

## **Clinical Policy: Interferon Beta-1a (Avonex, Rebif)**

Reference Number: CP.PHAR.255

Effective Date: 09.01.16

Last Review Date: 05.24

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Interferon beta-1a (Avonex<sup>®</sup>, Rebif<sup>®</sup>) is an amino acid glycoprotein.

### **FDA Approved Indication(s)**

Avonex and Rebif are indicated for the treatment of patients with 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.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Avonex and Rebif are **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;
  - b. Relapsing-remitting MS;
  - c. Secondary progressive MS;
2. Prescribed by or in consultation with a neurologist;
3. Age is one of the following (a or b):
  - a. Rebif:  $\geq 2$  years;
  - b. Avonex:  $\geq 18$  years;
4. Interferon beta-1a is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
5. Documentation of both baseline number of relapses per year and expanded disability status scale (EDSS) score;
6. Dose does not exceed one of the following (a or b):
  - a. Avonex: 30 mcg per week (1 syringe/autoinjector per week);
  - b. Rebif (i and ii):
    - i. 44 mcg three times per week;
    - ii. 1 syringe/autoinjector three times per week.

##### **Approval duration:**

**Medicaid/HIM** – 6 months

**Commercial** – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Multiple Sclerosis (must meet all):**

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
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  $\geq$  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  $\geq$  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. Interferon beta-1a 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 one of the following (a or b):
  - a. Avonex: 30 mcg per week (1 syringe/autoinjector per week);
  - b. Rebif (i and ii):
    - i. 44 mcg three times per week;
    - ii. 1 syringe/autoinjector three times per week.

**Approval duration:**

**Medicaid/HIM –**

**If member has received < 1 year of total treatment –** up to a total of 12 months of treatment

**If member has received ≥ 1 year of total treatment –** 12 months

**Commercial –** 6 months or to the member’s renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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*

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  
*\*The formerly available lyophilized vial formulation of Avonex is contraindicated in patients with a history of hypersensitivity to albumin (human). This contraindication does not apply to the other Avonex formulations.*

- Boxed warning(s): none reported

*Appendix D: General Information*

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone<sup>®</sup>, Glatopa<sup>®</sup>), interferon beta-1a (Avonex<sup>®</sup>, Rebif<sup>®</sup>), interferon beta-1b (Betaseron<sup>®</sup>, Extavia<sup>®</sup>), peginterferon beta-1a (Plegridy<sup>®</sup>), dimethyl fumarate (Tecfidera<sup>®</sup>), diroximel fumarate (Vumerity<sup>®</sup>), monomethyl fumarate (Bafiertam<sup>™</sup>), fingolimod (Gilenya<sup>®</sup>, Tascenso ODT<sup>™</sup>), teriflunomide (Aubagio<sup>®</sup>), alemtuzumab (Lemtrada<sup>®</sup>), mitoxantrone (Novantrone<sup>®</sup>), natalizumab (Tysabri<sup>®</sup>, and biosimilar Tyruko<sup>®</sup>), ocrelizumab (Ocrevus<sup>®</sup>), cladribine (Mavenclad<sup>®</sup>), siponimod (Mayzent<sup>®</sup>), ozanimod (Zeposia<sup>®</sup>), ponesimod (Ponvory<sup>™</sup>), ublituximab-xiiy (Briumvi<sup>™</sup>), and ofatumumab (Kesimpta<sup>®</sup>).

**V. Dosage and Administration**

Drug Name	Dosing Regimen	Maximum Dose
Interferon beta-1a (Avonex)	30 mcg IM Q week; may be titrated starting with 7.5 mcg for the first week, increased by 7.5 mcg each week for 3 weeks until target of 30 mcg is reached	30 mcg/week
Interferon beta-1a (Rebif)	Initial dose at 20% of prescribed dose TIW increased over 4 weeks to the targeted dose of either 22 mcg or 44 mcg SC TIW	44 mcg TIW

**VI. Product Availability**

Drug Name	Availability
Interferon beta-1a (Avonex)	Single-use prefilled autoinjector or syringe: 30 mcg/0.5 mL
Interferon beta-1a (Rebif)	Single-dose autoinjector or prefilled syringe: 8.8 mcg/0.2 mL, 22 mcg/0.5 mL, 44 mcg/0.5 mL

**VII. References**

1. Avonex Prescribing Information. Cambridge, MA: Biogen Inc.; July 2023. Available at <http://www.avonex.com>. Accessed January 10, 2024.
2. Rebif Prescribing Information. Rockland, MA: EMD Serono, Inc; July 2023. Available at <http://www.rebif.com>. Accessed January 10, 2024.
3. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis: Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*. 2002; 58(2): 169-178.
4. European Medicines Agency: Avonex: EPAR – Product Information; September 2023. Available at: <https://www.ema.europa.eu/en/medicines/human/EPAR/avonex>. Accessed January 24, 2024.
5. European Medicines Agency: Rebif: EPAR – Product Information; June 2023. Available at: <https://www.ema.europa.eu/en/medicines/human/EPAR/rebif>. Accessed January 24, 2024.

6. 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>. Reaffirmed on September 18, 2021.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1826	Injection, interferon beta-1a, 30 mcg
Q3027	Injection, interferon beta-1a, 1 mcg for intramuscular use
Q3028	Injection, interferon beta-1a, 1 mcg for subcutaneous use

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: no significant changes; references reviewed and updated.	01.27.20	05.20
Added requirements for documentation of baseline relapses/EDSS and objective measures of positive response upon re-authorization; modified Medicaid/HIM continued approval duration to 6 months for the first re-authorization and 12 months for second/subsequent re-authorizations; references reviewed and updated.	05.27.20	08.20
2Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; updated Appendix C to indicate the albumin contraindication only applies to the vial for Avonex per revised PI; removed Avonex vial per PI; references reviewed and updated.	02.08.21	05.21
2Q 2022 annual review: no significant changes; references reviewed and updated.	02.07.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.11.22	
2Q 2023 annual review: no significant changes; to be inclusive of members continuing therapy from a different benefit, revised Medicaid/HIM continued approval duration to reference the duration of total treatment received rather than the number of re-authorizations; references reviewed and updated.	01.30.23	05.23
2Q 2024 annual review: no significant changes; references reviewed and updated.	01.24.24	05.24

**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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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 clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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