

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- you are **sensitive** (allergic) to the active ingredient **cladribine** or to **any of the other ingredients** the medicine contains (see section 6)
 - you are an **HIV positive**, meaning you are infected with the human immunodeficiency virus (HIV)
 - you have active tuberculosis or liver inflammation (hepatitis)
 - you have a **weakened immune system** due to a medical condition or because **you are taking other medicines that weaken the immune system** or reduce the production of blood cells in the **bone marrow** including:
 - 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 section "Drug interactions"
- you have active cancer
 - you have **moderate or severe kidney problems**
 - you are **pregnant or breast-feeding** (see also section "Pregnancy and breast-feeding")

If you are unsure if any of the above applies to you, **do not take MAVENCLAD** and refer to your doctor or pharmacist.

Special warnings and precautions regarding use of this medicine

Infections

You will be tested to see if you have any infections before starting MAVENCLAD treatment. It is important to talk to your doctor if you think you have an infection. Symptoms of infections can include fever, aches, muscle pain, headache, general unwell feeling or yellowing of the eyes. Your doctor may delay or stop treatment until the infection passes.

Shingles

If necessary, you will be vaccinated against shingles before starting treatment. You will have to wait between 4 and 6 weeks until the vaccination begins to take effect. **Tell the doctor immediately if you have symptoms of shingles**, a common complication of MAVENCLAD (see section 4), which may require specific treatment.

Progressive multifocal leukoencephalopathy (PML)

If you think your **multiple sclerosis** is getting worse or if you **notice any new symptoms**, for example, changes in mood or behavior, memory problems, speech or 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 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 need to have a head MRI** (magnetic resonance imaging) before starting 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. The doctor will decide what is the best treatment option for you. As a precautionary measure, you should follow standard cancer screening recommendations, as recommended by your doctor.

Liver problems

MAVENCLAD may cause liver problems. **Tell 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.

Contraception

Men and women must use effective contraception during treatment and for at least 6 months after the last dose. This is important because MAVENCLAD may seriously harm your baby. See also section "Pregnancy and breast-feeding".

Blood transfusions

If you require a blood transfusion, tell the doctor that you are taking MAVENCLAD. To prevent complications, you may have to receive irradiated blood.

Changing treatment

If you change from another multiple sclerosis treatment to MAVENCLAD, your doctor will check that your blood cell count (lymphocytes) is normal before starting treatment.

If you change from MAVENCLAD to another multiple sclerosis treatment, talk to your doctor. There can be an overlap in the effect on your immune system.

Children and adolescents

Use of MAVENCLAD is not intended for patients under the age of 18. The medicine has not been tested in this age group.

Tests and follow-up

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

The doctor will also perform blood tests during and after treatment to check that you can continue taking MAVENCLAD, and that you are not developing any complications as a result of the treatment.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Do not start using 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 if recommended by your doctor.

Do not use MAVENCLAD together with other medicines for multiple sclerosis, unless specifically recommended by your doctor.

Do not take MAVENCLAD at the same time with any other medicines.

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.

Tell your doctor, if you are or have been treated in the past with:

- medicines which may affect your blood cells (for example carbamazepine, used to treat epilepsy). Your doctor may need to monitor you more closely.
- certain types of vaccines (live or live attenuated vaccines). If you have been vaccinated during the last 4-6 weeks, MAVENCLAD treatment must be delayed. You must not receive such vaccines during MAVENCLAD treatment. Your immune system must have recovered before you can be vaccinated; this will be checked by blood tests.
- dilazep, nifedipine, nimodipine, reserpine, cilostazol or sulindac (used to treat the heart, high blood pressure, vascular conditions or inflammations), 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), Hypericum (St. John's wort) (used to treat depression) or corticosteroids (used to suppress inflammations). 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. oral contraceptive pills). You will need to use an additional method of contraception during use of MAVENCLAD and for at least 4 weeks after the last dose.

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** in order 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. oral contraceptive pills). You will need to use an additional method of contraception during the use of MAVENCLAD and for at least 4 weeks after the last dose. If you become pregnant more than 6 months after the last dose in year 1, no safety risk is expected but you cannot receive treatment with MAVENCLAD while you are pregnant.

Men must use effective methods of contraception to prevent their partner from getting pregnant during treatment with MAVENCLAD and for 6 months after the last dose.

Your doctor will advise you regarding 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 the treatment and for at least one week after the last dose.

Driving and using machines

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

Important information about some of this medicine's ingredients
This medicine contains 64 mg sorbitol in each tablet.

3. HOW TO USE THIS MEDICINE

Always use this preparation according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this preparation.

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is as detailed below.

Treatment courses

You will be given MAVENCLAD in **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 will receive 1 or 2 tablets every day** (see Table 1).

Example: If you start the treatment in the middle of April, you must take the tablets as shown below:

	Year 1		Year 2
1st treatment week	1 or 2 tablets every day, for 4 or 5 days, mid-April	1st treatment week	1 or 2 tablets every day, for 4 or 5 days, mid-April
2nd treatment week	1 or 2 tablets every day, for 4 or 5 days, mid-May	2nd treatment week	1 or 2 tablets every day, for 4 or 5 days, mid-May

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

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

MAVENCLAD® 10 mg Tablets

The active ingredient:

Each tablet contains cladribine 10 mg

Inactive ingredients and allergens in the medicine: see section 2 under "Important information about some of this medicine's ingredients" and section 6 "Additional information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine.

If you have further questions, refer to the doctor or pharmacist. This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

In addition to the leaflet, the MAVENCLAD preparation has a Patient Guide. This guide contains important safety information that you should know before starting and during treatment with MAVENCLAD, and follow accordingly. Read the patient guide and the patient leaflet before starting to use the preparation. Keep the guide for further review, if needed.

1. WHAT IS THIS MEDICINE INTENDED FOR

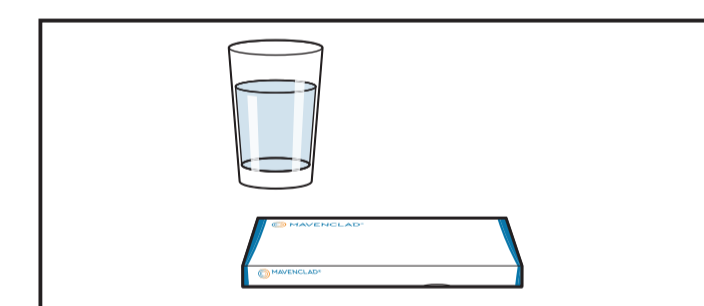
MAVENCLAD is intended for the treatment of adults with highly active relapsing multiple sclerosis.

Therapeutic group: selective immunosuppressants.

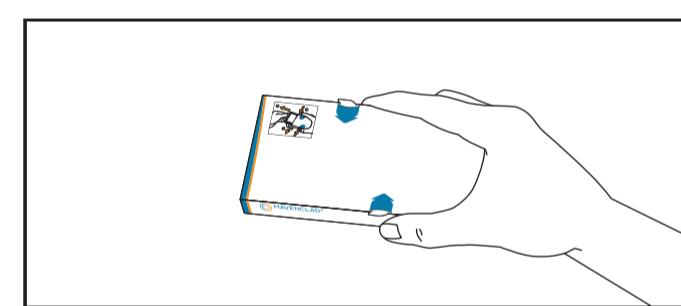
Multiple sclerosis is a disease in which inflammation destroys the protective sheath around the nerves.

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

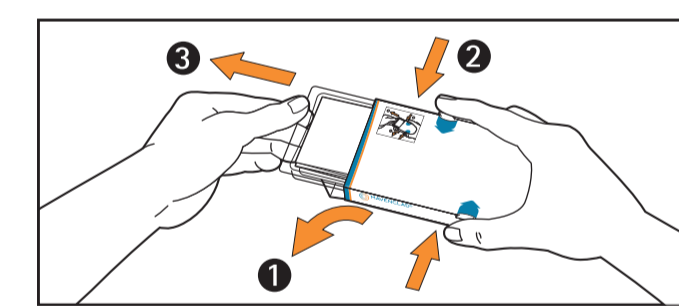
Treatment with MAVENCLAD has been shown to reduce flare-ups of symptoms and to slow down progression of disability.



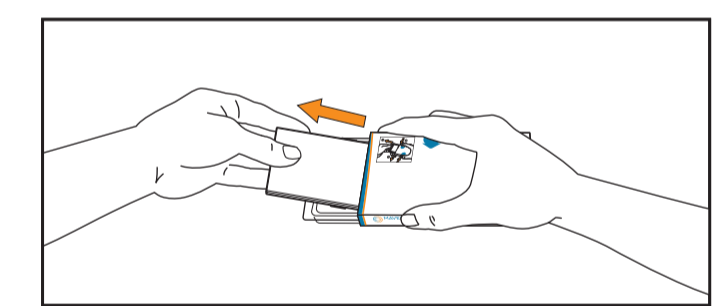
- 1** Prepare a glass of water and make sure that your hands are clean and dry before taking the tablet(s).



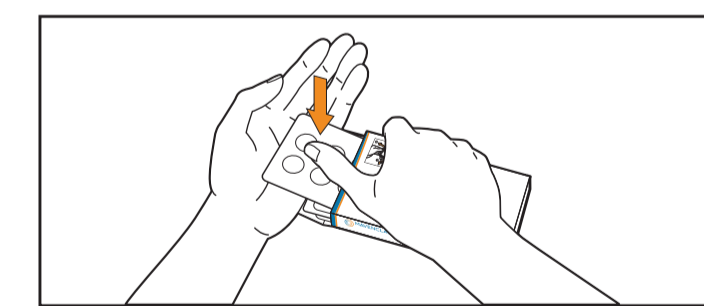
- 2** Pick up the carton with the instructions facing up.



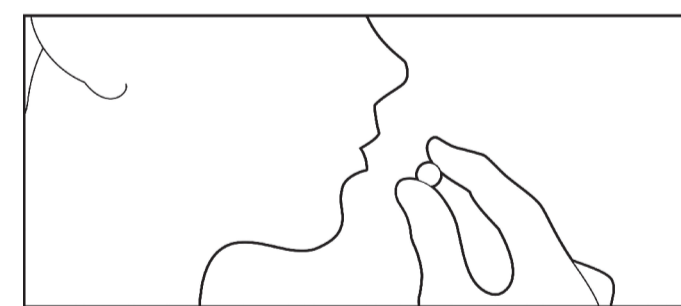
- 3** (1) Open the flap on the left end of the carton.
(2) Simultaneously push in the hooks marked on the sides of the carton with your index finger and thumb, and keep hooks pushed.
(3) Pull the tray out until it stops. **Caution:** Do not remove the tray from the carton.



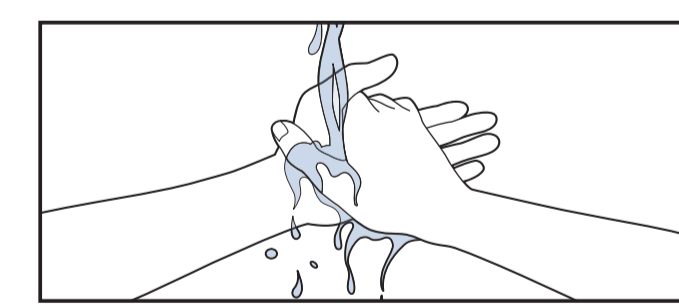
- 4** Take the leaflet out of the tray. Make sure that you have read the entire leaflet, including the guide for taking MAVENCLAD 10 mg tablets and keep it in a safe place.



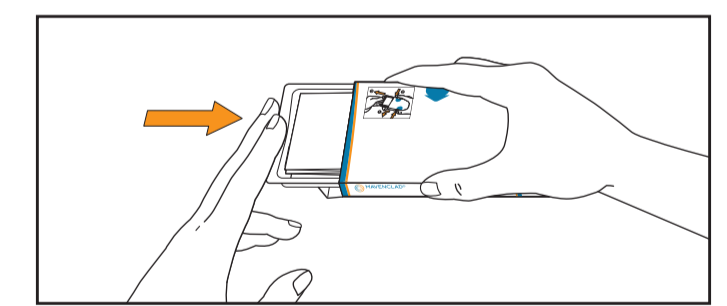
- 5** Raise the blister package by pushing your finger through the hole in the tray. Place your hand under the blister package and push 1 or 2 tablet(s) into your hand, according to your prescribed dosage.



- 6** Swallow the tablet(s) with water. Swallow the tablets whole, without chewing or allowing it to dissolve in your mouth. Limit contact with the skin. Avoid touching the nose, eyes and other parts of your body.



- 7** Wash your hands thoroughly with soap and water.



- 8** Push the tray back into the carton. Store below 25°C, in the original package in order to protect from moisture.

Keep the tablets in the blister until you take the next dose. Do not remove the tablets from the blister. Do not store the tablets in a different container.

GUIDE FOR TAKING MAVENCLAD 10 MG TABLETS

MAVENCLAD is packed in a reclosable, child-resistant carton package and must be kept out of the reach and sight of children. See below for a 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 instructions in the package leaflet.

Step-by-Step Guide for
MAVENCLAD® 10 mg
tablets
cladribine

MERCK

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

Dosage

1. You will be prescribed the correct number of tablets for each treatment week, based on your body weight, as shown in Table 2.
2. You will need one or more packages in order to provide the correct number of tablets.
3. When you receive the medicine, check that you have the correct number of tablets.
4. In the left column of table 2, find the row that matches your body weight (in kg), and then check the number of tablets that should be in the package(s) for the treatment week you will be starting.
5. If the number of tablets in the package(s) you received is different from the number shown for your weight in the table, talk to your doctor.
6. Note that for some weight ranges, the number of tablets may vary from one treatment week to the next.

Example: if you weigh 85 kg and are about to start treatment week 1, you will be given 8 tablets.

Table 2

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

Do not exceed the recommended dose.

How to take the medicine

Take the tablet(s) at about the same hour each day. Swallow them with water, without chewing. The tablets do not have to be taken at meal times. They can be taken with meals or between meals.

Read the guide for taking MAVENCLAD 10 mg tablets at the end of this leaflet regarding the handling of the child-resistant packages and how to take the tablets included in the package.

Important

- Ensure that your hands are dry before picking up the tablet(s).
- Push the tablet(s) through the blister and swallow immediately.
- Do not leave the tablet(s) exposed on surfaces, for example on a table, and do not handle the tablets longer than necessary.
- If a tablet was left on a surface or if a tablet breaks and fragments of it fall from the blister, wash the area thoroughly.
- Thoroughly wash your hands after taking the medicine.

- If you lose a tablet, consult with your doctor.

Duration of treatment

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.

Table 3 shows how many tablets (1 or 2 tablets) you have to take on each day.

If your daily dosage is 2 tablets, take them at the same time.

Example: if you have to take 8 tablets, you should take **2 tablets** on Day 1, Day 2 and Day 3, and **1 tablet** on Day 4 and Day 5.

Table 3

Total number of tablets per treatment week	Day 1	Day 2	Day 3	Day 4	Day 5
4	1	1	1	1	0
5	1	1	1	1	1
6	2	1	1	1	1
7	2	2	1	1	1
8	2	2	2	1	1
9	2	2	2	2	1
10	2	2	2	2	2

If you have accidentally taken a higher dose, 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 number of lymphocytes in your body may decline, resulting in lymphopenia (see section 4).

If you took an overdose, or if a child accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take MAVENCLAD

If you forgot a dose and you remember on the same day you were supposed to take it	If you forgot a dose and only remembered the following day
Take the forgotten dose on the same day.	Do not take the forgotten dose along with the next scheduled dose. Take the forgotten dose on the next day and extend the number of days in the current treatment week.

Example: If you forgot to take the Day 3 dose and do not remember it until Day 4, take the Day 3 dose on Day 4, and extend the total number of days in the treatment week by 1 day. If you forgot 2 consecutive doses (for example, both Day 3 and Day 4), take the forgotten doses on the next 2 days, and then extend the treatment week by 2 days.

Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions regarding use of the medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of MAVENCLAD may cause side effects in some users. Do not be alarmed by the list of side effects, you may not suffer from any of them.

Some side effects could be or could become serious

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

The most important side effect is a reduction in the number of white blood cells called lymphocytes (**lymphopenia**). This effect is very common and may be severe. Lymphopenia may increase the risk of getting infections. 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 be headache, burning sensation, tingling, numbness or itchiness of the skin in the affected area, general unwell feeling or fever in the early stages of the infection.

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

Liver problems (uncommon side effects - may affect up to 1 in 100 patients):

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 interrupted or stopped.

Other possible side effects

Common side effects - may affect up to 1 in 10 patients:

- cold sores (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 side effect - may affect up to 1 in 10,000 patients:

- tuberculosis

If you experience any side effect, if any side effect gets worse or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED

- **Avoid poisoning!** This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning.
- **Do not induce vomiting** unless explicitly instructed to do so by the doctor!
- **Do not use the medicine** after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- **Store below 25°C.** Store the medicine in the original package in order to protect from moisture.
- **Do not dispose of medicines** into the sewage system or household waste. Ask your pharmacist how to dispose of medicines that are not in use, in order to protect the environment.

6. ADDITIONAL INFORMATION

What MAVENCLAD contains

In addition to the active ingredient, the medicine also contains: hydroxypropylbetadex, sorbitol and magnesium stearate.

What MAVENCLAD looks like and the contents of the packages

MAVENCLAD tablets are white, round, biconvex, embossed with 'C' on one side and '10' on the other side. Each package contains 1, 4, 5, 6, 7 or 8 tablets in a blister, sealed in a cardboard wallet inside a child-resistant carton. Not all package sizes may be marketed.

Registration holder and importer's name and address: Merck Serono Ltd., 18 Hakishon St., Yavne 81220

Manufacturer's name and address: Merck Europe B.V., Amsterdam, The Netherlands

This leaflet was revised in May 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 159 78 35306 00

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