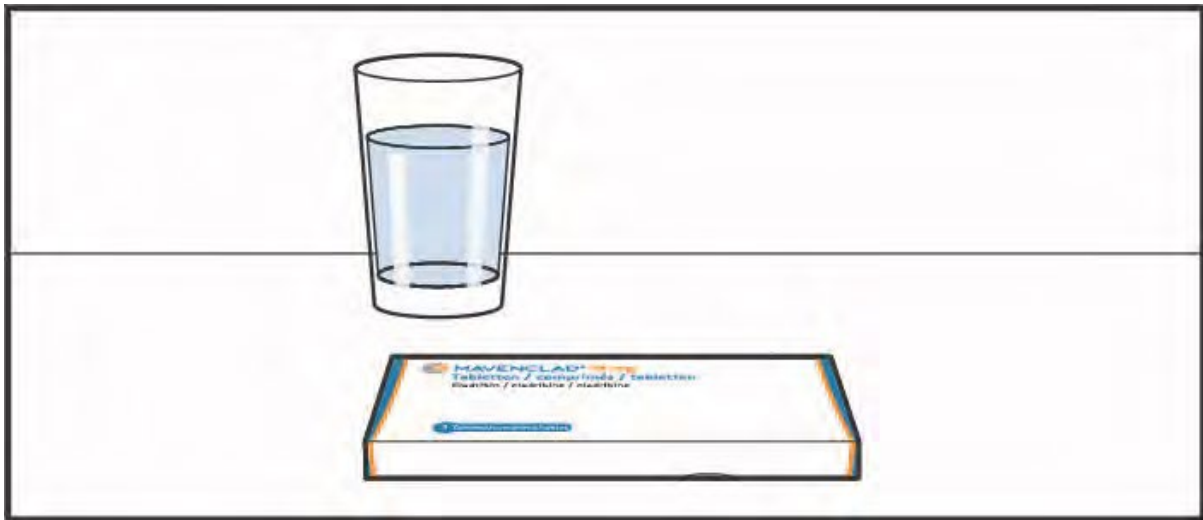
Before you start a treatment course, your doctor will do a blood test to check that the levels of lymphocytes (a type of white blood cells) are in an acceptable range. If this is not the case, your treatment will be delayed.

Once you have completed the 2 treatment courses over 2 years, your doctor will continue to monitor your health for another 2 years, in which you do not need to take the medicine.

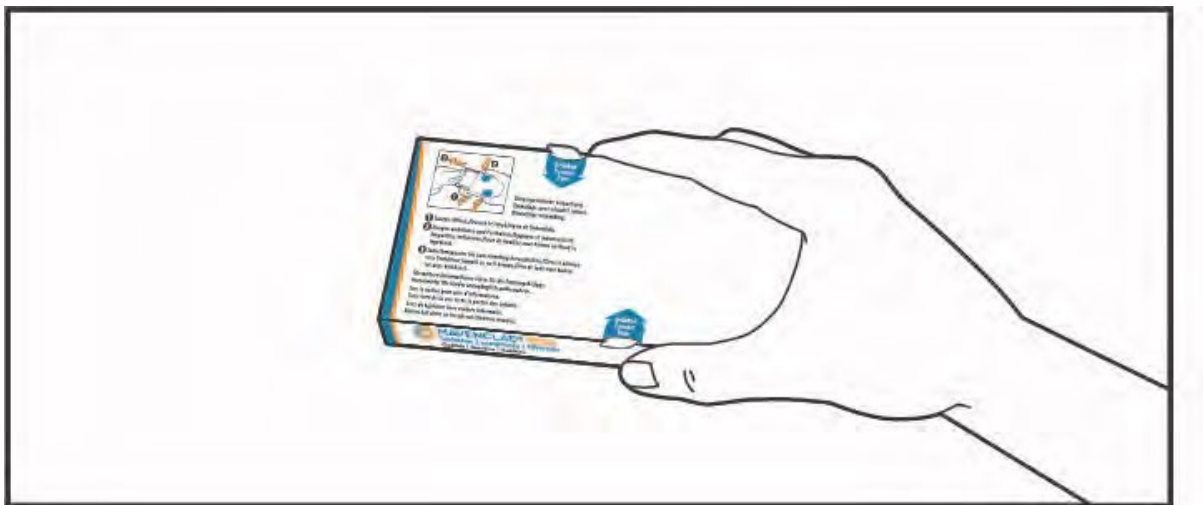
How to take your medicine

Take the tablet(s) at about the same time each day. Swallow them with water and without chewing. You do not have to take the tablets at meal times. You can take them with meals or between meals.

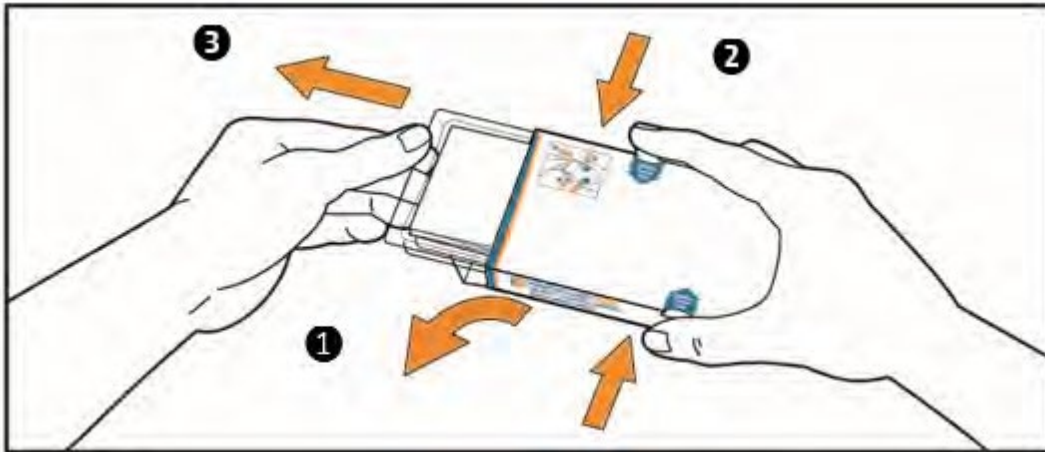
Step-by-Step Guide to taking your MAVENCLAD 10 mg tablets



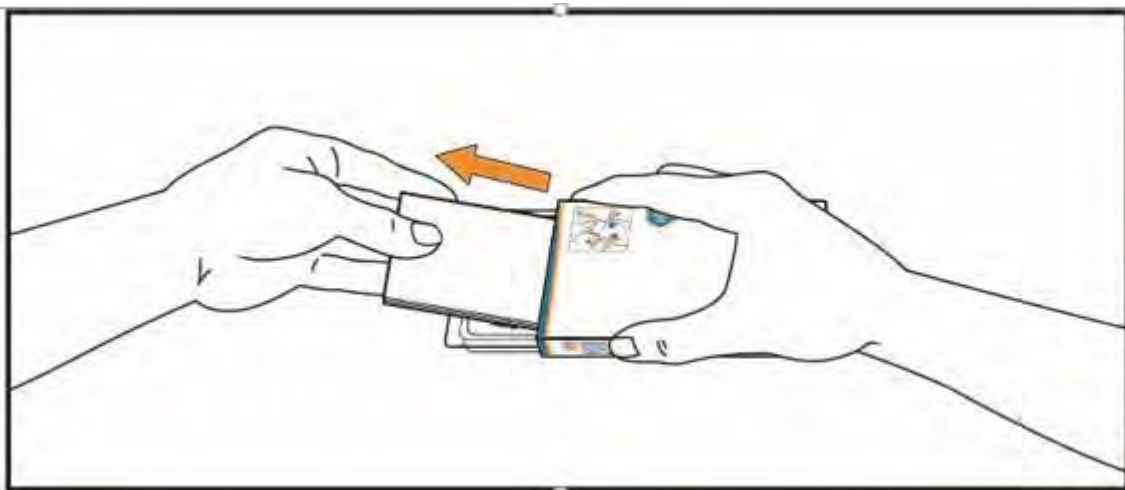
1. Have a glass of water ready and make sure your hands are clean and dry before taking the tablet(s).



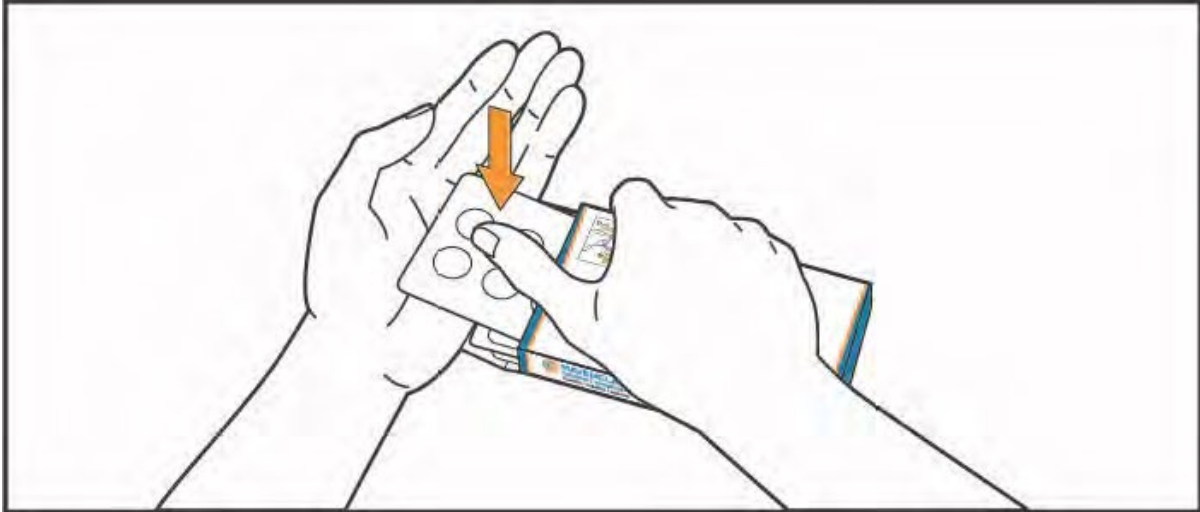
2. Pick up carton with the opening instructions facing up.



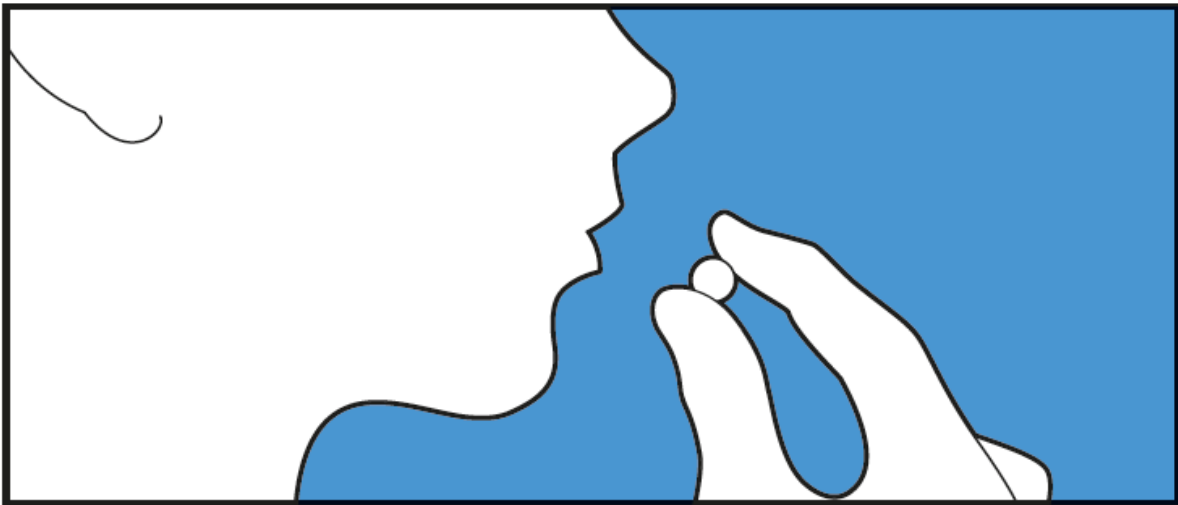
3. (1) Open the flap on the left end.
- (2) Push in the hooks on the sides of the carton simultaneously with your index finger and thumb, and keep hooks pushed.
- (3) Pull the tray out until it stops. **Caution:** Do not remove the tray from the carton.



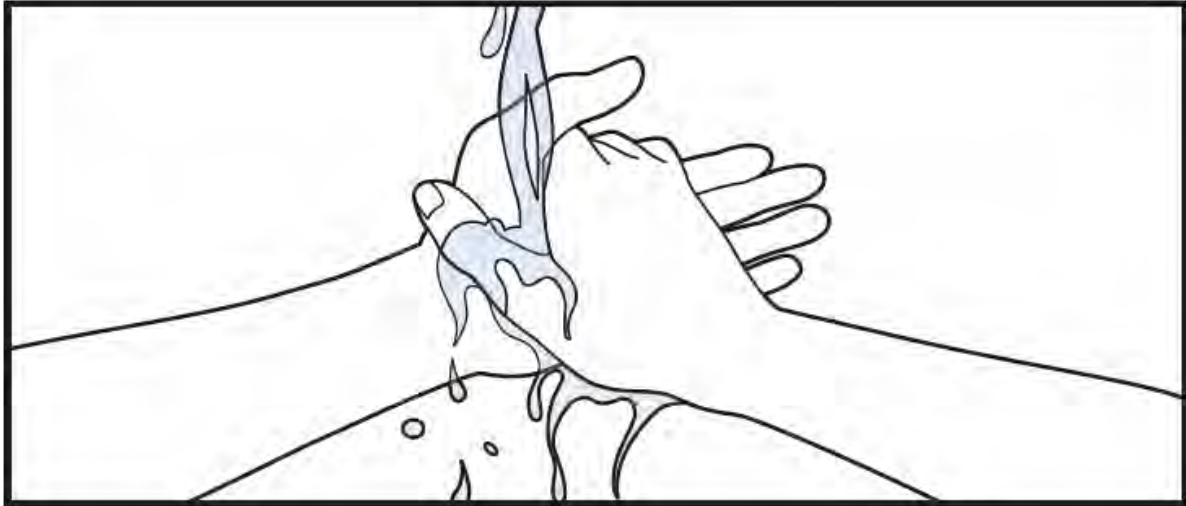
4. Take the leaflet from the tray. Make sure you have read all of the package leaflet including the step-by-step guide and keep it in a safe place.



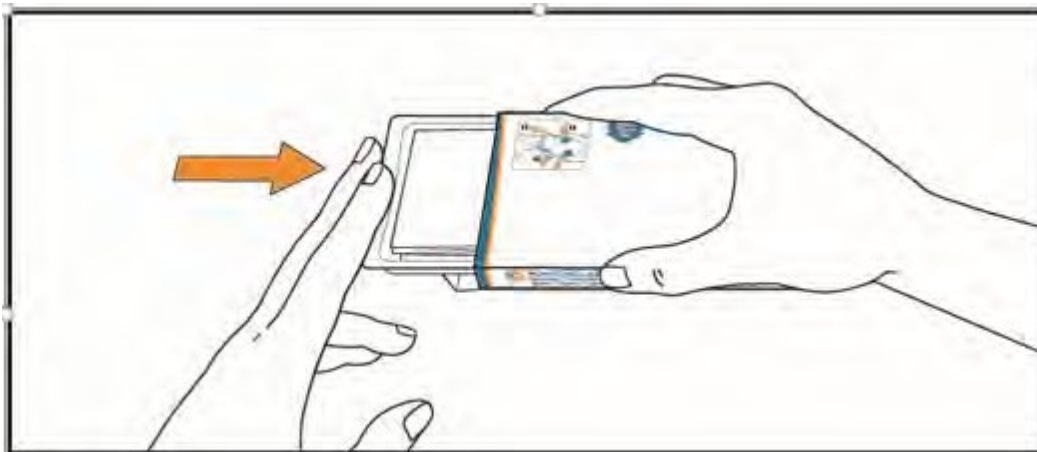
5. Raise the blister pack by pushing your finger through the hole in the tray. Place your hand under the blister pack and push 1 or 2 tablet(s) into your hand, according to your prescribed dose.



6. Swallow tablet(s) with water. Tablets must be swallowed whole and not chewed or allowed to dissolve in your mouth. Contact with skin should be limited. Avoid touching your nose, eyes, and other parts of the body.



7. Wash your hands thoroughly with soap and water.



8. Push the tray back into the carton. Store in the original package in order to protect from moisture.

Keep your tablets in the blister until your next dose. Do not pop the tablets out of the blister. Do not store the tablets in a different container.

Your doctor will tell you how long your treatment with MAVENCLAD will last. Do not stop treatment early without consulting your doctor or pharmacist. If you have the impression that the effect of MAVENCLAD is too strong or too weak, tell your doctor or pharmacist.

If you take more MAVENCLAD than you should

If you have taken more tablets than you should, contact your doctor immediately. Your doctor will decide if you need to stop treatment or not.

There is limited experience with overdose of MAVENCLAD. It is known that the more medicine you take the less lymphocytes may be present in your body, resulting in lymphopenia.

In the event of overdosage, consult your doctor or pharmacist. If neither your doctor or pharmacist is available, contact the nearest hospital or poison centre.

If you forget to take MAVENCLAD

If you miss a dose and you remember on the same day you were supposed to take it	If you miss a dose and do not remember it until the following day
Take the missed dose on that day.	Do not take the missed dose along with the next scheduled dose. Take the missed dose on the next day and extend the number of days in that treatment week.

Do not take a double dose to make up for forgotten individual doses.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

MAVENCLAD can have side effects.

Not all side effects reported for MAVENCLAD are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking MAVENCLAD, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop taking MAVENCLAD and tell your doctor immediately or go to the casualty department at your nearest hospital:

- allergic reactions, including itching, hives, rash and swelling of the lips, tongue or face

These are all very serious side effects. If you have them, you may have a serious reaction to MAVENCLAD. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- shingles such as a 'band' of severe pain and blistering rash, typically on one side of the upper body or the face, or other symptoms such as headache, burning, tingling, numbness or itchiness of the skin in the affected area, feeling generally unwell or feverish in the early stages of infection
- feeling sick (nausea), vomiting, stomach pain, tiredness (fatigue), loss of appetite, yellow skin or eyes (jaundice) or dark urine which may be symptoms of liver problems

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects

- cold sore (oral herpes)
- rash
- hair loss

- reduction in the number of certain white blood cells (neutrophils)

Less frequent side effect

- tuberculosis

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: <https://www.sahpra.org.za/Publications/Index/8>. By reporting side effects, you can help provide more information on safety of MAVENCLAD.

5. How to store MAVENCLAD

Keep this medicine out of the sight and reach of children.

Store at or below 30 °C.

Store in the original package in order to protect from moisture.

Do not use this medicine after the expiry date which is stated on the cardboard wallet and the carton after EXP. The expiry date refers to the last day of that month.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicines in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What MAVENCLAD contains

MAVENCLAD contains the active substance cladribine.

Each tablet contains 10 mg cladribine.

The other ingredients are hydroxypropyl betadex (2-hydroxypropyl- β -cyclodextrin) magnesium stearate and sorbitol.

MAVENCLAD[®] contains sugar (sorbitol 64,04 mg).

What MAVENCLAD looks like and contents of the pack

MAVENCLAD tablets are white, round, biconvex tablets engraved with 'C' on one side and '10' on the other side.

Each pack contains 1, 4, 5, 6, 7 or 8 tablets in a blister, sealed in a cardboard wallet and fixed in a child-resistant carton. Not all pack sizes may be marketed.

Holder of Certificate of Registration

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