

Clinical Policy: Ponesimod (Ponvory)

Reference Number: ERX.SPA.437

Effective Date: 06.01.21

Last Review Date: 05.21

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Ponesimod (Ponvory[™]) is a sphingosine 1-phosphate receptor modulator.

FDA Approved Indication(s)

Ponvory is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] that Ponvory is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all):

1. Diagnosis of one of the following (a, b, or c):
 - a. Clinically isolated syndrome, and member is contraindicated to all, or has experienced clinically significant adverse effects to two, of the following: Aubagio[®], glatiramer (Copaxone[®], Glatopa[®]), an interferon-beta agent (Betaseron[®] or Rebif[®]);
 - b. Relapsing-remitting MS, and failure of two of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Aubagio[®], dimethyl fumarate, Gilenya[®], glatiramer (Copaxone[®], Glatopa[®]), an interferon-beta agent (Betaseron[®] or Rebif[®]), Kesimpta[®], Mayzent[®], Ocrevus[®], Tysabri[®], Vumerity[®], Zeposia[®];^{*}
- c. Secondary progressive disease MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Ponvory is not prescribed concurrently with other disease modifying therapies (*see Appendix D*);
5. Documentation of baseline number of relapses per year and expanded disability status scale (EDSS) score;
6. Request meets the following:
 - a. Treatment initiation: Dose follows the 14-day titration schedule as outlined in Section V and does not exceed 1 tablet per day;
 - b. Treatment maintenance: Dose does not exceed 20 mg (1 tablet) per day.

**Prior authorization is required for all disease modifying therapies for MS.*

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Multiple Sclerosis (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
 - a. If member has received < 1 year of total treatment: Member is responding positively to therapy;
 - b. If member has received ≥ 1 year of total treatment: Member meets one of the following (i, ii, iii, or iv):
 - i. Member has not had an increase in the number of relapses per year compared to baseline;
 - ii. Member has not had ≥ 2 new MRI-detected lesions;
 - iii. Member has not had an increase in EDSS score from baseline;
 - iv. Medical justification supports that member is responding positively to therapy;
3. Ponvory is not prescribed concurrently with other disease modifying therapies for MS (see *Appendix D*);
4. If request is for a dose increase, new dose does not exceed 20 mg (1 tablet) per day.

Approval duration: first re-authorization: 6 months; second and subsequent re-authorizations: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;
- B.** Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
EDSS: expanded disability status scale
FDA: Food and Drug Administration

MS: multiple sclerosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Rebif® (interferon beta-1a)	22 mcg or 44 mcg SC TIW	44 mcg TIW
Betaseron® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
Aubagio® (teriflunomide)	7 mg or 14 mg PO QD	14 mg/day
Gilenya® (fingolimod)	0.5 mg PO QD	0.5 mg/day
Mayzent® (siponimod)	<i>All patients:</i> Day 1 and 2: 0.25 mg PO QD Day 3: 0.5 mg PO QD Day 4: 0.75 mg PO QD	2 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<p>CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: Day 5: 1.25 mg PO QD Day 6 and onward: 2 mg PO QD</p> <p>CYP2C9 genotypes *1/*3 or *2/*3: Day 5 and onward: 1 mg PO QD</p>	
dimethyl fumarate (Tecfidera®)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day
Tysabri® (natalizumab)	300 mg IV every 4 weeks	300 mg/4 weeks
Ocrevus® (ocrelizumab)	Initial 300 mg IV infusion with a second 300 mg IV infusion two weeks later, followed by subsequent doses of 600 mg via IV infusion every 6 months	600 mg/6 months
Kesimpta® (ofatumumab)	20 mg SC at weeks 0, 1, and 2, followed by 20 mg SC monthly starting at week 4	20 mg
Zeposia® (ozanimod)	Days 1-4: 0.23 mg PO QD Days 5-7: 0.46 mg PO QD Day 8 and thereafter: 0.92 mg PO QD	0.92 mg/day
Vumerity® (diroximel fumarate)	Starting: 231 mg PO BID for 7 days Maintenance: 462 mg PO BID	924 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): in the last 6 months, patients who have experienced myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III or IV heart failure; patients who have presence of Mobitz type II second-degree, third-degree atrioventricular block, or sick sinus syndrome, or sino-atrial block, unless patient has a functioning pacemaker
- Boxed warning(s): none reported

Appendix D: General Information

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), diroximel fumarate (Vumerity®), monomethyl fumarate (Bafiertam™), fingolimod (Gilenya®), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus®), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), ofatumumab (Kesimpta®), and ponesimod (Ponvory™).
- Of the disease-modifying therapies for MS that are FDA-labeled for clinically isolated syndrome, only the interferon products, glatiramer, and Aubagio have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the American Academy of Neurology 2018 MS guidelines.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MS	<p>Treatment initiation:</p> <ul style="list-style-type: none"> Days 1 and 2: 2 mg PO QD Days 3 and 4: 3 mg PO QD 	20 mg/day

Indication	Dosing Regimen	Maximum Dose
	<ul style="list-style-type: none"> Days 5 and 6: 4 mg PO QD Day 7: 5 mg PO QD Day 8: 6 mg PO QD Day 9: 7 mg PO QD Day 10: 8 mg PO QD Day 11: 9 mg PO QD Day 12, 13, and 14: 10 mg PO QD <p><u>Treatment maintenance:</u></p> <ul style="list-style-type: none"> Day 15 and thereafter: 20 mg PO QD <p><u>Missed doses:</u></p> <ul style="list-style-type: none"> If fewer than 4 consecutive doses are missed: <ul style="list-style-type: none"> During titration: Resume treatment with the first missed titration dose and resume the titration schedule at that dose and titration day. During maintenance: Resume treatment with the maintenance dosage. If 4 or more consecutive doses are missed during titration or maintenance: <ul style="list-style-type: none"> Treatment should be reinitiated with Day 1 of the titration regimen (new starter pack). 	

VI. Product Availability

- Tablets, starter pack: 2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg
- Tablets, maintenance dose bottle: 20 mg

VII. References

- Ponvory Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; March 2021. Available at: <https://www.ponvory.com>. Accessed March 24, 2021.
- Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018; 90(17): 777-788. Full guideline available at: <https://www.aan.com/Guidelines/home/GetGuidelineContent/904>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	03.24.21	05.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2021 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.