Clinical Policy Title:	interferon beta-1b
Policy Number:	RxA.652
Drug(s) Applied:	Betaseron®
Original Policy Date:	8/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Interferon beta-1b (Betaseron®) is an interferon beta indicated for the treatment of relapsing forms of multiple sclerosis, 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 (Betaseron®)	Relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults	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	Dose of 0.25 mg (1 mL) every other day subcutaneously

Dosage Forms

- For injection: 0.3 mg 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), and
   b. Secondary progressive MS (SPMS);
   c. Clinically isolated syndrome;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Betaseron is not prescribed concurrently with other disease modifying therapies for MS; (see Appendix D);

5. 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. Betaseron is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
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
SPMS: Secondary progressive multiple sclerosis
CHF: Congestive Heart Failure
TMA: Thrombotic Microangiopathy

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		
Tysabri®	300 mg intravenous infusion over one hour every four weeks	300 mg every 4 weeks intravenously
mitoxantrone	recommended dosage is 12 mg/m^2 given as a short (approximately 5 to 15 minutes) intravenous infusion every 3 months.	140 mg/m^2 intravenously
(Ocrevus™)	Initial dose: 300 mg intravenous infusion, followed two weeks later by a second 300 mg intravenous infusion. Subsequent doses: single 600 mg intravenous infusion every 6 months.	600 mg/dose intravenously
Lemtrada®	12 mg/day intravenously	12 mg/dose intravenously
Injectable therapies		

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
glatiramer (Copaxone®, Glatopa®)	20 mg/mL subcutaneously per day, 40 mg/ml subcutaneously three times per week	20 mg/mL subcutaneously per day, 40 mg/ml subcutaneously three times per week
Avonex®, Rebif®	Avonex®: 30 micrograms intramuscularly once a week Rebif®: 22 mcg or 44 mcg injected subcutaneously three times per week.	For Avonex®, 30 mcg intramuscularly once a week For Rebif®, 44 mcg subcutaneously every 48 hours
Extavia®	0.25 mg subcutaneously 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.	250 mcg every other day subcutaneously
Plegridy®	125 micrograms every 14 days intramuscularly or subcutaneously	125 mcg intramuscularly or subcutaneously once every 14 days.
Oral therapies		
dimethyl fumarate (Tecfidera®)	Starting dose: 120 mg orally twice daily for 7 days Maintenance dose after 7 days: 240 mg orally twice daily	480 mg/day orally
Bafiertam™	Starting dose: 95 mg orally twice daily for 7 days Maintenance dose after 7 days: 190 mg (administered as two 95 mg capsules) orally twice daily	380 mg/day orally
(Vumerity®)	Starting dose: 231 mg orally twice daily for 7 days Maintenance dose after 7 days: 462 mg (administered as two 231 mg capsules) orally twice daily	924 mg/day orally
(Aubagio®)	7 mg or 14 mg orally once daily, with or without food	14 mg/day orally
(Gilenya™)	For adults and pediatric patients (≥ 10 years of age) weighing more than 40 kg: 0.5 mg orally once daily, with or without food For pediatric patients (10 years of age and above) weighing less than or equal to 40 kg: 0.25 mg orally once daily, with or without food.	Adults: 0.5 mg/day orally Pediatric: 10 to 12 years > 40 kg: 0.5 mg/day orally 10 to 12 years ≤ 40 kg: 0.25 mg/day orally
(Mayzent®)	Maintenance dose: 2 mg orally daily	2 mg/day orally
(Zeposia®)	Maintenance dose: 0.92 mg orally daily	0.92 mg/day orally
(Mavenclad®)	Cumulative dosage of 3.5 mg/kg administered orally and divided into 2 treatment courses (1.75 mg/kg per treatment course). Each treatment course is divided into 2 treatment cycles.	20 mg (2 tablets)/cycle day orally and 1.75 mg/kg PO per course for 2 courses up to cumulative 3.5 mg/kg orally in 2 years

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
dalfampridine (Ampyra®)	10 mg tablet orally twice daily	20 mg/day orally, administered as 10 mg every 12 hours

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):
  - In patients with a history of hypersensitivity to natural or recombinant interferon beta, Albumin (Human), or any other component of the formulation.

- Boxed Warning(s):
  - None Reported.

APPENDIX D: General Information

- Hepatic Injury: Monitor liver function tests and signs and symptoms of hepatic injury.
- Depression and Suicide: Advise patients to immediately report any symptom of depression and/or suicidal ideation; consider discontinuation of Betaseron® if depression occurs.
- Congestive Heart Failure (CHF): Monitor patients with CHF for worsening of cardiac symptoms; consider discontinuation of Betaseron® if worsening of CHF occurs.
- Injection Site Necrosis and Reactions: Do not administer Betaseron® into affected area until fully healed; if multiple lesions occur, discontinue Betaseron® until healing of skin lesions.
- Leukopenia: Monitor complete blood count.
- Thrombotic Microangiopathy: Cases of thrombotic microangiopathy have been reported. Discontinue Betaseron® 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 Betaseron if patients develop new characteristic signs and symptoms.

References

1. Betaseron Prescribing Information. Whippany, NJ: Bayer Corporation.; March 2021. Available at: https://labeling.bayerhealthcare.com/html/products/pi/Betaseron_PI.pdf . Accessed June 28, 2021.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at https://www.clinicalkey.com/pharmacology/. Accessed June 28, 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 June 28, 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. Accessed at https://pubmed.ncbi.nlm.nih.gov/29686117/. Accessed June 28, 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 June 28, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	08/2020	9/14/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial and Continued therapy criteria approval duration was updated to remove HIM approval duration. 3. Appendix A was updated to include SPMS, CHF and TMA. 4. Therapeutic alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance..". 5. Appendix B Therapeutic Alternate table was updated with Dosing regimen and Max Dose limit. 6. 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®...”. 7. Appendix B: Therapeutic alternative was updated to remove “natalizumab, ocrelizumab, alemtuzumab , interferon beta-1a , interferon beta-1b, peginterferon beta-1a, monomethyl fumarate, diroximel fumarate” as they were not present on ESM. 8. Appendix B: Therapeutic alternative was updated to remove “teriflunomide, fingolimod, siponimod, ozanimod, cladribine” as they were not present on ESM.	06/28/2021	09/14/2021

9. References were reviewed and updated.		