Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Ponvory 20 mg film-coated tablets

Ponvory 2, 3, 4, 5, 6, 7, 8, 9 and 10 mg film-coated tablets

(ponesimod)

PLGB 00242/0739 and 0743

Janssen-Cilag Ltd

LAY SUMMARY

Ponvory 20 mg film-coated tablets

Ponvory 2, 3, 4, 5, 6, 7, 8, 9 and 10 mg film-coated tablets (ponesimod)

This is a summary of the Public Assessment Report (PAR) for Ponvory 20 mg film-coated tablets and Ponvory 2, 3, 4, 5, 6, 7, 8, 9 and 10 mg film-coated tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Ponvory in this lay summary for ease of reading.

For practical information about using Ponvory, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Ponvory and what is it used for?
These products have been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 19 May 2021 (EMEA/H/C/005163/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

These applications are full-dossier applications. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that these medicines are suitable for treating the specified indications.

Ponvory is used to treat adults with relapsing forms of multiple sclerosis (RMS) with active disease. Active disease in RMS is when there are relapses or when MRI (magnetic resonance imaging) results show signs of inflammation.

What is multiple sclerosis
Multiple sclerosis (MS) affects the nerves in the brain and spinal cord (the central nervous system).

In MS, the immune system (one of the body's main defence systems) does not work properly. The immune system attacks a protective covering of nerve cells called myelin sheath – this causes inflammation. This breakdown of the myelin sheath (called demyelination) stops the nerves working properly.

Symptoms of MS depend on which part of the brain and spinal cord are affected. These can include problems with walking and balance, weakness, numbness, double vision and blurring, poor coordination and bladder problems.

Symptoms of a relapse may disappear completely when the relapse is over – but some problems may remain.

How does Ponvory work?
Ponvory contains the active substance ponesimod. Ponesimod belongs to a group of medicines called sphingosine-1-phosphate (S1P) receptor modulators.

Ponvory reduces circulating lymphocytes, which are white blood cells involved in the immune system. It does this by keeping them in the lymphoid organs (lymph nodes). This means that fewer lymphocytes are available to attack the myelin sheath around the nerves in the brain and spinal cord.

Decreasing nerve damage in patients with MS reduces the number of attacks (relapses) and slows down worsening of the disease.

How is Ponvory used?
The pharmaceutical form of these medicines is a film-coated tablet, and the route of administration is oral (via the mouth).

How to take
The patient should take Ponvory exactly as their doctor tells them. The patient should not change their dose or stop taking Ponvory unless their doctor tells them to.

- **Take only 1 tablet each day.** To help the patient remember to take their medicine they should take it at the same time each day.
- Take with or without food.

Treatment initiation pack (14-day)

- The patient should **only** start their treatment with Ponvory using the treatment initiation pack, with which their dose will be gradually increased over 14 days. The purpose of the titration phase is to reduce any side effects due to slowing the heart rate at the start of treatment.
- The patient should write down the date they start taking the medicine next to day 1 on the Ponvory treatment initiation pack.
- Follow this 14-day treatment schedule

Treatment initiation pack day	Daily dose
Day 1	2 mg
Day 2	2 mg
Day 3	3 mg
Day 4	3 mg
Day 5	4 mg
Day 6	4 mg
Day 7	5 mg
Day 8	6 mg
Day 9	7 mg
Day 10	8 mg
Day 11	9 mg
Day 12	10 mg
Day 13	10 mg
Day 14	10 mg

Maintenance dose

- **After** the patient finishes taking the tablets in the treatment initiation pack, they should continue treatment using the 20 mg maintenance dose.
- The patient should write down the date they start taking the 20 mg maintenance dose, next to week 1 of the Ponvory 20 mg blister pack.

For further information on how Ponvory is used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Ponvory have been shown in studies?
A main study involving 1,133 adults with relapsing forms of multiple sclerosis showed that Ponvory was more effective than another multiple sclerosis medicine, teriflunomide, at reducing the number of relapses (flare-ups). After two years of treatment, the average number of relapses a year in patients taking Ponvory was 0.2 compared with 0.3 in patients taking teriflunomide. The average number of relapses in a year was reduced by about a third in patients taking Ponvory compared with patients taking teriflunomide.

What are the possible side effects of Ponvory?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Why was Ponvory approved?
A main study showed that Ponvory was more effective than teriflunomide at reducing the number of relapses in patients with relapsing forms of multiple sclerosis. The side effects that occur with Ponvory are similar to those seen with medicines of the same class and are considered manageable.

The MHRA therefore decided that Ponvory's benefits are greater than its risks and that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Ponvory?
A Risk Management Plan (RMP) has been developed to ensure that Ponvory is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Ponvory
Marketing authorisations were granted in Great Britain on 29 July 2021.

The full PAR for Ponvory follows this summary.

This summary was last updated in October 2021.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Ponvory 20 mg film-coated tablets and Ponvory 2, 3, 4, 5, 6, 7, 8, 9 and 10 mg film-coated tablets (PLGB 00242/0739 and 0743) could be approved.

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

Ponesimod is a sphingosine 1-phosphate (S1P) receptor 1 modulator. Ponesimod binds with high affinity to S1P receptor 1 located on lymphocytes.

Ponesimod blocks the capacity of lymphocytes to egress from lymph nodes reducing the number of lymphocytes in peripheral blood. The mechanism by which ponesimod exerts therapeutic effects in multiple sclerosis may involve reduction of lymphocyte migration into the central nervous system.

These products have been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 19 May 2021 (EMEA/H/C/005163/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

These applications were approved under Regulation 50 of The Human Medicines Regulation 2012, as amended (previously Article 8(3) of Directive 2001/83/EC, as amended), a full-dossier application.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a paediatric investigation plan (PIP) P/0066/2021.

At the time of the submission of the application the PIP was not yet completed as some measures were deferred.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Marketing Authorisations were granted on 29 July 2021.

II. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPCs are in line with current guidelines and are satisfactory.

PATIENT INFORMATION LEAFLET
The PIL is in line with current guidelines and is satisfactory.

LABEL
The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS
MHRA considered that the quality data submitted for these applications is satisfactory.

The grant of marketing authorisations is recommended.

IV. NON-CLINICAL ASPECTS
MHRA considered that the non-clinical data submitted for these applications is satisfactory.

The grant of marketing authorisations is recommended.

V. CLINICAL ASPECTS
MHRA considered that the non-clinical data submitted for these applications is satisfactory.

The grant of marketing authorisations is recommended.

VI. RISK MANAGEMENT PLAN (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional risks and safety measures have been proposed:

Table: Summary table of pharmacovigilance activities and risk minimisation activities by safety concern

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
Important Identified Risks		
Bradyarrhythmia occurring post-first dose	**Routine risk minimisation measures:** • SmPC Section 4.2 • SmPC Section 4.3 • SmPC Section 4.4 • SmPC Section 4.5 • SmPC Section 4.8 • SmPC Section 4.9 • SmPC Section 5.1 • PL Section 2 • PL Section 3 • PL Section 4 • An ECG should be obtained before treatment initiation with ponesimod and before treatment re-initiation when 4 or more consecutive doses are missed, as described in SmPC Sections 4.2 and 4.4, and PL Section 2. • Ponesimod treatment must be started with a 14-day up-titration scheme using a treatment initiation pack which should also be used before treatment re-initiation if 4 or more consecutive doses are missed, as described in SmPC Sections 4.2 and 4.4 and PL Section 3. • Advice from a cardiologist should be sought before treatment initiation with ponesimod if treatment is considered in patients with certain pre-existing heart conditions, as described in SmPC Section 4.4. Before starting treatment, patients are advised to tell their doctor if they have certain heart or blood vessel conditions, have suddenly passed out or fainted, as described in PL Section 2. • First-dose monitoring is recommended for patients with certain heart conditions, as described in SmPC Section 4.4 and PL Section 2.	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	• Appropriate management should be initiated in case certain post-dose heart-related disorders or symptoms occur, as described in SmPC Section 4.4. • Advice from a cardiologist should be sought before treatment initiation with ponesimod if treatment is considered in patients who receive concomitant therapy with medicinal products that decrease HR. Switching to non-HR-lowering medicinal products should be considered, as described in SmPC Section 4.4. Patients are advised to tell their doctor or pharmacist, before starting treatment, if they are taking, have recently taken or might take any medicine to control the heart rhythm or heart beat, as described in PL Section 2. • Patients who receive an overdose of ponesimod, especially upon initiation/re-initiation of treatment, should be observed for signs and symptoms of bradycardia as well as AV conduction blocks, which may include overnight monitoring, as described in SmPC Section 4.9. • Patients who experience signs and symptoms indicative of slow HR should call their physician immediately, as described in PL Section 2. • Pack size: ponesimod treatment initiation pack for 14-day up-titration • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	
Macular oedema	**Routine risk minimisation measures:** • SmPC Section 4.4 • SmPC Section 4.8 • PL Section 2 • PL Section 4 • An ophthalmic evaluation of the fundus, including the macula, is recommended in all patients before ponesimod treatment initiation and again at any time if a patient reports any change in vision while on ponesimod therapy, as described in SmPC Section 4.4 and PL Section 2. • Ponesimod therapy should not be initiated in patients with macular oedema until resolution, and patients with visual symptoms of macular oedema should be evaluated and, if confirmed, treatment should be discontinued, as described in SmPC Section 4.4. • Patients with a history of uveitis or diabetes mellitus should have regular examinations of the fundus, including the macula, prior to treatment initiation with ponesimod, and	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	have follow-up evaluations while receiving therapy, as described in SmPC Section 4.4. Before starting treatment, patients are advised to tell their doctor, if they have diabetes or eye problems, as described in PL Section 2. • Patients who experience symptoms of macular oedema should call their physician immediately, as described in PL Sections 2 and 4. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	
Bronchoconstriction	**Routine risk minimisation measures:** • SmPC Section 4.4 • SmPC Section 4.8 • SmPC Section 5.1 • PL Section 2 • PL Section 4 • Spirometry evaluation of respiratory function should be performed during ponesimod therapy, if clinically indicated, as described in SmPC Section 4.4. • Patients who develop new or worsening breathing problems should call their physician immediately, as described in PL Sections 2 and 4. Before starting treatment, patients are advised to tell their doctor if they have breathing problems, as described in PL Section 2. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024 • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection
Important Potential Risks		
Severe liver injury	**Routine risk minimisation measures:** • SmPC Section 4.2 • SmPC Section 4.3 • SmPC Section 4.4 • SmPC Section 4.8 • SmPC Section 5.2 • PL Section 2 • PL Section 4 • Recent (ie, within the last 6 months) transaminase and bilirubin levels should be reviewed before treatment initiation with ponesimod, as described in SmPC Section 4.4 and PL Section 2. • Patients who develop symptoms suggestive of hepatic dysfunction should be monitored for hepatotoxicity. Ponesimod treatment should be discontinued in case significant	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024 • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	liver injury is confirmed, as described in SmPC Section 4.4. • Patients who develop symptoms of liver problems should call their physician immediately, as described in PL Section 2. Before starting treatment, patients are advised to tell their doctor if they have liver problems, as described in PL Section 2. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	
Serious opportunistic infections including PML	**Routine risk minimisation measures:** • SmPC Section 4.3 • SmPC Section 4.4 • SmPC Section 4.5 • SmPC Section 4.8 • PL Section 2 • PL Section 4 • Results from a recent (ie, within 6 months or after discontinuation of prior therapy) CBC with differential (including lymphocyte count) should be reviewed before treatment initiation with ponesimod, as described in SmPC Section 4.4 and PL Section 2.	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • TFUQ to obtain structured information on reported AEs • Independent review of cases of suspected PML by external adjudication committee **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024 • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	• Assessments of CBC are recommended periodically during treatment with ponesimod; confirmed absolute lymphocyte counts <0.2x10^9/L should lead to interruption of ponesimod therapy; re-initiation of ponesimod can be considered when the level reaches >0.8x10^9/L, as described in SmPC Section 4.4. • Treatment initiation with ponesimod should be delayed in patients with severe active infection until resolution. Vigilance for signs and symptoms of infection should be continued for 1 to 2 weeks after treatment discontinuation, as described in SmPC Section 4.4. Before starting treatment, patients are advised to tell their doctor if they have a fever or infection, as described in PL Section 2. • Effective diagnostic and therapeutic strategies should be used in patients with symptoms of infection while on ponesimod therapy. Suspension of ponesimod treatment should be considered if a patient develops a serious infection, as described in SmPC Section 4.4. • Patients without an HCP-confirmed history of varicella (chickenpox) or without documentation of a full course of vaccination against VZV should be tested for antibodies to VZV before treatment initiation with ponesimod, as described in SmPC Section 4.4 and PL Section 2. Before starting treatment, patients are advised to tell their doctor if they never had chickenpox (varicella) or have not received a vaccine for chickenpox, as described in PL Section 2. • Physicians should be vigilant for clinical signs or symptoms of CM. Patients with signs or symptoms consistent with a cryptococcal infection should undergo prompt diagnostic evaluation and treatment. Ponesimod treatment should be suspended until a cryptococcal infection has been excluded; if CM is diagnosed, appropriate treatment should be initiated, as described in SmPC Section 4.4. • Physicians should be vigilant for clinical symptoms or MRI findings suggestive of PML. If PML is suspected, ponesimod treatment should be suspended until PML is excluded. Treatment with ponesimod should be discontinued if PML is confirmed, as described in SmPC Section 4.4. • The half-life and mode of action of medicinal products with prolonged immune effects should be considered when switching from these medicinal products to	

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	avoid unintended additive effects on the immune system while at the same time minimizing risk of disease reactivation when initiating ponesimod, as described in SmPC Section 4.4. For the same reason, caution should be applied during concomitant administration and in the weeks following administration or, if there is a history of prior use before initiating, during and up to 1 week after the last dose of ponesimod, as described in SmPC Sections 4.4 and 4.5. • A full course of vaccination with varicella vaccine is recommended for antibody-negative patients before treatment initiation with ponesimod, and treatment should be delayed for 4 weeks after vaccination, as described in SmPC Section 4.4 and PL Section 2. • The use of live, attenuated vaccines should be avoided while on ponesimod therapy and up to 1 week after treatment discontinuation. If immunisation with a live attenuated vaccine is required, ponesimod treatment should be paused from 1 week prior to 4 weeks after a planned vaccination, as described in SmPC Sections 4.4 and 4.5 and PL Section 2. Before starting treatment, patients are advised to tell their doctor if they have recently received any vaccinations or are planning to receive a vaccination, as described in PL Section 2. • Patients who experience symptoms of infection during treatment or 1 week after the last dose should call their physician immediately, as described in PL Sections 2 and 4. • Before starting treatment, patients are advised to tell their doctor if they have an immune system that does not work properly due to a disease or are taking medicines that weaken their immune system, as described in PL Section 2. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
Skin cancer	**Routine risk minimisation measures:** • SmPC Section 4.3 • SmPC Section 4.4 • SmPC Section 4.5 • SmPC Section 4.8 • PL Section 2 • PL Section 4 • Patients treated with ponesimod should be cautioned against exposure to sunlight and UV light without protection, and they should not receive concomitant phototherapy with UVB radiation or PUVA photochemotherapy, as described in SmPC Section 4.4 and PL Section 2. PL Section 2 also advises patients on how to limit such exposure. • The half-life and mode of action of medicinal products with prolonged immune effects should be considered when switching from these medicinal products to avoid unintended additive effects on the immune system while at the same time minimizing risk of disease reactivation when initiating ponesimod, as described in SmPC Section 4.4. For the same reason, caution should be applied during concomitant administration and in the weeks following administration or, if there is a history of prior use before initiating, during and up to 1 week after the last dose of ponesimod, as described in SmPC Sections 4.4 and 4.5. • Before starting treatment, patients are advised to tell their doctor if they have an immune system that does not work properly due to a disease or are taking medicines that weaken their immune system, as described in PL Section 2. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024 • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection
Non-skin malignancy	**Routine risk minimisation measures:** • SmPC Section 4.3 • SmPC Section 4.4 • SmPC Section 4.5 • PL Section 2 • The half-life and mode of action of medicinal products with prolonged immune effects should be considered when switching from these medicinal products to avoid unintended additive effects on the immune system while at the same time minimizing risk of disease reactivation when initiating ponesimod, as described in SmPC Section 4.4. For the same reason,	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	caution should be applied during concomitant administration and in the weeks following administration, or if there is a history of prior use before initiating, during and up to 1 week after the last dose of ponesimod, as described in SmPC Sections 4.4 and 4.5. • Before starting treatment, patients are advised to tell their doctor if they have an immune system that does not work properly due to a disease or are taking medicines that weaken their immune system, as described in PL Section 2. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • None	
Reproductive and embryofetal toxicity	**Routine risk minimisation measures:** • SmPC Section 4.3 • SmPC Section 4.4 • SmPC Section 4.6 • SmPC Section 5.3 • PL Section 2 • Before initiation of ponesimod treatment in women of childbearing potential, a negative pregnancy test result must be available, as described in SmPC Sections 4.4 and 4.6 and PL Section 2. • Women of childbearing potential should be counseled before treatment initiation on the potential for a serious risk to the fetus and the need for effective contraception during treatment with ponesimod and for 1 week after treatment discontinuation, as described in SmPC Sections 4.4 and 4.6 and PL Section 2. • Patients are advised not to use ponesimod during pregnancy, if they are trying to become pregnant, or if they could become pregnant and are not using effective contraception, as described in PL Section 2. • Ponesimod treatment should be discontinued immediately if a woman becomes pregnant during treatment, as described in SmPC Section 4.6 and PL Section 2. • If a woman becomes pregnant during treatment with ponesimod, medical advice should be given regarding the risk of harmful effects to the fetus associated with treatment. Follow-up examinations should be performed, as described in SmPC Section 4.6. Patients are advised to tell their doctor if they become pregnant within 1 week after stopping treatment, as described in PL Section 2.	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • Ponesimod POEM Final report: 1 year after the end of data collection. • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	• Patients are advised to talk to their doctor about reliable methods of contraception, as described in PL Section 2. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide • Pregnancy-specific patient reminder card	
Convulsions	**Routine risk minimisation measures:** • SmPC Section 4.8 • PL Section 2 • PL Section 4 • Patients who experience symptoms of a seizure should call their physician immediately, as described in PL Section 2. • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • TFUQ to obtain structured information on reported AEs • Cumulative reviews of events of convulsion in the PBRER **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024 • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection
Unexpected neurological or psychiatric symptoms/signs (PRES, ADEM, atypical MS relapses)	**Routine risk minimisation measures:** • SmPC Section 4.4 • PL Section 2 • A complete physical and neurological examination should be scheduled in ponesimod-treated patients who develop any unexpected neurological or psychiatric symptoms/signs, any symptom/sign suggestive of an increase of intracranial pressure, or accelerated neurological deterioration, and an MRI should be considered, as described in SmPC Section 4.4. • If PRES is suspected, ponesimod treatment should be discontinued, as described in SmPC Section 4.4. • Patients who experience symptoms suggestive of PRES should call their physician immediately, as described in PL Section 2.	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • TFUQ to obtain structured information on reported AEs **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024 • HCP survey to assess the effectiveness of HCP and patient/caregiver educational materials Final report: 1 year after the end of data collection
	• Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • Healthcare professional checklist • Patient/caregiver guide	
Missing Information		
Use in elderly patients	**Routine risk minimisation measures:** • SmPC Section 4.2	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:**

Safety Concern	Risk Minimisation Measures	Pharmacovigilance Activities
	• Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • None	• Cumulative reviews of reports of ponesimod use in elderly patients in the PBRER. **Additional pharmacovigilance activities:** • None
Long-term safety of ponesimod	**Routine risk minimisation measures:** • Legal status: medicinal product subject to restricted medical prescription **Additional risk minimisation measures:** • None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** • None **Additional pharmacovigilance activities:** • Trial AC-058B303/ OPTIMUM-LT Final report: 15/02/2025 • Trial AC-058B202 Final report: 14/12/2024

ADEM: acute disseminated encephalomyelitis; AEs: Adverse Events; CBC: complete blood count; CM: cryptococcal meningitis; ECG: electrocardiogram; HCP: healthcare professional; HR: heart rate; MS: multiple sclerosis; MRI: magnetic resonance imaging; PBRER: Periodic Benefit-Risk Evaluation Report; PL: package leaflet; PML: progressive multifocal leukoencephalopathy; PRES: posterior reversible encephalopathy syndrome; PUVA: psoralen and ultraviolet A; SmPC: summary of product characteristics; TFUQ: targeted follow-up questionnaire; UVB: ultraviolet B; VZV: varicella zoster virus.

This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

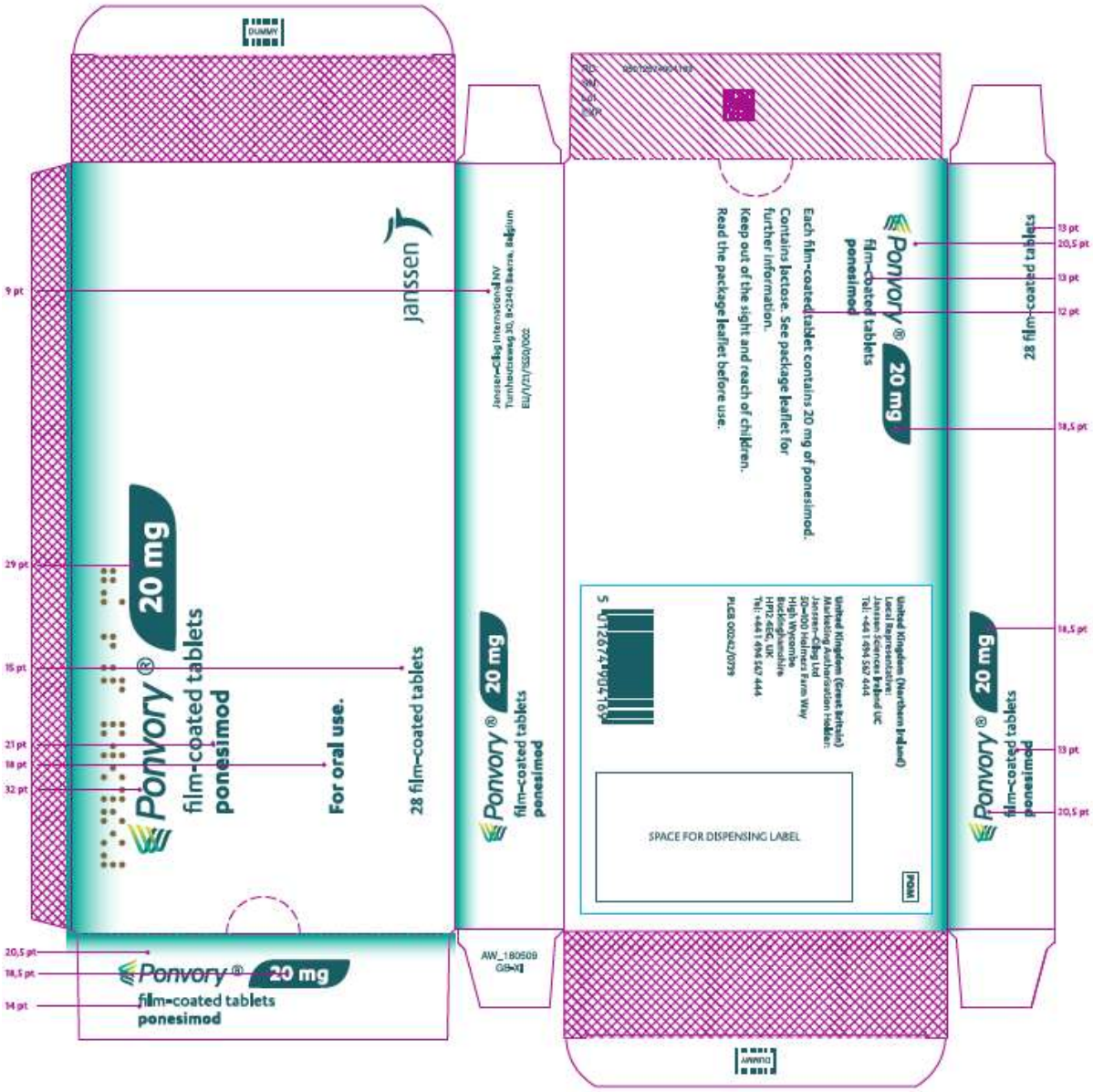
VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

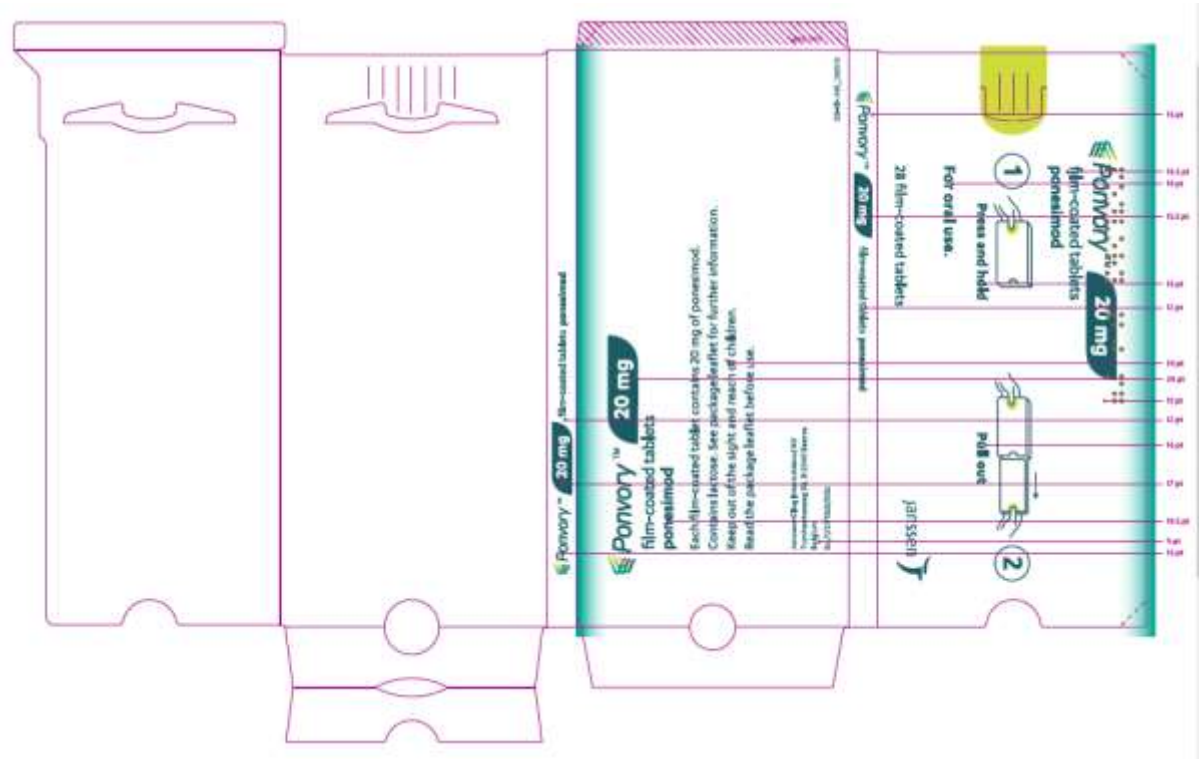
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

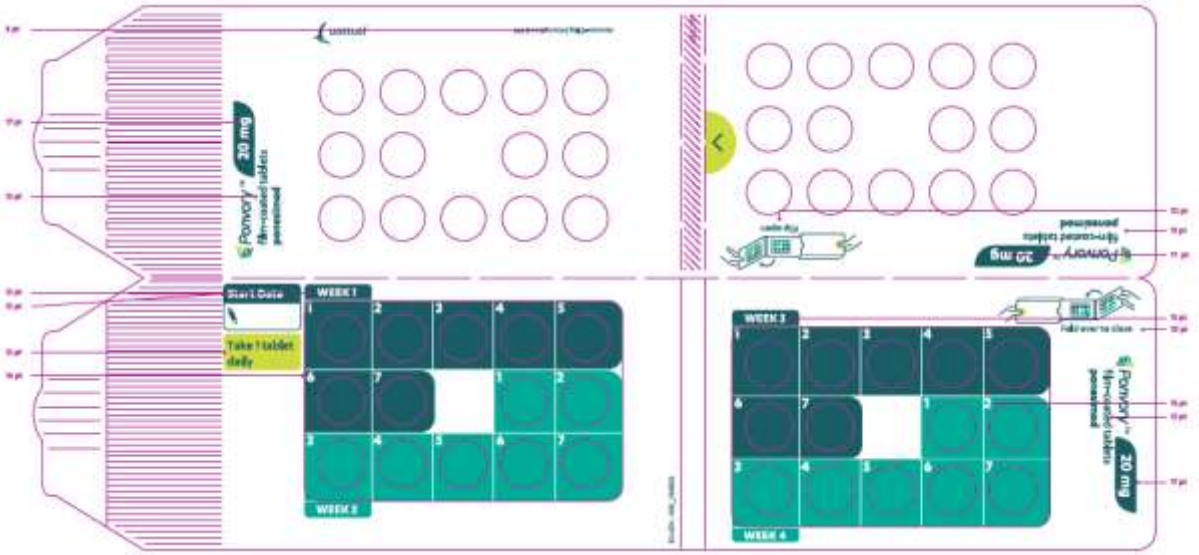
The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory.

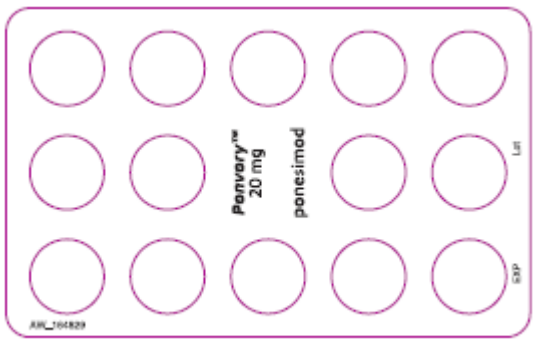
In accordance with legal requirements, the current approved GB versions of the SmPCs and PIL for these products are available on the MHRA website.

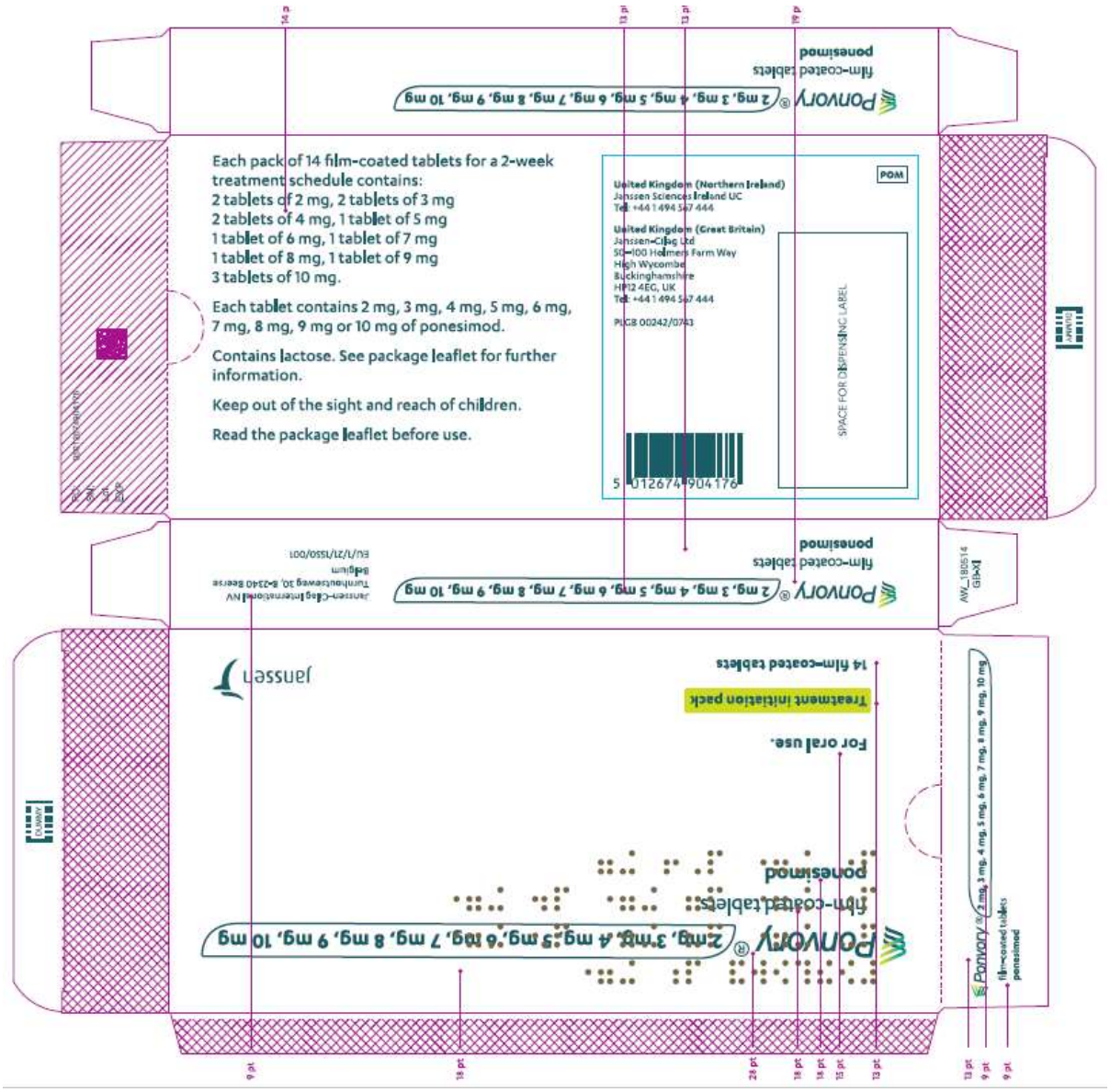
Representative copies of the labels at the time of GB licensing are provided below.

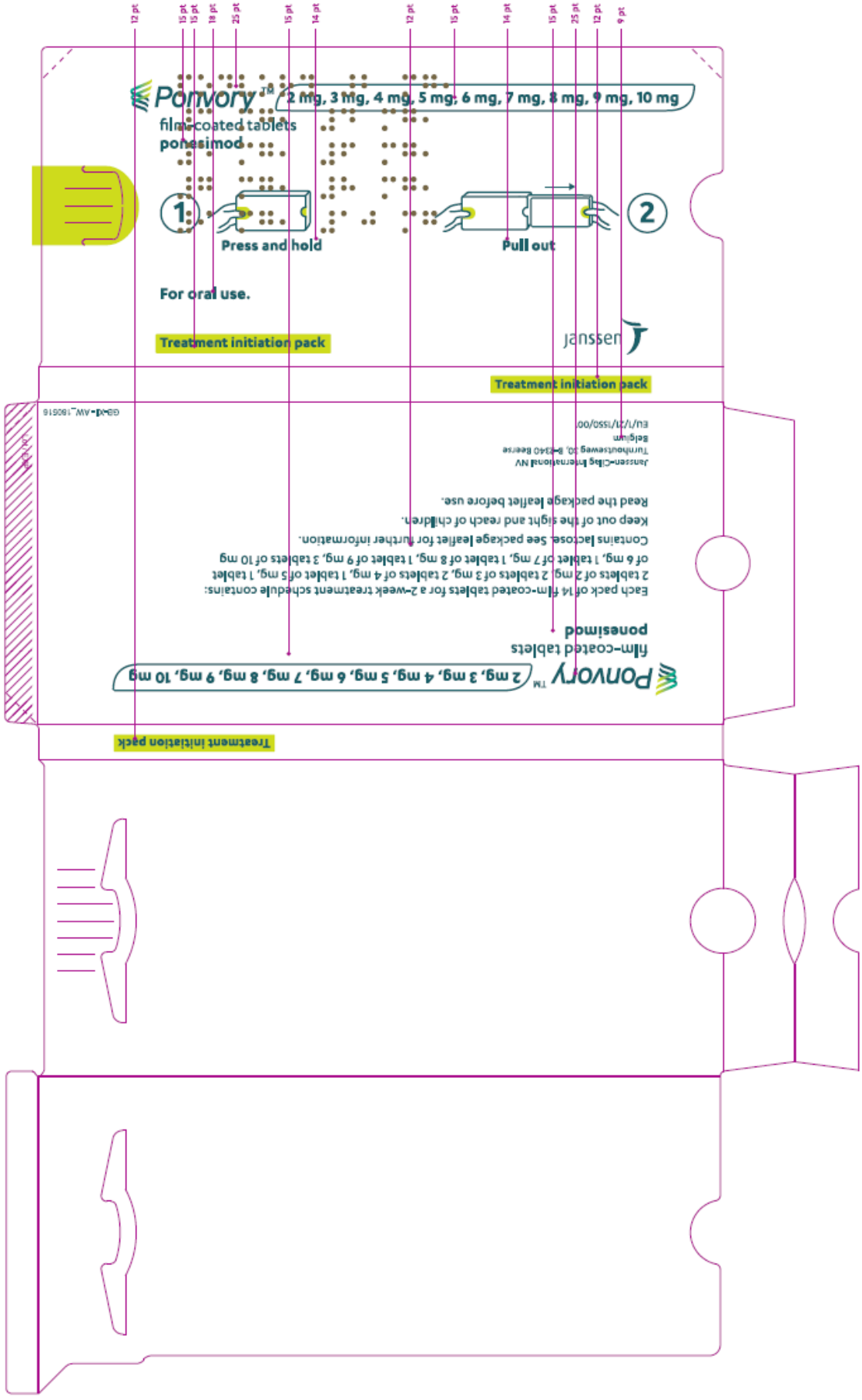

DUMMY
Janssen
Janssen-Cilag International NV
Turnhoutseweg 30, B-2340 Beerse, Belgium
EU/1/21/1530/002
Ponvory® 20 mg
film-coated tablets
ponesimod
For oral use.
28 film-coated tablets
Each film-coated tablet contains 20 mg of ponesimod.
Contains lactose. See package leaflet for further information.
Keep out of the sight and reach of children.
Read the package leaflet before use.
PLGB 00242/0739
SPACE FOR DISPENSING LABEL
POM
AW_180509
GB-XI
9 pt
29 pt
15 pt
21 pt
18 pt
32 pt
20,5 pt
18,5 pt
14 pt
13 pt
12 pt

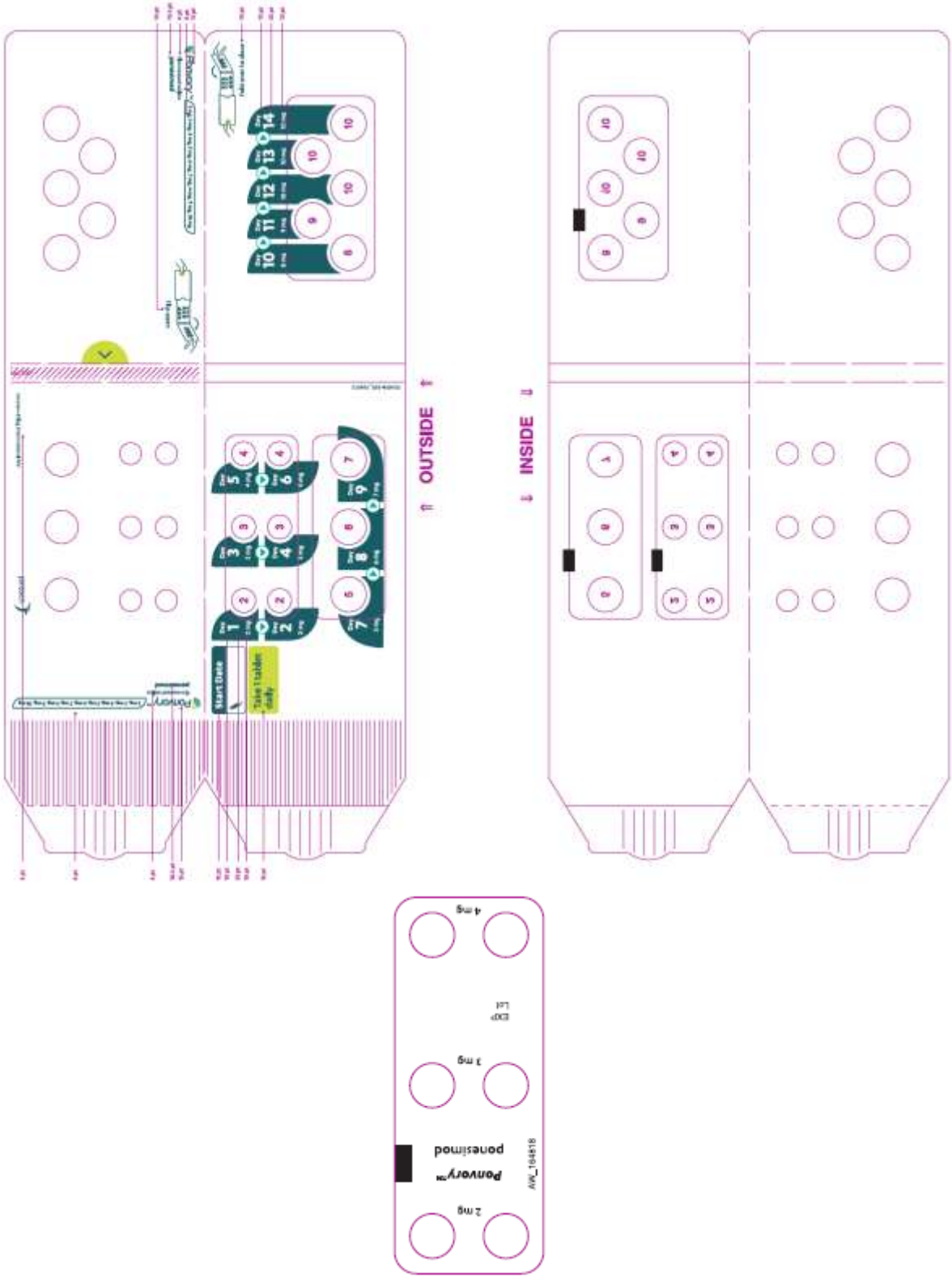

Ponvory™
20 mg
film-coated tablets
ponesimod
28 film-coated tablets
For oral use.
Press and hold
Pull out
Tissue

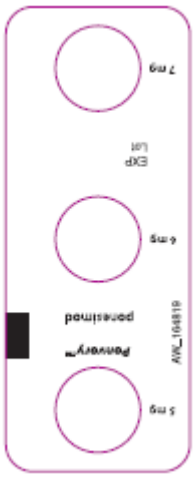

Ponvory™
20 mg
film-coated tablets
ponesimod
Start Date
Take 1 tablet daily
WEEK 1
WEEK 2
WEEK 3
WEEK 4


Ponvory™
20 mg
ponesimod
Lot
EXP


Each pack of 14 film-coated tablets for a 2-week treatment schedule contains:
2 tablets of 2 mg, 2 tablets of 3 mg
2 tablets of 4 mg, 1 tablet of 5 mg
1 tablet of 6 mg, 1 tablet of 7 mg
1 tablet of 8 mg, 1 tablet of 9 mg
3 tablets of 10 mg.
Each tablet contains 2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg or 10 mg of ponesimod.
Contains lactose. See package leaflet for further information.
Keep out of the sight and reach of children.
Read the package leaflet before use.
POM
United Kingdom (Northern Ireland)
Janssen Sciences Ireland UC
Tel: +44 1494 567 444
United Kingdom (Great Britain)
Janssen-Cilag Ltd
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG, UK
Tel: +44 1494 567 444
PLGB 00242/0743
5 012674 904176
SPACE FOR DISPENSING LABEL
PONVORY® (2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg)
film-coated tablets
ponesimod
Janssen-Cilag International NV
Turnhoutseweg 30, B-2340 Beerse
Belgium
EU/1/21/1550/001
AW_1805614
GB×XI
Janssen
14 film-coated tablets
Treatment initiation pack
For oral use.
Ponvory® film-coated tablets ponesimod
2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg


12 pt
15 pt
15 pt
18 pt
25 pt
15 pt
14 pt
12 pt
15 pt
14 pt
15 pt
25 pt
12 pt
9 pt
Ponvory™
2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg
film-coated tablets
ponesimod
1
Press and hold
Pull out
2
For oral use.
Treatment initiation pack
janssen
Treatment initiation pack
GB-XD-AW_180516
Each pack of 14 film-coated tablets for a 2-week treatment schedule contains:
2 tablets of 2 mg, 2 tablets of 3 mg, 2 tablets of 4 mg, 1 tablet of 5 mg, 1 tablet of 6 mg, 1 tablet of 7 mg, 1 tablet of 8 mg, 1 tablet of 9 mg, 3 tablets of 10 mg
Contains lactose. See package leaflet for further information.
Keep out of the sight and reach of children.
Read the package leaflet before use.
Janssen-Cilag International NV
Turnhoutseweg 30, B-2340 Beerse
Belgium
EU/1/21/1550/007
Treatment initiation pack
Ponvory™
2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg
film-coated tablets
ponesimod
Treatment initiation pack


OUTSIDE
INSIDE
Start Date
Take 1 tablet daily
Ponvory™
ponesimod
2 mg
3 mg
4 mg


7 mg
EXP
6 mg
ponesimod
Ponvory™
5 mg
AW_164819

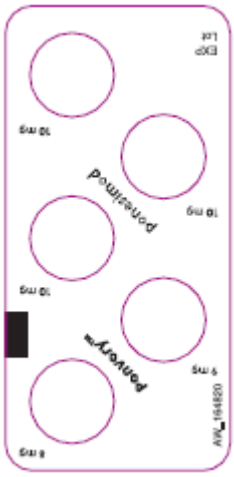

EXP
10 mg
ponesimod
10 mg
10 mg
Ponvory™
9 mg
8 mg
AW_164820

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**
IB	To submit an Updated Environmental Risk Assessment Report with required accompanying studies.	No	11 June 2024	Granted	N