Clinical Policy Title:	interferon beta-1b
Policy Number:	RxA.653
Drug(s) Applied:	Extavia®
Original Policy Date:	09/14/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Extavia® is an interferon beta 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
interferon beta-1b (Extavia®)	Multiple Sclerosis	The recommended dose is 0.25 mg every other day. Generally, start at 0.0625 mg (0.25 mL) every other day, and increase over a six-week period to 0.25 mg (1 mL) every other day. Reconstitute lyophilized powder with supplied diluent; the removable diluent cap contains natural rubber latex	0.25 mg (1 mL) every other day

Dosage Forms

- For injection: 0.3 mg of lyophilized powder in a single-dose vial for reconstitution

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. Relapsing-remitting MS (RRMS);
   b. Secondary progressive MS (SPMS);
   c. Clinically isolated syndrome;
2. Trial and failure of at least two (2) preferred disease modifying therapies (Avonex®, Betaseron®,

Copaxone®, Vumerity®, Bafiertam®, or Kesimpta®), at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
*Prior authorization is required for all disease modifying therapies for MS

3. Prescribed by or in consultation with a neurologist;
4. Age 18 ≥ years;
5. Extavia® is not prescribed concurrently with other disease modifying therapies for MS (see Appendix B);
6. Dose does not exceed 0.25 mg (1 mL) every other day.

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 the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Extavia® is not prescribed concurrently with other disease modifying therapies for MS (see Appendix B);
4. Dose does not exceed 0.25 mg (1 mL) every other day**.**

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. APPENDICES

APPENDIX A: Abbreviation/Acronym Key
CIS: clinically isolated syndrome
FDA: Food and Drug Administration
MS: Multiple Sclerosis
RRMS: relapsing-remitting multiple sclerosis

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
Infusion therapies		
mitoxantrone	12 mg/m^2 given as a short (approximately 5 to 15 minutes) intravenous infusion every 3 months	Cumulative lifetime dose of ≥ 140 mg/m^2
Tysabri®	300 mg intravenously every 4 weeks. In CD, discontinue in patients who have not experienced therapeutic benefit by 12 weeks of induction therapy and in patients that cannot discontinue chronic concomitant steroids within six months of starting therapy	300 mg/4 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Ocrevus™	Initial 300 mg intravenous infusion with a second 300 mg intravenous infusion two weeks later, followed by subsequent doses of 600 mg via intravenous infusion every 6 months	600 mg/6 months
Lemtrada®	Intravenous infusion for 2 or more treatment courses: • First course: 12 mg/day on 5 consecutive days • Second course: 12 mg/day on 3 consecutive days 12 months after first course • Subsequent courses as needed: 12 mg/day on 3 consecutive days 12 months after any prior course	See regimen
Injectable therapies		
glatiramer (Copaxone®, Glatopa®)	20 mg subcutaneously daily or 40 mg subcutaneously three times weekly	20 mg/day or 40 mg three times weekly
Avonex®, Rebif®	Avonex: 30 mcg intramuscularly weekly Rebif: 22 mcg or 44 mcg subcutaneously three times weekly	Avonex: 30 mcg /week Rebif: 44 mcg three times weekly
Betaseron®, Extavia®	250 mcg subcutaneously every other day	250 mg every other day
Plegridy®	125 mcg subcutaneously every 2 weeks	125 mcg/2 weeks
Oral therapies		
dimethyl fumarate (Tecfidera®)	120 mg orally twice daily for 7 days, followed by 240 mg orally twice daily	480 mg/day
Bafiertam™	Initial: 95 mg twice daily; after 7 days, increase to the maintenance dose: 190 mg twice daily.	380mg/day
Vumerity®	Starting: 231 mg orally twice daily for 7 days Maintenance: 462 mg orally twice daily	924 mg/day
Aubagio®	7 mg or 14 mg orally once daily	14 mg/day
Gilenya®	0.5 mg orally once daily	0.5 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Mayzent®	All patients: Day 1 and 2: 0.25 mg orally once daily Day 3: 0.5 mg orally once daily Day 4: 0.75 mg orally once daily CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: Day 5: 1.25 mg orally once daily Day 6 and onward: 2 mg orally once daily CYP2C9 genotypes *1/*3 or *2/*3: Day 5 and onward: 1 mg orally once daily	2 mg/day
Zeposia®	Initial: 0.23 mg once daily on days 1 through 4; then 0.46 mg once daily on days 5 through 7; maintenance dose: 0.92 mg once daily starting on day 8	0.92mg/day
Mavenclad®	3.5 mg/kg over 2-year treatment course, administered as 1.75 mg/kg in each year. Divide the 1.75 mg/kg dose over 2 cycles, each cycle lasting 4 to 5 consecutive days	20mg/day
Ampyra® (dalfampridine)	10 mg orally twice daily (approximately 12 hours apart)	20 mg/day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - History of hypersensitivity to natural or recombinant interferon beta, albumin or mannitol.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Depression and Suicide: Advise patients to immediately report any symptom of depression and/or suicidal ideation; consider discontinuation of Extavia® if depression occurs.
- Congestive Heart Failure (CHF): Monitor patients with CHF for worsening of cardiac symptoms; consider discontinuation of Extavia® if worsening of CHF occurs.
- Injection Site Necrosis and Reactions: Do not administer Extavia® into affected area until fully healed; if multiple lesions occur, discontinue Extavia® until healing of skin lesions.

- Leukopenia: Monitor complete blood count.
- Thrombotic Microangiopathy: Cases of thrombotic microangiopathy have been reported. Discontinue Extavia® if clinical symptoms and laboratory findings consistent with TMA occur.
- Flu-like Symptom Complex: Consider analgesics and/or antipyretics on injection days.
- Drug-induced Lupus Erythematosus: Cases of drug-induced lupus erythematosus have been reported. Discontinue Extavia® if patients develop new characteristic signs and symptoms.
- Hepatic Injury: Monitor liver function tests and signs and symptoms of hepatic injury.

References

1. Extavia® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corp.; October 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125290s070lbl.pdf . Accessed July 2, 2021.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at https://www.clinicalkey.com/pharmacology/. Accessed June 10, 2021. Accessed July 2, 2021
3. 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;90:777-788. doi:10.1212/WNL.0000000000005347. Available at: https://pubmed.ncbi.nlm.nih.gov/29686116/. Accessed July 2, 2021
4. Rae-Grant A, Day GS, Marrie RA, et al. Comprehensive systematic review 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;90:789-800. doi:10.1212/WNL.0000000000005345. Available at: https://pubmed.ncbi.nlm.nih.gov/29686117/. Accessed July 2, 2021
5. Costello K, Kalb R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. Revised September 2019. Available at: http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c- 4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed July 2, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	08/2020	9/14/2020
Policy was reviewed: 1. Dosing Information updated with "Reconstitute lyophilized powder with supplied diluent; the removable diluent cap contains natural rubber latex"; 2. Statement about provider sample "The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 3. Initial Approval Criteria I.A.2 was updated to include "(Avonex®, Betaseron®, Copaxone®, Vumerity®, Bafiertam®, Kesimpta®)". 4. HIM was removed from Initial and continued approval criteria.	7/2/2021	9/14/2021

5. Continued therapy criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…” 6. Therapeutic alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance…”. 7. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 8. Appendix B: Therapeutic alternative was updated to remove “natalizumab, ocrelizumab, alemtuzumab , interferon beta-1a , interferon beta-1b, peginterferon beta-1a, monomethyl fumarate, diroximel fumarate, teriflunomide, fingolimod, Siponimod, ozanimod, cladribine” generic as they were not available on ESM. 9. Appendix D was updated with Warning and Precautions. 10. References were reviewed and updated.		