Patient and Caregiver Guide

Important things to remember about your MAYZENT® (siponimod)▼ treatment

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

If you have any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet.

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Contents

Introduction

This guide contains important information about MAYZENT® (siponimod) dosing, side effects and their potential risks, including guidance on pregnancy.

Before you start your treatment, read this guide and the leaflet, which is inside your MAYZENT® medication package, thoroughly. The package leaflet contains additional information on the potential side effects.

Save this guide together with the package leaflet in case you need to refer to it during treatment. Tell any doctor you see that you are being treated with MAYZENT®.

Use the medication schedule as shown on page 11 when you start treatment with MAYZENT®.

If you get any side effects, it's important that you report these to your doctor. This includes any possible side effects not listed in the package leaflet.

What is MS (multiple sclerosis)

Multiple sclerosis (MS) is a neurological disease that affects the brain and spinal cord.

In patients with MS, the body's own immune cells mistakenly attack nerve cells in the brain and spinal cord. Over time, these nerve cells are lost, leading to increasing disability.

For some people, symptoms gradually worsen from the beginning of the disease following a progressive pattern (progressive MS), but for others they come and go (relapsing-remitting MS).

Within ten years more than 50% of patients with relapsing-remitting MS will eventually develop sustained worsening of symptoms, independent of relapses, which results in disability. This is called secondary progressive multiple sclerosis (SPMS).

What MAYZENT® is and how it works

MAYZENT® contains an active substance called siponimod, which is a sphingosine-1-phosphate (S1P) receptor modulator.

It is used to treat adults with active (SPMS) disease.

MAYZENT® works by reducing the ability of the body's own immune cells (white blood cells) from travelling into the brain and spinal cord and attacking nerve cells.

During the EXPAND trial (study reference number A2304) which is a large phase 3 trial, it was found that MAYZENT® could slow down the effects of disease activity, such as worsening disability, brain lesions and relapses.

Before you take MAYZENT®

Testing and getting ready for treatment

Before you start treatment, your doctor will perform a blood or saliva test (buccal swab) to determine how well MAYZENT® is broken down in your body in order to determine the appropriate dose for you. In certain cases, the test may show that MAYZENT® is not the right treatment option for you.

Your blood may also be tested to check your white blood cell count and your liver function, if these have not been measured recently (within the last 6 months).

Your doctor will perform a skin examination to check for any abnormal growth or change on your skin.

If you have not previously had chickenpox or if you can't remember if you've had it, please tell your doctor. If you are not protected against this virus, you will need a vaccination before you start treatment with MAYZENT®. If this is the case, your doctor will delay the start of treatment with MAYZENT® until one month after the full course of vaccination is completed.

Before you take MAYZENT®

Testing and getting ready for treatment

Tell your doctor if you have, or have previously had, visual disturbances or vision problems in the centre of the eye (macular oedema), inflammation or infection of the eye (uveitis), or if you have high blood sugar levels (diabetes). If you have a history of any of these conditions, your doctor may suggest you have an eye examination before you can start treatment with MAYZENT®.

If you have an underlying heart problem or are taking medication that can cause your heart rate to slow down, your doctor will take your blood pressure and do a test called an electrocardiogram (ECG) to check the rhythm of your heart before starting treatment with MAYZENT®. Your doctor may also refer you to a heart specialist (cardiologist) for advice on how you should start treatment with MAYZENT®, and how you should be monitored.

Before you take MAYZENT®

Other medication

Tell your doctor if you are taking any medications that alter your immune system or medication that can cause your heart rate to slow down.

You may have to change or temporarily stop your usual medication for a short period of time. This is because the effects of these medicines can be increased when used together with MAYZENT®.

MAYZENT® is not recommended if you have certain cardiac disease or are taking other medicines known to decrease heart rate.

The first time you take MAYZENT®

Slow heart rate

At the beginning of treatment, MAYZENT® may cause the heart rate to slow down temporarily, which can make you feel dizzy or lightheaded. For most patients, the heart rate returns to normal within 10 days.

- You should not drive or use machines during the first day of treatment initiation with MAYZENT®, as you may feel dizzy.

Inform your doctor immediately if you experience dizziness, vertigo, nausea, fatigue or palpitations after your first dose or during the first six days of treatment.

If you have underlying heart problems, your doctor may ask you to stay at the doctor's office or hospital for at least 6 hours after taking the first dose so that your blood pressure and pulse can be checked regularly and an electrocardiogram (ECG) can be performed to check the rhythm of your heart. If your ECG shows any abnormalities during this time, you may need to be monitored for a longer period of time (possibly overnight) until these have resolved.

Starting treatment with MAYZENT®

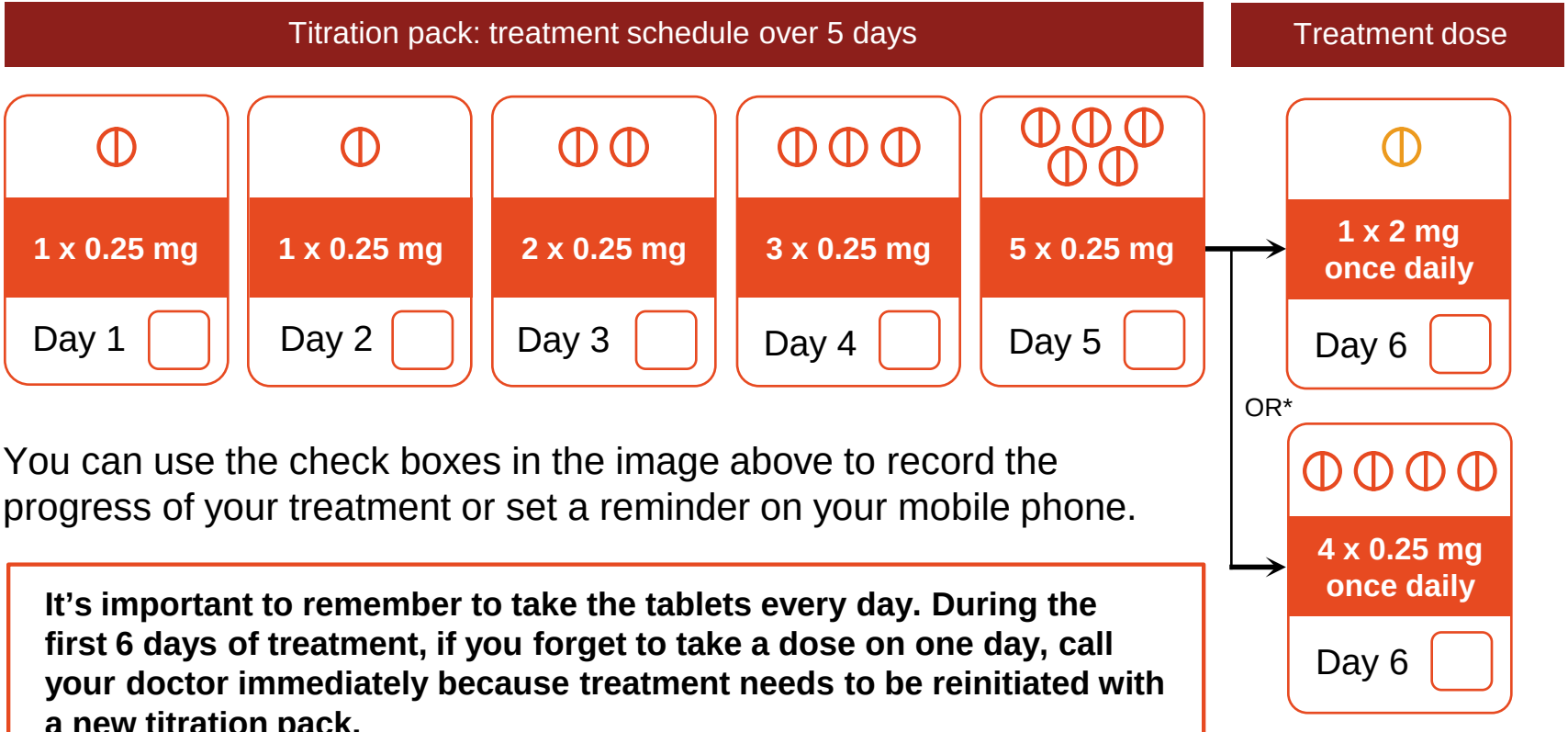
Your treatment will start with a five-day titration pack.

You will start with a dose of 0.25 mg (1 tablet) on days 1 and 2, followed by 0.5 mg on Day 3 (two tablets), 0.75 mg on Day 4 (three tablets) and 1.25 mg on Day 5 (five tablets), to reach the recommended treatment dose (either 2 mg or 1 mg depending on the results of your blood or saliva test performed before the start of treatment) from Day 6 onward.

Gradually increasing the dose of MAYZENT® over a period of time helps to reduce the temporary effect on your heart at the beginning of your treatment.

Take your MAYZENT® tablets once a day. Ideally, this should be at the same time each day. For the first 6 days, it is recommended that you take your tablets in the morning. Take your tablets with or without food.

MAYZENT® medication schedule



You can use the check boxes in the image above to record the progress of your treatment or set a reminder on your mobile phone.

It's important to remember to take the tablets every day. During the first 6 days of treatment, if you forget to take a dose on one day, call your doctor immediately because treatment needs to be reinitiated with a new titration pack.

Side effects and important risks: visual symptoms

MAYZENT® may cause swelling at the back of the eye. This condition is known as macular oedema and is reversible if caught early.

Possible symptoms may include:

- Blurry or wavy vision in the centre of the eye
- Vision loss
- Colours appearing faded or changed

Your doctor may request an eye examination before you start treatment with MAYZENT® and during treatment.

Tell your doctor immediately about any changes in your vision, during treatment and up to one month after you have stopped treatment with MAYZENT®.

Side effects and important risks: infections

Because MAYZENT® affects the immune system, you may be more vulnerable to infections. If you have any of the following symptoms during treatment, and up to one month after stopping treatment, let your doctor know straight away.

Possible symptoms of a serious infection (e.g. meningitis) are:

- Fever
- Flu-like symptoms
- Headache accompanied by a stiff neck
- Nausea and/or confusion

If you believe your MS is getting worse much more quickly (e.g. weakness, seizures or visual changes) or if you notice new or unusual symptoms (e.g. headache, forgetfulness, changes in mood or behaviour), talk to your doctor as soon as possible. These may be due to a very rare brain infection called progressive multifocal leukoencephalopathy (PML) which can occur in patients taking medicines like MAYZENT® and other medicines used for treating MS.

Side effects and important risks: liver function

MAYZENT® can cause abnormal results in liver function tests.

Contact your doctor if you notice symptoms such as:

- Unexplained nausea
- Vomiting
- Abdominal pain
- Fatigue
- Rash
- Yellowing of the eyes or the skin
- Dark urine

These symptoms could be signs of liver problems and you should contact your doctor who will perform a liver function test.

Side effects and important risks: malignancies

Whilst you are treated with MAYZENT®, there is an increased risk of skin malignancies.

You should limit your exposure to the sun and UV rays and protect yourself by wearing appropriate clothing and regularly applying sunscreen with a high degree of UV protection.

You should not receive phototherapy with UV-B radiation or PUVA-photochemotherapy (treatments used for some skin conditions) whilst you are being treated with MAYZENT®.

Inform your doctor immediately if you notice any skin nodules (e.g. shiny, pearly nodules), patches or open sores that do not heal within weeks. Symptoms of skin cancer may include abnormal growth or changes of skin tissue (e.g., unusual moles) with a change in colour, shape or size over time

Your doctor will carry out regular skin examinations during your treatment with Mayzent.

Side effects and important risks: Neurological and psychiatric symptoms/signs

Inform your doctor of any unexpected neurological or psychiatric symptoms/signs (such as sudden onset of severe headache, confusion, seizures and vision changes) or worsening of neurological condition.

Female patients

You must avoid becoming pregnant while taking MAYZENT® because there is a risk of harm to the unborn baby. You will need to have a negative pregnancy test before starting treatment and at regular intervals.

Talk with your doctor about reliable methods of birth control that you should use during MAYZENT® treatment and for at least 10 days after you stop treatment.

If you get pregnant during treatment, or within 10 days following discontinuation of treatment with MAYZENT®, let your doctor know immediately.

If you are a female of childbearing potential, you will also receive a Pregnancy Reminder Card.

MAYZENT® must not be used if you are pregnant or if you are a women of childbearing potential who is not using effective contraception.

Forgetting to take your tablets and stopping the medication

DO NOT RESTART TREATMENT WITH YOUR REGULAR DOSE IF:

- You forget to take your treatment on any day during the first 6 days of your treatment
- You forget or had to stop your treatment for 4 or more days in a row when on your prescribed treatment dose

If either of the above situations occurs, treatment will need to be restarted with a new titration pack, including first dose monitoring in patients with certain heart problems. Contact your doctor to arrange restarting your treatment.

Stopping treatment with MAYZENT®

After stopping treatment with MAYZENT®, inform your doctor immediately if you believe disease symptoms are getting worse (e.g. weakness or visual changes) or if you notice any new symptoms.

Contact details of your doctor

Name .....

Address .....

.....

Telephone no .....

Suspected Adverse Drug Reactions (side effects) and medication errors may be reported using the Medicines Authority ADR reporting form, which is available online at http://www.medicinesauthority.gov.mt/adrportal and sent by post or email to;

P: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann. SGN 3000.

E: postlicensing.medicinesauthority@gov.mt.

Healthcare Professionals may also report any adverse events associated with the use of **Mayzent** to Novartis Pharma Services Inc., Representative Office, Malta, by phone on +356 21222872, online on www.report.novartis.com or by e-mail at drug_safety.malta@novartis.com.

Marketing Authorization Holder: Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, Dublin 4, Ireland.

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