Clinical Policy Title:	interferon beta-1a
Policy Number:	RxA.274
Drug(s) Applied:	Avonex®, Rebif®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Interferon beta-1a (Avonex®, Rebif®) is an amino acid glycoprotein 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-1a (Avonex®)	Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults	30 mcg intramuscularly once weekly; may be titrated starting with 7.5 mcg for the first week, increased by 7.5 mcg each week for 3 weeks until target dose of 30 mcg is reached.	30 mcg/week
interferon Beta-1a (Rebif®)		Start dose at 20% of prescribed dose three times weekly; dose increased over 4 weeks to the targeted dose of either 22 mcg or 44 mcg subcutaneously three times weekly.	44 mcg three times weekly (132 mcg/week)

Dosage Forms

- Avonex®: Single-use prefilled autoinjector or syringe: 30 mcg/0.5 mL
- Rebif®: Single-dose prefilled autoinjector or syringe: 8.8 mcg/0.2 mL, 22 mcg/0.5 mL, 44 mcg/0.5 mL

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 (CIS);
   b. Relapsing-remitting MS;
   c. Active secondary progressive MS;
2. Prescribed by or in consultation with a neurologist;
3. Age 2 years of age or older (for Rebif® requests) or 18 years of age or older (for Avonex® requests);
4. Not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
5. If the request is for Rebif, trial and failure of at least (2) preferred agents: Avonex®, Betaseron®, Copaxone®, Vumerity®, Bafiertam®, or Kesimpta®.
6. Dose does not exceed one of the following (a or b):
   a. Avonex®: 30 mcg per week (1 vial/syringe/autoinjector per week);
   b. Rebif®: 44 mcg three times per week (1 syringe/autoinjector three times per week).

Approval Duration
Commercial: 12 months
Medicaid: 12 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 therapy;
3. 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 one of the following (a or b):
   a. Avonex®: 30 mcg per week (1 vial/syringe/autoinjector per week);
   b. Rebif®: 44 mcg three times per week (1 syringe/autoinjector three times per week.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MS: Multiple Sclerosis
CIS: Clinically isolated syndrome

APPENDIX B: Therapeutic Alternatives
Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - History of hypersensitivity to natural or recombinant interferon beta, albumin or any other component of the formulation.

- Boxed Warning(s):
  - None.

APPENDIX D: General Information

Disease-modifying therapies for MS include:

- Infusion therapies
  - natalizumab (Tysabri®)
  - mitoxantrone (Novantrone®)
  - ocrelizumab (Ocrevus®)
  - alemtuzumab (Lemtrada®)
  - rituximab (Rituxan®) (off-label)
- Injectable therapies
  - glatiramer (Copaxone®, Glatopa®)
  - interferon beta-1a (Avonex®, Rebif®)
  - interferon beta-1b (Betaseron®, Extavia®)
  - peginterferon beta-1a (Plegridy®)
- Oral therapies
  - dimethyl fumarate (Tecfidera®)
  - diroximel fumarate (Vumerity®)
  - teriflunomide (Aubagio®)
  - fingolimod (Gilenya®)
  - siponimod (Mayzent®)
  - ozanimod (Zeposia®)
  - cladribine (Mavenclad®)

References

1. Avonex® Prescribing Information. Cambridge, MA: Biogen Inc.; March 2020. Available at http://www.avonex.com. Accessed August 20, 2021.
2. Rebif® Prescribing Information. Rockland, MA: EMD Serono, Inc; October 2020. Available at http://www.rebif.com. Accessed August 20, 2021.
3. Costello K, Halper J, Kalb R, Skutnik L, Rapp R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. June 2019. Accessed August 20, 2021.
4. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology 2002; 58(2): 169-178. Available at: https://n.neurology.org/content/58/2/169.short. Accessed August 20, 2021.
5. European Medicines Agency: Avonex®: EPAR – Product Information; November 2018. Available at: https://www.ema.europa.eu/documents/product-information/avonex-eparproduct-information_en.pdf. Accessed August 20, 2021.
6. European Medicines Agency: Rebif®: EPAR – Product Information; December 2018. Available at: https://www.ema.europa.eu/documents/product-information/rebif-epar-productinformation_en.pdf. Accessed August 20, 2021.
7. 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. Accessed August 20, 2021.
8. Avonex® & Rebif®. In: Lexicomp Online Drug Database [database on the Internet]. Hudson, Ohio: Lexicomp, Inc.; 2020 [updated January 27, 2021]. Available at: http://online.lexi.com. Subscription required to view. Accessed August 20, 2021.

9. Yamout B, Sahraian M, Bohlega S, et al. Consensus recommendations for the diagnosis and treatment of multiple sclerosis: 2019 revisions to the MENACTRIMS guidelines. Mult Scler Relat Disord. 2020 Jan;37:101459. doi: 10.1016/j.msard.2019.101459. Epub 2019 Oct 18. PMID: 31670208. Accessed August 20, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy updated. 1. Formatting updated. 2. Clinical title updated. 3. Continued criteria for approval updated. 4. Approval duration updated. 5. Reference Updated	07/28/2020	09/14/2020
Policy was reviewed: 1. Dosing regimens updated for clarity. 2. Dosing frequency abbreviations expanded. 3. Clinical policy section standard verbiage was updated to include “The provision of provider samples…”. 4. Continued therapy criteria II.A.1 was rephrased to “Member is currently receiving medication…”. 5. Appendix A for abbreviations was updated. 6. References were updated.	04/01/2021	06/10/2021
Policy was reviewed. 1. Initial Approval Criteria I.A.5, trial and failure criteria, was updated from requiring member to try/fail at least two alternative therapies in order to receive either Avonex or Rebif, to requiring member to try/fail at least two alternative therapies to obtain Rebif only. 2. Appendix A was updated to remove abbreviation SC. 3. References were reviewed and updated.	08/20/2021	09/14/2021