

MAVENCLAD[®] 10MG TABLETS

Cladribine 10 mg

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What Mavenclad[®] is used for

MAVENCLAD is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, MAVENCLAD is generally used in people who have tried another MS medicine that they could not tolerate or that has not worked well enough.

MAVENCLAD is not recommended for use in people with clinically isolated syndrome (CIS).

It is not known if MAVENCLAD is safe and effective in children under 18 years of age.

How Mavenclad[®] works

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

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

Before you use Mavenclad[®]

When you must not take it

Do not take MAVENCLAD[®]:

- if you are allergic to cladribine or any of the other ingredients of this medicine (listed in excipients)

- 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:
 - 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). See also 'Other medicines and MAVENCLAD[®]'.
- if you have active cancer.
- if you have moderate or severe kidney problems.
- if you are pregnant or breast-feeding (see also 'Pregnancy and breast-feeding').

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

Before you start to take it

Talk to your doctor or pharmacist before taking MAVENCLAD[®].

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. These could be serious and possibly even life-threatening. 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[®] (see section "Before you use 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

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recommendations, as advised by your doctor.

Liver problems

MAVENCLAD may cause liver problems. Talk to your doctor before taking MAVENCLAD if you have or have ever 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 eye (jaundice) or dark urine. These could be symptoms of serious liver problems.

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.

See also 'Pregnancy and breast-feeding'.

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.

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.

Taking other 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 MS unless specifically advised by your doctor.

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 which 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.
- diltiazem, 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.

Pregnancy and breast-feeding

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. 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.

Men must use effective methods of contraception to prevent their partner from getting pregnant, while being 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 breast-feeding. If your doctor believes that MAVENCLAD® is essential for you, your doctor will advise you to stop breast-feeding during treatment and at least one week after the last dose.

Driving and using machines

MAVENCLAD® is not expected to affect your ability to drive or use machines.

Others

MAVENCLAD® contains sorbitol. If you have been told by your doctor that you have an intolerance to some

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sugars, contact your doctor before taking this medicine.

How to take Mavenclad®

How much to take

Always take this medicine 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.

Example:

If you start your treatment mid April, you take your tablets as shown:

	Year 1		Year 2
1st treatment week	1 or 2 tablets daily for 4 or 5 days; mid-April	1st treatment week	1 or 2 tablets daily for 4 or 5 days; mid-April
2nd treatment week	1 or 2 tablets daily for 4 or 5 days; mid-May	2nd treatment week	1 or 2 tablets daily for 4 or 5 days; mid-May

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.

Dose

1. You will be prescribed the correct number of tablets for each treatment week, based on your body weight.
2. You will need one or more packs to provide the correct number of tablets.
3. When you receive your supply of medicine, check that you have the correct number of tablets.
4. Based on your weight, you will be prescribed, your doctor will tell you the number of tablets to take.
5. If the number of tablets in your pack(s) is different from the numbers shown in the package insert, speak to your doctor.
6. Note that for some weight ranges the number of tablets may vary from one treatment week to the next.

Year 1

Your weight	Number of tablets to take	
	Year 1 treatment course	
	Treatment week 1	Treatment week 2
< 40 kg	Your doctor will tell you the number of tablets to take	
40 to < 50 kg	4	4
50 to < 60 kg	5	5
60 to < 70 kg	6	6
70 to < 80 kg	7	7
80 to < 90 kg	8	7
90 to < 100 kg	9	8
100 to < 110 kg	10	9
> 110 kg	10	10

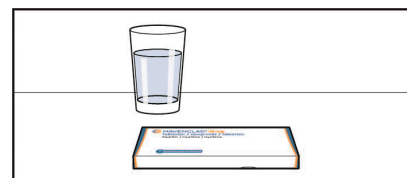
Year 2

Your weight	Number of tablets to take	
	Year 2 treatment course	
	Treatment week 1	Treatment week 2
< 40 kg	Your doctor will tell you the number of tablets to take	
40 to < 50 kg	4	4
50 to < 60 kg	5	5
60 to < 70 kg	6	6
70 to < 80 kg	7	7
80 to < 90 kg	8	7
90 to < 100 kg	9	8
100 to < 110 kg	10	9
> 110 kg	10	10

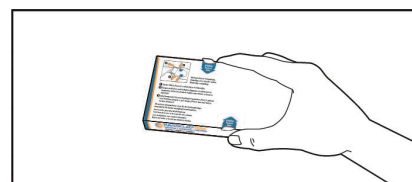
A Step-by-Step Guide to taking your MAVENCLAD® 10 mg tablets

MAVENCLAD® is packed in a reclosable, child-resistant carton and must be kept out of the sight and reach

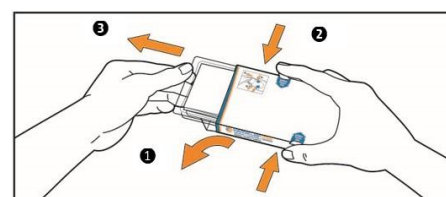
of children. See below for a step-by-step guide on how to handle the package and to take the MAVENCLAD® tablets. Make sure you know how many tablets are contained in the package. See package leaflet for guidance.



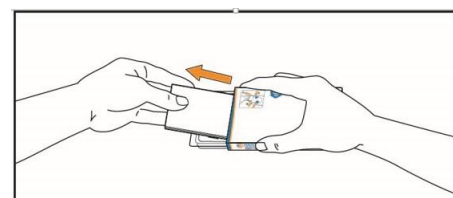
1. Have a glass of water ready and make sure your hands are clean and dry before taking the tablet(s).



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

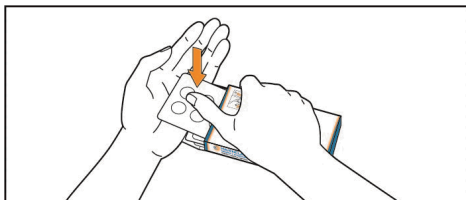


3. (1) Open the flap on the left end.
- (2) Push in the hooks on the sides of the carton simultaneously with your index finger and thumb, and keep hooks pushed.
- (3) Pull the tray out until it stops. Caution: Do not remove the tray from the carton.



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



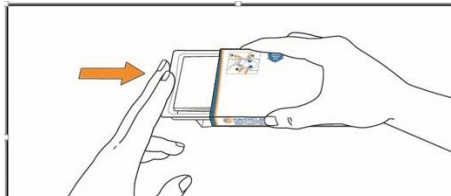
5. Raise the blister pack by pushing your finger through the hole in the tray. Place your hand under the blister pack and push 1 or 2 tablet(s) into your hand, according to your prescribed dose.



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.

When to take it

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

How long to take it

Depending on the total number of tablets you have been prescribed, you have to take them over 4 or 5 days, in each treatment week. The tables under “Treatment Courses” and “Dose” show how many tablets (1 or 2 tablets) you must take on each day. If your daily dose is 2 tablets, take them at the same time.

If you forget to take it

If you miss a dose and you remember on the same day you were supposed to take it - Take the missed dose on that day.

If you miss a dose and do not remember it until the following 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.

If you take too much (overdose)

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.

While you are using Mavenclad®

Things you must do

- Ensure your hands are dry before picking up your tablet(s).
- Push your tablet(s) through the blister and swallow immediately.
- If a tablet is left on a surface or if it breaks and fragments fall from the blister, the area must be thoroughly washed.
- Thoroughly wash your hands after handling the tablets.
- If you lose a tablet, contact your doctor for advice.

Things you must not do

- Do not leave your tablet(s) exposed on surfaces, for example on a table, or handle the tablet longer than necessary.

Things to be careful of

To ensure doctor monitors your blood count and screening for latent infections

Side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some side effects could be or could become serious.

Lymphopenia and shingles (may affect more than 1 in 10 people)

The most important side effect is a reduction in the number of white blood cells called lymphocytes (lymphopenia), which is very common and may be severe. Lymphopenia may increase the risk of getting an infection. An infection commonly seen with MAVENCLAD® is shingles.

Tell your doctor immediately if you have symptoms of shingles such as a 'band' of severe pain and blistering rash, typically on one side of the upper body or the face. Other symptoms may

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be headache, burning, tingling, numbness or itchiness of the skin in the affected area, feeling generally unwell or feverish in the early stages of infection.

Shingles will need to be treated, and MAVENCLAD® treatment may need to be stopped until the infection is cleared.

Liver problems (uncommon – may affect up to 1 in 100 people)

Tell your doctor immediately if you have symptoms such as feeling sick (nausea), vomiting, stomach pain, tiredness (fatigue), loss of appetite, yellow skin or eyes (jaundice) or dark urine. MAVENCLAD treatment may need to be stopped or interrupted.

Other possible side effects

Common side effects (may affect up to 1 in 10 people):

- cold sore (oral herpes)
- rash
- hair loss
- reduction in the number of certain white blood cells (neutrophils)
- allergic reactions, including itching, hives, rash, and swelling of the lips, tongue or face

Very rare – (may affect up to 1 in 10,000 people)

- tuberculosis

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website nptra.moh.gov.my (Public → Reporting Medicinal Problems / Side Effects / AEFI).

Storage and disposal of Mavenclad®

Storage

Store below 30°C.

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

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.

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

Disposal

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Product description

What it looks like

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.

Ingredients

- The active substance is cladribine. Each tablet contains 10 mg cladribine.
- The other ingredients are hydroxypropylbetadex, sorbitol and magnesium stearate.

MAL Number

MAL20096001ARZ

Manufacturer

NerPharMa S.R.L.

Viale Pasteur, 10

20014 Nerviano (MI)

Italy

Product Registration Holder

Merck Sdn Bhd (178145-V)

B-23A-1, Level 23A, The Ascent

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