Janssen Neuroscience

PHARMACEUTICAL COMPANIES OF Johnson&Johnson

PONVORY®▼(ponesimod)

PRESCRIBER'S CHECKLIST

Important points to remember before, during, and after treatment

▼This medicinal product is subject to additional monitoring.
This will allow quick identification of new safety information.
You can help by reporting any side effects you may get.
For more information, see the section on reporting of side effects.

Suspected Adverse Drug Reactions (side effects) or 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 Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000
E: postlicensing.medicinesauthority@gov.mt

Alternatively, to report Suspected Adverse Drug Reactions, contact Janssen's Local Representative, AM Mangion, on the following:
Phone (24/7): 00356 2397 6333
Email: pv@ammangion.com
Address: AM Mangion Ltd, Mangion Building, N/S Off Valletta Road, Luqa, LQA 6000, MALTA

For further information please contact Janssen's Local Representative, AM Mangion Medical Information by using one of the following methods:
Phone: 00356 2397 6888
Email: medicalaffairs@ammangion.com
Website: www.ammangion.com.mt

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The additional Risk Minimization Materials are a condition of the Marketing Authorisation.

Contents

Introduction to the Prescriber's checklist

This guide provides essential information on the most important identified and potential risks associated with Ponvory and the activities required to minimise these risks (as defined within the Ponvory Risk Minimisation Plan).

This checklist does not contain all of the information related to the adverse drug reaction profile of Ponvory, or the relevant prescribing information. The prescriber's checklist should therefore be read in conjunction with the Ponvory Summary of Product Characteristics (SmPC).

A patient/caregiver guide and a pregnancy-specific patient reminder card have also been developed as part of the risk minimisation plan and should be used to inform your discussion with the patient.

Therapeutic indication:

Ponvory is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features.

Further information:

For more detailed guidance on Ponvory, please refer to the SmPC included in this educational material or contact Janssen's Local Representative, AM Mangion Medical Information by using one of the following methods:
Phone: 00356 2397 6888
Email: medicalaffairs@ammangion.com
Website: www.ammangion.com.mt

Ponvory® (ponesimod) Prescriber's checklist

This checklist is intended to assist in the management of patients being treated with Ponvory. Important points to remember before, during, and after treatment are included.

Patient identification:
Name:
Date of birth:

Prescriber/Treating Healthcare Professional details:
Name:
Signature:
Date:

Prior to initiating treatment

Ponvory is contraindicated in patients who have:

- Hypersensitivity to the active substance or to any of the excipients
- An immunodeficient state
- Experienced myocardial infarction, unstable angina, stroke, transient ischaemic attack (TIA), decompensated heart failure requiring hospitalisation, or New York Heart Association (NYHA) Class III/IV heart failure in the previous 6 months
- Presence of Mobitz type II second-degree atrioventricular (AV) block, third-degree AV block, or sick sinus syndrome, unless the patient has a functioning pacemaker
- Severe active infections or active chronic infections
- Active malignancies
- Moderate or severe hepatic impairment (Child-Pugh Class B and C respectively)
- Become pregnant and in women of childbearing potential not using effective contraception

Ponvory is not recommended in the following patients:

- Patients with unstable ischemic heart disease, cardiac decompensated failure occurring more than 6 months prior to treatment initiation, history of cardiac arrest, cerebrovascular disease (TIA, stroke occurring more than 6 months prior to treatment initiation), and uncontrolled hypertension, since significant bradycardia may be poorly tolerated in these patients, treatment is not recommended
- Ponvory has not been studied in children and adolescents, therefore it is not recommended for use in children and adolescents aged less than 18 years

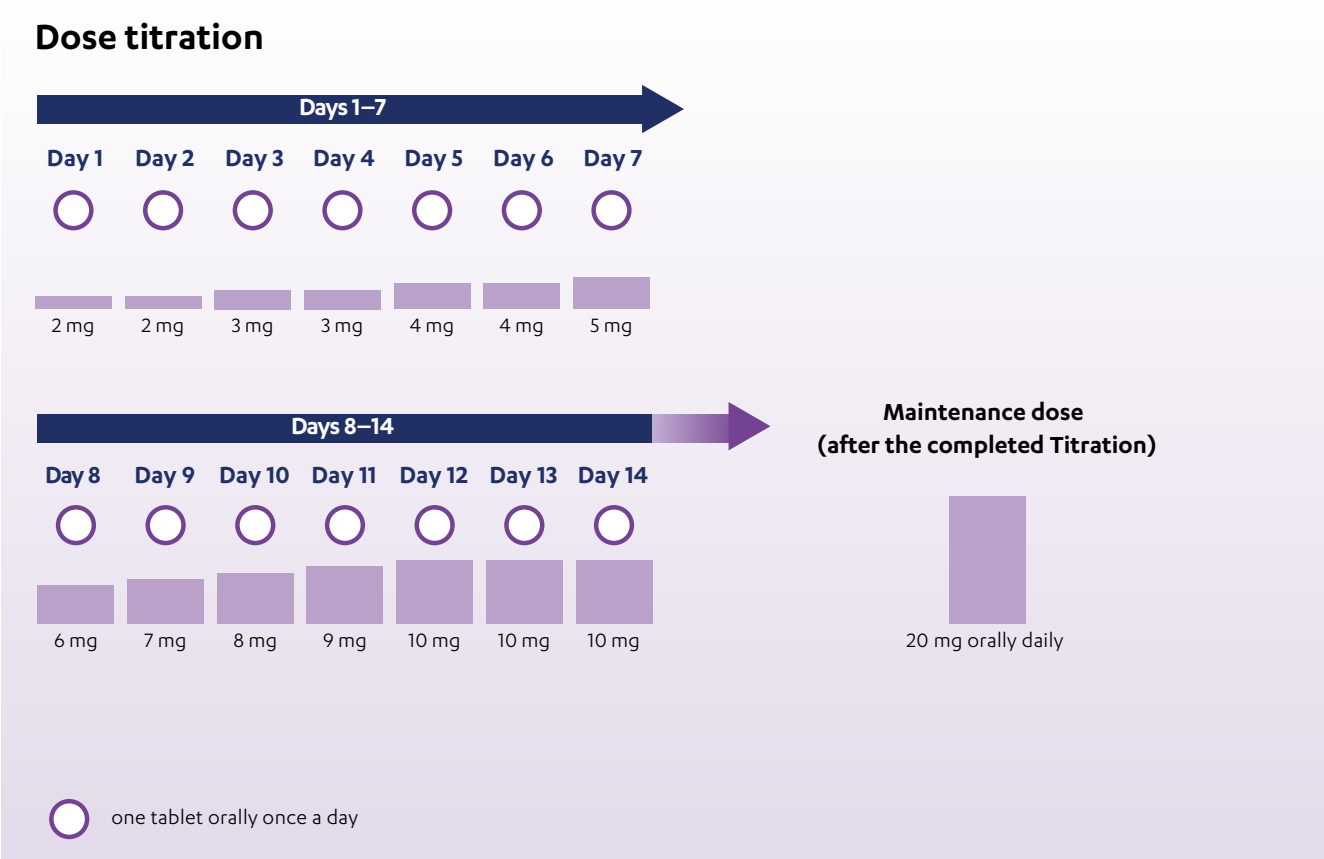
Mandatory requirements before initiating treatment

☐	Perform an electrocardiogram (ECG) to determine whether any pre-existing cardiac abnormalities are present • In patients with certain pre-existing conditions, first-dose monitoring is recommended (see "first-dose monitoring" section)
☐	Consult a cardiologist before initiation of Ponvory in the following patients to determine overall benefit-risk and the most appropriate monitoring strategy: • Patients with significant QT prolongation (QTc >500 ms) or who are already being treated with QT-prolonging medicinal products with known arrhythmogenic properties (risk of torsades de pointes) • Patients with atrial flutter/fibrillation or arrhythmias treated with Class Ia (e.g. quinidine, procainamide) or Class III (e.g. amiodarone, sotalol) anti-arrhythmic medicinal products • Patients with unstable ischaemic heart disease, cardiac decompensated failure occurring more than 6 months prior to treatment initiation, history of cardiac arrest, cerebrovascular disease (TIA, stroke occurring more than 6 months prior to treatment initiation) and uncontrolled hypertension • As significant bradycardia may be poorly tolerated in these patients, treatment is not recommended • Patients with a history of Mobitz Type II second-degree AV block or higher-grade AV block, sick-sinus syndrome, or sinoatrial heart block • Patients with a history of recurrent syncope or symptomatic bradycardia • Patients receiving concurrent therapy with drugs that decrease heart rate (HR) (e.g. beta blockers, non-dihydropyridine calcium channel blockers [diltiazem and verapamil] and other drugs that may decrease HR, such as digoxin); consider the need to switch to non-HR-lowering medicinal products Concomitant use of these medicinal products during Ponvory initiation may be associated with severe bradycardia and heart block
☐	A cardiology consultation is not applicable for this patient
☐	Review results of a recent (obtained within 6-months prior to treatment initiation or after discontinuation of prior multiple sclerosis (MS) therapy) complete blood cell count (CBC) with differential (including absolute lymphocyte count)
☐	Review results of a recent (within 6 months prior to treatment initiation) liver function test for transaminase and bilirubin levels
☐	Obtain an evaluation of the fundus, including the macula, prior to treatment initiation. Ponvory should not be initiated in patients with macular oedema until resolution • Patients with a history of uveitis or diabetes mellitus should have regular examinations of the fundus, including the macula, prior to treatment initiation with Ponvory
☐	Confirm a negative pregnancy test result prior to treatment initiation in women of childbearing potential or that a pregnancy test is not applicable to this patient
☐	Counsel women of childbearing potential on the potential for a serious risk to the fetus and the need for effective contraception during treatment with Ponvory
☐	Counsel women of childbearing potential on the potential risk of teratogenicity and the need for effective contraception during treatment with PONVORY® and for at least 1 week following treatment discontinuation
☐	Counsel women of childbearing potential to discontinue treatment with PONVORY® at least 1 week before attempting to conceive • Explain to the patient that their disease activity may return when treatment with PONVORY® is discontinued due to pregnancy or attempting to conceive
☐	Instruct women receiving PONVORY® that they should not breastfeed
☐	Perform a varicella zoster virus (VZV) antibody test in patients without documentation of a HCP-confirmed history of varicella or a full course of vaccination against VZV • If negative, VZV vaccination is recommended at least 4 weeks prior to treatment initiation with Ponvory to allow the full effect of vaccination to occur
☐	Initiation of treatment with Ponvory should be delayed in patients with severe active infection until resolution
☐	Review current or prior medications. If patients are taking antineoplastic, immunosuppressive, or immune-modulating therapies, or if there is a history of prior use of these medicinal products, consider possible unintended additive effects on the immune system before treatment initiation
☐	Determine whether patients are taking medicinal products that could slow down heart rate (HR) or atrioventricular (AV) conduction
☐	Review current or prior medications. If patients are taking antineoplastic, immunosuppressive, or immune-modulating therapies, or if there is a history of prior use of these medicinal products, consider possible unintended additive effects on the immune system before treatment initiation

Treatment initiation (including re-initiation criteria)

Dose escalation at treatment initiation

Initiate treatment with the 14-day treatment initiation pack. Start treatment on Day 1 with one 2 mg tablet orally once daily and progress with the 14-day titration schedule outlined in the following diagram:



- After dose titration is complete, the recommended maintenance dose of Ponvory is one 20 mg tablet taken orally once daily.

Re-initiation of Ponvory therapy following treatment interruption during dose titration or maintenance period

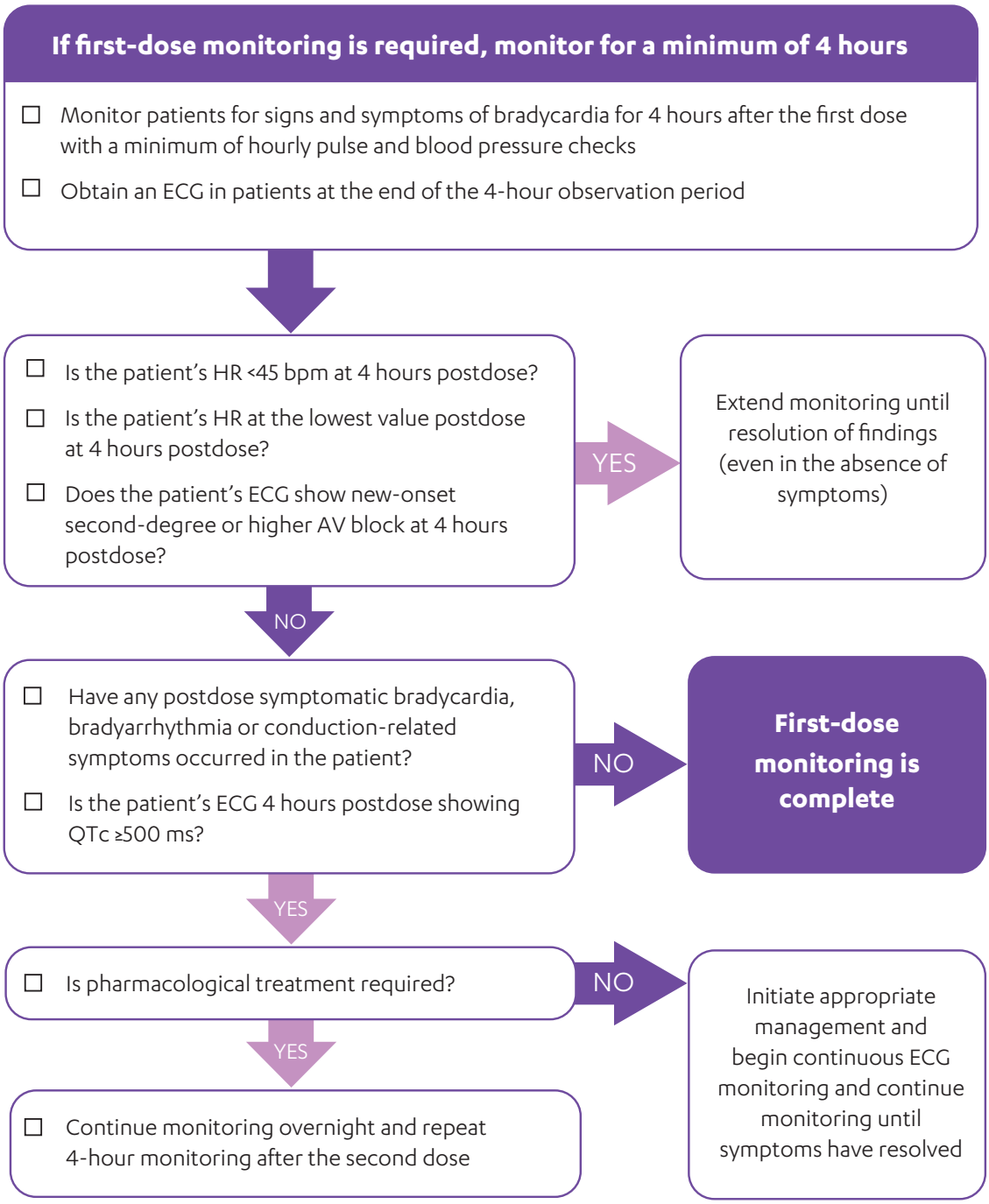
- **If fewer than 4 consecutive doses are missed**, resume treatment with the first missed dose
- **If 4 or more consecutive doses are missed**, re-initiate treatment with Day 1 (2 mg) of the titration regimen (using a new treatment initiation pack)
    - The same first-dose monitoring as for treatment initiation is recommended when 4 or more consecutive doses of Ponvory are missed during the titration or maintenance periods

First-dose monitoring

First-dose monitoring is recommended for patients with **certain pre-existing cardiac conditions**:

- Sinus bradycardia (HR <55 beats per minute [bpm])
- First- or second-degree (Mobitz Type I) AV block, or
- A history of myocardial infarction or heart failure occurring more than 6 months prior to treatment initiation

If first-dose monitoring for patients with pre-existing cardiac conditions is required, follow the steps outlined below:



bpm, beats per minute; ECG, electrocardiogram; HR, heart rate; QTc, Heart-rate-corrected QT interval.

☐ The patient does not have applicable pre-existing cardiac conditions and therefore first-dose monitoring is not required

During treatment

Peripheral blood lymphocyte counts

Ponvory reduces peripheral blood lymphocyte counts. Results of a CBC with lymphocyte count should be checked in all patients prior to initiation (refer to section 'Prior to initiation').

- ☐ Assess CBC periodically during Ponvory treatment
  - Absolute lymphocyte counts <0.2×10^9/L, if confirmed, should lead to interruption of Ponvory therapy until the level reaches >0.8×10^9/L, after which re-initiation of Ponvory can be considered

Considerations relating to immunosuppressive effect

Ponvory has an immunosuppressive effect that predisposes patients to infections, including opportunistic infections that can be fatal, and may increase the risk of developing malignancies, particularly those of the skin.

- ☐ Carefully monitor patients, especially those with concurrent conditions or known risk factors, such as previous immunosuppressive therapy. Discontinuation of treatment in patients at increased risk of infections or malignancies should be considered on a case-by-case basis
- ☐ Consider suspension of treatment during serious infection
- ☐ Apply caution when co-administering antineoplastic, immune-modulating or immunosuppressive therapies, due to the risk of additive immune system effects. For the same reason, a decision to use prolonged concomitant treatment with corticosteroids should be taken after careful consideration and the half-life and mode of action of medicinal products with prolonged immune effects should be considered when switching from these
- ☐ Vigilance for skin malignancies is recommended:
  - Caution patients against exposure to UV light and sunlight without protection
  - Ensure patients are not receiving concomitant phototherapy with ultraviolet B (UVB) radiation or psoralen and ultraviolet A (PUVA) photochemotherapy
  - Patients with pre-existing skin disorders and patients with new or changing skin lesions should be referred to a dermatologist to determine appropriate monitoring
- ☐ Vigilance for signs and symptoms of infection is recommended. Instruct patients to report signs and symptoms of infections immediately to their prescriber during treatment, and for up to 1 week after the last dose of Ponvory
  - Cases of fatal cryptococcal meningitis (CM) and disseminated cryptococcal infections have been reported in patients treated with other sphingosine-1-phosphate (S1P) receptor modulators
    - Suspend treatment with Ponvory if CM is suspected until cryptococcal infection has been excluded
    - Initiate appropriate treatment if CM is diagnosed
  - Cases of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain caused by the John Cunningham polyoma virus, have been reported in patients treated with another S1P receptor modulator and other MS therapies. Physicians should be vigilant for clinical signs and symptoms or MRI findings suggestive of PML
    - Suspend treatment with Ponvory if PML is suspected until PML has been excluded
    - Discontinue treatment with Ponvory if PML is confirmed
- ☐ Use of live attenuated vaccines may carry a risk of infection and should therefore be avoided during treatment and for up to 1 week after its discontinuation
  - If the use of live attenuated vaccines during treatment with Ponvory is required, treatment should be paused 1 week prior and for 4-weeks after a planned vaccination

Ophthalmic evaluation

☐	Obtain an ophthalmic evaluation of the fundus, including the macula, at any time if a patient reports any change in vision while on Ponvory therapy
☐	Instruct patients to report changes in vision
☐	Evaluate patients who present with visual symptoms of macular oedema • Discontinue treatment with Ponvory if macular oedema is confirmed • Consider the potential benefits and risks of Ponvory after resolution of macular oedema before treatment re-initiation
☐	Conduct regular follow-up examinations of the fundus, including the macula, in patients with a history of uveitis or diabetes mellitus

For women of childbearing potential

Ponvory is contraindicated during pregnancy and in women of childbearing potential not using effective contraception

☐	Repeat pregnancy tests at suitable intervals during treatment
☐	Before initiation and during treatment with Ponvory, counsel women of childbearing potential on the possibility of serious risk to the foetus during treatment with Ponvory, using the pregnancy-specific patient reminder card
☐	Instruct women of childbearing potential to use effective contraception during treatment with Ponvory and for at least 1 week following treatment discontinuation
☐	Counsel women of childbearing potential to discontinue treatment with Ponvory at least 1 week before attempting to conceive • Explain to patient that their disease activity may return when treatment with Ponvory is discontinued due to pregnancy or attempting to conceive
☐	Immediately discontinue treatment with Ponvory if a woman becomes pregnant during treatment. Provide medical advice regarding the risk of harmful effects to the fetus associated with Ponvory treatment and ensure follow-up examinations are performed
☐	Instruct women receiving Ponvory that they should not breastfeed
☐	If a pregnancy occurs during treatment with Ponvory, regardless of it being associated with an adverse event or not, please report it to Janssen's Local Representative, AM Mangion, on the following: • **Phone (24/7):** 00356 2397 6333 • **Email:** pv@ammangion.com • **Address:** AM Mangion Ltd, Mangion Building, N/S Off Valletta Road, Luqa, LQA 6000, MALTA Pregnancy cases during treatment with Ponvory 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 Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 • **E:** postlicensing.medicinesauthority@gov.mt Janssen has a developed a **P**regnancy **O**utcomes **E**nhanced **M**onitoring (POEM) programme designed to collect information about pregnancy in patients exposed to Ponvory immediately before or during pregnancy and on infant outcomes 12 months post-delivery

☐	Physicians are encouraged to enrol pregnant patients in the POEM programme by contacting Janssen's Local Representative, AM Mangion, on the following: • **Phone (24/7):** 00356 2397 6333 • **Email:** pv@ammangion.com • **Address:** AM Mangion Ltd, Mangion Building, N/S Off Valletta Road, Luqa, LQA 6000, MALTA As detailed above for more information, refer to the pregnancy reminder card for women of childbearing potential
☐	A pregnancy test is not applicable to this patient
☐	Counselling on pregnancy precautions is not applicable to this patient

Considerations relating to liver function

Elevation of transaminases and bilirubin may occur in patients taking Ponvory.

☐	Monitor patients who develop symptoms suggestive of hepatic dysfunction during treatment with Ponvory for hepatotoxicity
☐	Discontinue treatment if significant liver injury is confirmed (e.g. alanine aminotransferase [ALT] exceeds 3× upper limit of normal [ULN] and total bilirubin exceeds 2×ULN)

Respiratory considerations

Ponvory may cause a decline in pulmonary function

☐	Perform spirometry evaluation of respiratory function during treatment with Ponvory if clinically indicated

Blood pressure considerations

☐	Regularly monitor blood pressure during treatment with Ponvory

Neurological considerations

☐	Seizures have been reported in patients treated with Ponvory. Physicians should be vigilant for seizures, especially in patients with a pre-existing history of seizures or a family history of epilepsy
☐	Rare cases of posterior reversible encephalopathy syndrome (PRES) have been reported in patients receiving an S1P receptor modulator • Promptly schedule a complete physical and neurological examination if a Ponvory-treated patient develops unexpected neurological or psychiatric signs or symptoms, signs or symptoms suggestive of increased intracranial pressure, or accelerated neurological deterioration and an MRI should be considered • Discontinue treatment with Ponvory if PRES is suspected • Symptoms of PRES are usually reversible but may evolve into ischaemic stroke or cerebral haemorrhage. Delay in diagnosis and treatment may lead to permanent neurological sequelae

Additional considerations

☐	Provide all patients with the patient/caregiver guide
☐	Provide all patients with the pregnancy-specific patient reminder card if appropriate

Notes

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