Clinical Policy Title:	ponesimod
Policy Number:	RxA.686
Drug(s) Applied:	Ponvory™
Original Policy Date:	05/07/2021
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ponesimod (Ponvory™)	Multiple Sclerosis	A starter pack must be used for patients initiating treatment with Ponvory™. **Initiate treatment with a 14-day titration:** **Titration day** / **Daily dose** Days 1 and 2 — 2 mg Days 3 and 4 — 3 mg Days 5 and 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, 13 and 14 — 10 mg **Maintenance:** 20 mg once daily, beginning on day 15	20 mg PO once daily

Dosage Forms

- Tablets: 2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg, and 20 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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;
   b. Relapsing-remitting MS;
   c. Secondary progressive MS;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Trial and failure of at least two (2) preferred agents: Aubagio, Avonex, Betaseron, Copaxone, Glatopa, Kesimpta, Ocrevus, Plegridy, or Zeposia.
5. Ponvory™ is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
6. Dose does not exceed 20 mg once daily.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Multiple sclerosis (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to the therapy;
3. Ponvory™ is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
4. Dose does not exceed 20 mg once daily.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
MS: Multiple sclerosis
VZV: Varicella zoster virus

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum dose
Ocrevus® (ocrelizumab)	300 mg, followed by a second 300 mg dose 2 weeks later followed by subsequent doses of 600 mg via intravenous infusion every 6 months	600 mg/6 months

Drug Name	Dosing Regimen	Dose Limit/ Maximum dose
dimethyl fumarate (Tecfidera®)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day
Aubagio® (teriflunomide)	7 mg or 14 mg PO once daily	14 mg/day
Gilenya® (fingolimod)	0.5 mg PO once daily	0.5 mg/day
Copaxone® (glatiramer acetate)	20 mg SC once daily or 40 mg SC TIW	20 mg/day or 40 mg TIW
Zeposia® (ozanimod hydrochloride)	**Initial dose:** Days 1 -4: 0.23 mg once daily Days 5-7: 0.46 mg once daily Day 8 and thereafter: 0.92 mg once daily **Maintenance:** 0.92 mg taken orally once daily starting on Day 8	0.92 mg once daily
Bafiertam™ (monomethyl fumarate)	**Starting dose:** 95 mg twice a day, orally, for 7 days **Maintenance dose** after 7 days: 190 mg (administered as two 95 mg capsules) twice a day, orally	300 mg/day
Ocrevus® (ocrelizumab)	**Start dose:** 300 mg intravenous infusion, followed two weeks later by a second 300 mg intravenous infusion. **Subsequent doses:** 600 mg intravenous infusion every 6 months	600 mg/dose IV

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, experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure.
  - Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker.

- Boxed Warning(s):
  - None

APPENDIX D: General Information

Disease-modifying therapies for MS include:

- Infusion therapies
  - natalizumab (Tysabri®)
  - mitoxantrone
  - ocrelizumab (Ocrevus®)
  - alemtuzumab (Lemtrada®)

- Injectable therapies
  - glatiramer (Copaxone®, Glatopa®)
  - interferon beta-1a (Avonex®, Rebif®)
  - interferon beta-1b (Betaseron®, Extavia®)
  - peginterferon beta-1a (Plegridy®)
- Oral therapies
  - dimethyl fumarate (Tecfidera®)
  - monomethyl fumarate (Bafiertam™)
  - diroximel fumarate (Vumerity®)
  - teriflunomide (Aubagio®)
  - fingolimod (Gilenya®)
  - siponimod (Mayzent®)
  - ozanimod (Zeposia®)
  - cladribine (Mavenclad®)
  - dalfampridine (Ampyra®)

References

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2. Ponvory. In: Lexicomp Online Drug Database [database on the Internet]. Hudson, Ohio: Lexicomp, Inc.; 2020 [updated March 22, 2021]. Available at: http://online.lexi.com. Subscription required to view. Accessed May 07, 2021.
3. Clinical Pharmacology [database online]. Elsevier; Gold Standard, Inc.; 2021. Available at: https://www.clinicalkey.com/pharmacology/ . Accessed May 07, 2021
4. IPD Analytics. [Internet database]. Updated periodically. Available at: https://secure.ipdanalytics.com/User/Pharma/RxStrategy/Search?q=Ponvory . Accessed May 07, 2021

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	05/07/2021	06/10/2021