Info-Table - Version 03

IDENTIFICATION OF THE COMPONENT		
Material component code:	594207	
Local brand:	MAVENCLAD	
Strength(s):	10 mg	
TECHNICAL DATA		
Packaging site:	R-Pharm DEU	
Technical layout ref:	PIL_473x598mm, folded to 60x120mm_V04	
BARCODE		
Barcode type:	Laetus	
Alpha numeric content:	166	
Spotmark:	Yes	
Spotmark value:	Position: 55,5 mm; color: green	
TRACEABILITY (VERSIONS)		
Vx	Date	Designer
01	17.10.2022	Eugene Tyson
02	n/a	n/a
03	n/a	n/a

COLOURS			
Printed colour(s)		Technical information(s)	
	Cyan		Keyline
	Magenta		
	Yellow		
	Black		

MAVENCLAD® 10 mg
tablets
cladribine

594207

Package leaflet:
Information for the user

Package leaflet:
Information for the user

MAVENCLAD® 10 mg
tablets
cladribine

594207

Package leaflet:
Information for the user

MAVENCLAD® 10 mg
tablets
cladribine

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

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 substance 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**. MS 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:
  - 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.

Warnings and precautions

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. Symptoms of infections can include: fever, aching, painful muscles, headache, generally feeling unwell or yellowing of the eyes. 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 4), 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.

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.

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.

Other medicines and MAVENCLAD

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. 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 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.
- 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 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. **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 breast-feeding. If your doctor believes that MAVENCLAD is essential for you, your doctor will advise you to stop breast-feeding.

Driving and using machines

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

MAVENCLAD contains sorbitol

This medicine contains 64 mg sorbitol in each tablet.

3. How to take MAVENCLAD

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 (see Table 1)**.

Example: if you start your treatment mid April, you take your tablets as shown.

Table 1

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 as shown in Table 2.
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. In the left column of the table below find the row that fits your body weight (in kg), and then check the number of tablets that should be in the pack(s) for the treatment week you will be starting.
5. If the number of tablets in your pack(s) is different from the number shown for your weight in the table below, speak 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 treatment course		Year 2 treatment course	
	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 to less than 50 kg	4	4	4	4
50 to less than 60 kg	5	5	5	5
60 to less than 70 kg	6	6	6	6
70 to less than 80 kg	7	7	7	7
80 to less than 90 kg	8	7	8	7
90 to less than 100 kg	9	8	9	8
100 to less than 110 kg	10	9	10	9
110 kg and above	10	10	10	10

How to take your medicine

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

Read the 'Step-by-Step Guide' at the end of this package leaflet on how to handle the child- resistant package and how to take the tablets included in the pack.

Important

- Ensure your hands are dry before picking up your tablet(s).
- Push your tablet(s) through the blister and swallow immediately.
- Do not leave your tablet(s) exposed on surfaces, for example on a table, or handle the tablet longer than necessary.
- 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.

Duration of a treatment week

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 dose is 2 tablets, take them at the same time.

Example: if you have to take 8 tablets, you would take **2 tablets** on Day 1, Day 2, Day 3, then **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

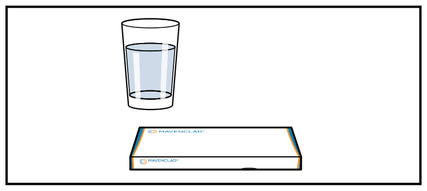
If you take more MAVENCLAD than you should

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.

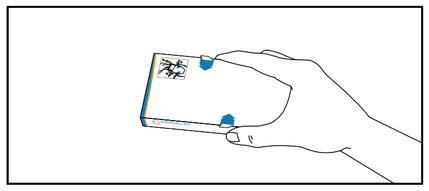
There is limited experience with overdose of MAVENCLAD. It is known that the more medicine you take the less lymphocytes may be present in your body, resulting in lymphopenia (see section 4).

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

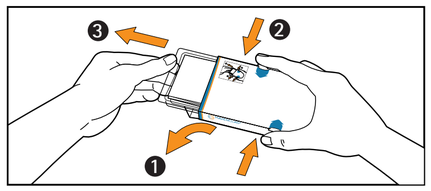
MAVENCLAD is packed in a reclosable, child-resistant carton and must be kept out of the sight and reach of children. See below for a step-by-step guide on how to handle the package and to take the MAVENCLAD tablets. Make sure you know how many tablets are contained in the package. See package leaflet for guidance.



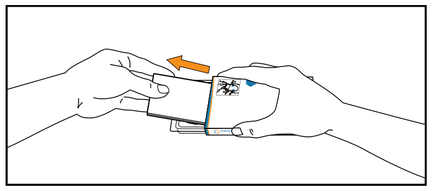
1. Have a glass of water ready and make sure your hands are clean and dry before taking the tablet(s).



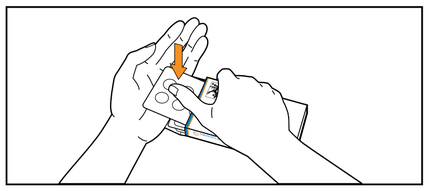
2. Pick up carton with the opening instructions facing up.



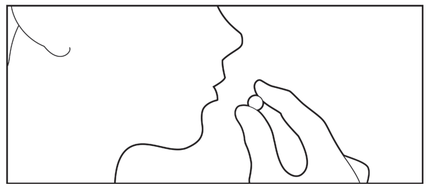
3. (1) Open the flap on the left end.
   (2) Push in the hooks on the sides of the carton simultaneously with your index finger and thumb, and keep hooks pushed.
   (3) Pull the tray out until it stops. **Caution:** Do not remove the tray from the carton.



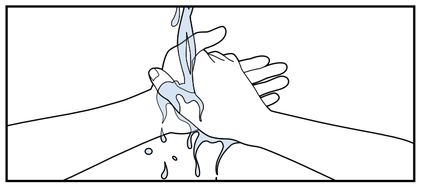
4. Take the leaflet from the tray. Make sure you have read all of the package leaflet including the step-by-step guide and keep it in a safe place.



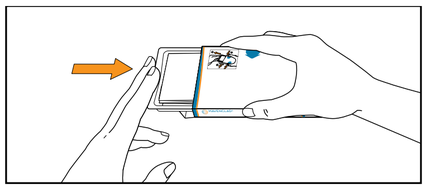
5. Raise the blister pack by pushing your finger through the hole in the tray. Place your hand under the blister pack and push 1 or 2 tablet(s) into your hand, according to your prescribed dose.



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.

MAVENCLAD® 10 mg
tablets
cladribine

Info-Table - Version 03

IDENTIFICATION OF THE COMPONENT		
Material component code:	594207	
Local brand:	MAVENCLAD	
Strength(s):	10 mg	
TECHNICAL DATA		
Packaging site:	R-Pharm DEU	
Technical layout ref:	PIL_473x598mm, folded to 60x120mm_V04	
BARCODE		
Barcode type:	Laetus	
Alpha numeric content:	166	
Spotmark:	Yes	
Spotmark value:	Position: 55,5 mm; color: green	
TRACEABILITY (VERSIONS)		
Vx	Date	Designer
01	17.10.2022	Eugene Tyson
02	n/a	n/a
03	n/a	n/a

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.

Example: If you forget 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 miss 2 consecutive doses (for example both Day 3 and Day 4 doses), take the missed doses for the next 2 days, and then extend the treatment week by 2 days.

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

4. Possible 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

The most important side effect is a reduction in the number of white blood cells called lymphocytes (**lymphopenia**), which is very common (may affect more than 1 in 10 people) 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 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 side effect - may affect up to 1 in 10,000 people

- tuberculosis

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store MAVENCLAD

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 label 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.

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.

6. Contents of the pack and other information What MAVENCLAD contains

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

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.

Marketing Authorisation Holder

Merck Europe B.V.
Gustav Mahlerplein 102
1082 MA Amsterdam
The Netherlands

Manufacturer

NerPharMa S.R.L.
Viale Pasteur, 10
20014 Nerviano (MI)
Italy

Releasing Site

R-Pharm Germany GmbH
Heinrich-Mack-Strasse
35 89257 Illertissen Germany

This leaflet was last revised in {04/2022}.

This is a medicine

- A medicine is a product which affects your health and its consumption, contrary to instructions, is dangerous for you.
- Closely follow your doctor's prescription, the method of use and the instructions of the pharmacist who sold the product
- Your doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not interrupt the period of treatment prescribed without your doctor's permission.
- Do not repeat the same prescription without consulting your doctor.

Keep medicines out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists