MAYZENT®
0.25 mg, 1 mg and 2 mg
film-coated tablets (siponimod)

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

Healthcare Professionals Checklist

Important points to remember before, during, and after treatment with MAYZENT®

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Contents

Adverse drug reactions

Adverse drug reactions should be reported to Novartis Patient Safety; online at report.novartis.com, email to patientsafety.aunz@novartis.com or by telephone on 1800 671 203. Adverse drug reactions can also be reported to the TGA at tga.gov.au/reporting-problems.

Introduction

This checklist provides essential information on important risks associated with MAYZENT® treatment and the activities required to minimise these risks.

A patient and caregiver guide, and a pregnancy reminder card for women of childbearing potential have also been developed as part of the risk minimisation plan, and may be used to inform your discussion with the patient.

It is advised that this checklist is read alongside the approved Product Information for MAYZENT®.

Patient selection

Therapeutic indication[1]

MAYZENT® is indicated for the treatment of adult patients with secondary progressive multiple sclerosis (SPMS).

Considerations for patient selection[2]

Contraindications[1]

MAYZENT® is contradicted in patients:

- With known hypersensitivity to siponimod or any of the excipients
- With a CYP2C9*3*3 genotype
- Who in the last 6 months had myocardial infarction (MI), unstable angina pectoris, stroke/transient ischaemic attack (TIA), decompensated heart failure (requiring inpatient treatment), or New York Heart Association Class III/IV heart failure
- With second-degree Mobitz type II atrioventricular (AV) block, third-degree AV block, sino-atrial heart block or sick-sinus syndrome, if they do not have a pacemaker

Not recommended

Treatment with MAYZENT® is not recommended in the following patients:[2]

- History of symptomatic bradycardia or recurrent syncope
- Uncontrolled hypertension
- Severe untreated sleep apnoea
- QTc prolongation >500 msec
- Taking the following medications at treatment initiation
  - class Ia (quinidine, procainamide) or Class III (amiodarone, sotalol) antiarrhythmic drugs
  - calcium channel blockers (e.g. verapamil, diltiazem)
  - other medications (e.g. ivabradine or digoxin) which are known to decrease the heart rate

Consider MAYZENT® only after performing risk/benefit analysis and consulting a cardiologist to determine the most appropriate monitoring strategy and possibility of switch to a non-heart rate lowering drug before initiation of treatment.

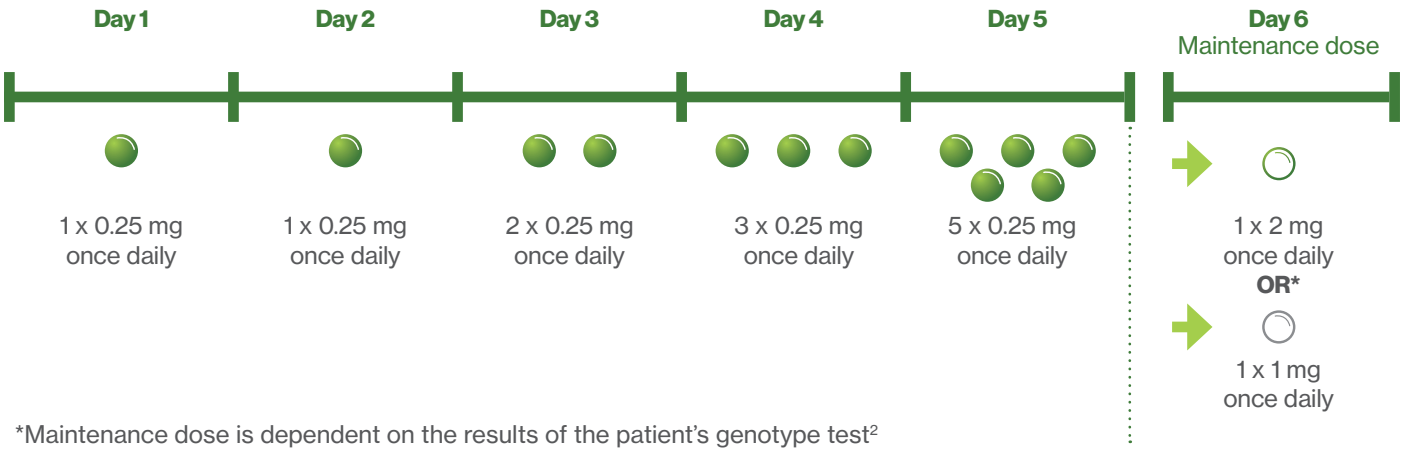
Prior to initiating treatment

The checklists and schematic that follow are intended to assist in the management of patients on MAYZENT®. Key steps and considerations while initiating, continuing or discontinuing treatment are provided.

- [ ] Ensure to select patients according to contraindications and recommendations for non-treatment
- [ ] Identify the CYP2C9 genotype of the patient to determine the correct MAYZENT® maintenance dose. Genotyping can be conducted with a DNA sample obtained via a blood test as tested and confirmed by NATA/RCPA accredited Pathology Lab. *A testing program is in place with a local Australian provider at no cost to the patient. Pathology requests can be obtained from the provider. For further information, contact Novartis on 1800 671 203. Results of the test will be available within 10 working days following the collection of the blood sample.*
  - Patients with CYP2C9*3*3 should not receive MAYZENT®
  - Patients with CYP2C9*1*3 or CYP2C9*2*3 should receive the 1 mg maintenance dose (following the titration schedule)
  - All other patients (CYP2C9 *1*1, *1*2, *2*2) can receive 2 mg (following the titration schedule)
- [ ] Establish whether the patient requires first-dose observation. As a precautionary measure, patients with sinus bradycardia (heart rate (HR) <55 bpm), first or second-degree (Mobitz type I) atrioventricular block (AV block), or a history more than 6 months ago of myocardial infarction or heart failure should be observed for a period of 6 hours after the first dose of MAYZENT® for signs and symptoms of bradycardia[1]
- [ ] Caution should be exercised in elderly patients with multiple comorbidities, or advanced disease/disability (due to possible increased risks of events such as infections or bradyarrhythmia during treatment initiation)[2]
- [ ] Check availability of a recent complete blood count (CBC) and liver function tests (i.e. within 6 months or after discontinuation of prior therapy)[2]
- [ ] Do not initiate treatment with MAYZENT® in patients with severe active infection until infection is resolved[2]
- [ ] Take caution if patients are concomitantly treated with anti-neoplastic, immunomodulatory or immunosuppressive therapies (including corticosteroids) due to the risk of additive immune system effects
- [ ] Instruct patients to report signs and symptoms of infections immediately during treatment
- [ ] Check varicella zoster virus (VZV) antibody status in patients without a healthcare professional-confirmed history of varicella or without documentation of a full course of vaccination against VZV. If tested negative, vaccination is recommended and treatment with MAYZENT® should be postponed for 1 month to allow the full effect of vaccination to occur[2]
- [ ] Counsel patients to report visual disturbances at any time while on treatment
- [ ] Arrange an ophthalmologic evaluation prior to initiating therapy in patients with diabetes mellitus, uveitis or underlying/co-existing retinal disease[1]
- [ ] Use with caution in patients with asthma. Asthma status should be reviewed and medications (including preventers) should be optimised before MAYZENT® treatment is considered[1]
- [ ] Perform skin examination and be vigilant for skin malignancies
- [ ] A negative pregnancy test result is required prior to initiation of treatment in women of childbearing potential
- [ ] Do not initiate treatment in patients with macular oedema until resolution
- [ ] Counsel women of childbearing potential about the serious risks of MAYZENT® to the foetus and the need to use effective contraception during treatment and for at least 10 days following discontinuation of treatment, facilitated by the pregnancy-specific patient reminder card[2]
- [ ] **Provide patients with a Patient and Caregiver Guide**
- [ ] **Inform patients of the importance of reporting adverse events to either their doctor or directly to Novartis**
- [ ] **Women of childbearing potential should also be provided with the Pregnancy Reminder Card**
- [ ] **Be familiar with the MAYZENT® Product Information**

Treatment initiation schedule

Initiation of treatment with MAYZENT® results in a transient decrease in heart rate. For this reason, a 5-day up-titration scheme is required before a daily maintenance dose of 2 mg once daily can be achieved from Day 6 onwards (see figure). In patients with a CYP2C9*1*3 or CYP2C9*2*3 genotype, the recommended maintenance dose is 1 mg once daily (starting on Day 6). Titration and maintenance doses can be taken with or without food.[2]



*Maintenance dose is dependent on the results of the patient's genotype test[2]

Important information[2]

If a dose is missed on one day during the first 6 days of treatment, repeat the titration schedule with a new titration pack.

Similarly, if treatment (maintenance dose) is interrupted for 4 or more consecutive days, treatment must be re-initiated with a new titration pack.

Treatment initiation: Recommendations for patients with certain pre-existing cardiac conditions

MAYZENT® causes transient heart rate reduction and may cause indirect AV conduction delays following initiation of treatment. Treatment initiation with a titration phase is usually well tolerated in most patients.[2]

Patients with:

- sinus bradycardia (heart rate <55 bpm),
- first- or second-degree (Mobitz type I) AV block **or**
- a history of myocardial infarction (MI) or heart failure if not contraindicated*

should be observed for signs and symptoms of bradycardia for a period of 6 hours after the first dose of MAYZENT®. Measurement of hourly vitals during this period and ECG measurements both pre- and 6 hours post-dose are recommended. If necessary, the decrease in heart rate induced by MAYZENT® can be reversed by parenteral doses of atropine or isoprenaline.

*Patients who have experienced an MI or heart failure within the past 6 months should not be treated with MAYZENT®.

☐ **Perform baseline ECG and BP measurement**

☐ **Patient to take first titration dose**

☐ **Monitor patients with cardiovascular risk for a minimum of 6 hours, with hourly pulse and BP checks**
ECG measurements prior to dosing, and at the end of observation period are recommended

☐ **Did the patient develop post-dose bradyarrhythmia or conduction-related symptoms?**

YES

- **Initiate appropriate management**
- **Continue to observe until the findings have resolved**

NO

☐ **Did the patient require pharmacological intervention at any time during the monitoring period?**

YES

- **Monitor overnight in a medical facility**
- **Monitoring as for the first dose, should be repeated after the second dose of MAYZENT®**

NO

At the end of the 6-hour monitoring period, did ECG show:

☐ New-onset second-degree or higher AV block?

☐ QTc ≥500 msec?

YES

Initiate appropriate management

- **Continue to observe until the findings have resolved**
- **If pharmacological intervention is required, continue monitoring overnight and repeat 6-hour monitoring**

NO

☐ **At the end of the 6-hour monitoring period, is the HR the lowest since the first dose was administered?**

YES

Extend monitoring by at least 2 hours and until the heart rate increases

NO

First-dose monitoring is complete

The above first-dose monitoring procedure should be repeated in these patients if:

- A titration dose is missed for one day in the first 6 days
- Treatment is interrupted for >4 consecutive days during the maintenance phase

During treatment

- [ ] An ophthalmological evaluation 3–4 months after treatment initiation is recommended[1,2]
  - Conduct periodic ophthalmologic evaluations in patients with diabetes mellitus, uveitis, or a history of retinal disorders
  - Counsel patients to report any visual disturbance during treatment
- [ ] Assessments of complete blood count are recommended 3–4 months following treatment initiation, and at least yearly thereafter, as well as in case(s) of signs of infection
  - If absolute lymphocyte counts <0.2 x 10^9/L, reduce MAYZENT® dose to 1 mg
  - If absolute lymphocyte counts <0.2 x 10^9/L in a patient already receiving MAYZENT® 1 mg, temporarily stop treatment with siponimod until levels reach 0.6 x 10^9/L. Re-initiation with MAYZENT® may then be considered
- [ ] Monitor patients carefully for signs and symptoms of infections:
  - Prompt diagnostic evaluation should be performed in patients with symptoms and signs consistent with encephalitis, meningitis or meningoencephalitis. MAYZENT® treatment should be suspended until such infections are excluded. Appropriate treatment of infection, if diagnosed, should be initiated
  - Cases of herpes viral infection (including cases of meningitis or meningoencephalitis caused by varicella zoster viruses) have occurred with MAYZENT® at any time during treatment
  - Cases of cryptococcal meningitis (CM) have been reported for MAYZENT®
  - Cases of progressive multifocal leukoencephalopathy (PML) have been reported for S1P receptor modulators, including MAYZENT®, and other therapies for MS. Healthcare professionals should be vigilant for clinical symptoms (e.g., weakness, visual changes, new/worsening symptoms of MS) or MRI findings suggestive of PML. If PML is suspected, treatment should be suspended until PML has been excluded. If PML is confirmed, treatment with MAYZENT® should be discontinued
- [ ] Exercise caution when administering concomitant treatment with anti-neoplastic, immune-modulating or immunosuppressive therapies (including corticosteroids) due to the risk of additive immune system effects[2]
- [ ] Be vigilant for skin malignancies while on treatment with MAYZENT®
  - Perform skin examination every 6 to 12 months taking into consideration clinical judgement
  - Careful skin examinations should be maintained with longer treatment duration. Patients should be referred to a dermatologist if suspicious lesions are detected
  - Patients should not receive concomitant phototherapy with UV-B radiation or PUVA-photochemotherapy
- [ ] Should a patient develop any unexpected neurological or psychiatric symptoms/signs or accelerated neurological deterioration, promptly schedule a complete physical and neurological examination and consider an MRI
- [ ] If patients develop symptoms suggestive of hepatic dysfunction request a liver enzyme check. Discontinue treatment if significant liver injury is confirmed
- [ ] Counsel women of childbearing potential regularly about the serious risks of MAYZENT® to the foetus[2]
- [ ] Discontinue treatment if a patient becomes pregnant or is planning to become pregnant[2]
  - MAYZENT® should be stopped at least 10 days before a pregnancy is planned. When stopping MAYZENT® therapy, the possible return of disease activity should be considered
  - Counsel the patient in case of inadvertent pregnancy. If a woman becomes pregnant whilst on treatment, they should be advised of potential serious risks to the foetus and an ultrasound examination should be performed
- [ ] Should a pregnancy occur during treatment with MAYZENT®, regardless of it being associated with an adverse outcome, please report it to Novartis by email to patientsafety.aunz@novartis.com or by telephone on 1800 671 203

After discontinuation

- [ ] After discontinuation, MAYZENT® remains in the blood for up to 10 days[2]
  - Exercise caution when starting other therapies during this time due to risk of additive effects
- [ ] Repeat titration schedule with a new titration pack if treatment was discontinued by mistake and:
  - A titration dose is missed on any day during the first 6 days

    OR
  - Treatment is interrupted for ≥4 consecutive days during the maintenance phase
  - First-dose monitoring in specific patients (patients with sinus bradycardia (HR <55 bpm), first- or second-degree AV block, or a history of MI or heart failure) will also need to be repeated
- [ ] If MAYZENT® is discontinued, the possibility of recurrence of high disease activity should be considered and the patient monitored accordingly
- [ ] Instruct patients to report signs and symptoms of infection immediately and for up to one month after treatment discontinuation[2]
- [ ] Counsel female patients that effective contraception is needed for at least 10 days after discontinuation.[2] Should a pregnancy occur within 10 days after stopping MAYZENT®, regardless of it being associated with an adverse event or not, please report it to Novartis by email patientsafety.aunz@novartis.com or by telephone on 1800 671 203

  Novartis has put in place a Pregnancy outcomes Intensive Monitoring (PRIM) program, which is a registry based on enhanced follow-up mechanisms to collect information about pregnancy in patients exposed to MAYZENT® immediately before or during pregnancy and on infant outcomes 12 months post-delivery

Further information

For more detailed guidance on MAYZENT®, please refer to the MAYZENT® Product Information.

PBS Information: Authority Required (STREAMLINED).
For use in patients with multiple sclerosis who meet certain criteria.
Refer to PBS Schedule for full Authority Required information.

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PMAY0625

For healthcare professionals only.
Please review full Product Information before prescribing.
Scan QR code for full MAYZENT Product Information.

Alternatively, please contact med info at 1 800 671 203 or visit www.novartis.com.au/products/healthcare-professionals/products to access the full Product Information.

References: 1. MAYZENT® approved Product Information. Novartis Pharmaceuticals Australia Pty Ltd. **2.** MAYZENT® Risk Management Plan. Europe. Healthcare professionals' checklist. September 2024.

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