Clinical Policy: Mitoxantrone (Novantrone)

Reference Number: CP.PHAR.258
Effective Date: 08.01.16
Last Review Date: 05.18
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Mitoxantrone (Novantrone®) is a synthetic antineoplastic anthracenedione.

FDA Approved Indication(s)
Novantrone is indicated for:
- Reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (MS) (i.e., patients whose neurologic status is significantly abnormal between relapses)
- Treatment of patients with pain related to advanced hormone-refractory prostate cancer as initial chemotherapy in combination with corticosteroids
- Initial therapy of acute nonlymphocytic leukemia (ANLL) (including myelogenous, promyelocytic, monocytic, and erythroid acute leukemias) in adults in combination with other approved drug(s)

Limitation(s) of use: Novantrone is not indicated in the treatment of patients with primary progressive MS.

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® that Novantrone is **medically necessary** when the following criteria are met:

I. **Initial Approval Criteria**
   A. **Multiple Sclerosis** (must meet all)**:**
      1. Diagnosis of relapsing-remitting or secondary-progressive MS;
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 18 years;
      4. If relapsing-remitting MS, failure of one of the following (a or b) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:
         a. Tecfidera or Gilenya and any of the following: an interferon-beta agent *(Avonex and Plegridy are preferred agents)* or glatiramer *(Glatopa 20 mg and Copaxone 40 mg are preferred agents)*;
         b. Tecfidera and Gilenya;

5. Novantrone is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix C*);
6. Dose does not exceed 12 mg/m^2 every 3 months (total cumulative lifetime dose of 140 mg/m^2).

Approval duration: 6 months

B. Prostate Cancer (must meet all)**:**
1. Diagnosis of advanced or metastatic prostate cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is hormone-refractory (i.e., castration-recurrent);
5. Novantrone is prescribed concurrently with a corticosteroid;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 14 mg/m^2 every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*);
7. Total cumulative lifetime dose does not exceed 140 mg/m^2.

Approval duration: 6 months

C. Acute Nonlymphocytic Leukemia (must meet all)**:**
1. Diagnosis of ANLL (including myelogenous [i.e., acute myelogenous leukemia], promyelocytic, monocytic, and erythroid acute leukemias);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 12 mg/m^2 per infusion;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*);
5. Total cumulative lifetime dose does not exceed 140 mg/m^2.

Approval duration: 6 months

D. Lymphoma (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Hodgkin's lymphoma;
   b. Non-Hodgkin's lymphoma which has relapsed following treatment with other chemotherapy;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*);
5. Total cumulative lifetime dose does not exceed 140 mg/m^2.

Approval duration: 6 months

E. Other diagnoses/indications
1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Multiple Sclerosis (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Novantrone is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix C*);
4. If request is for a dose increase, new dose does not exceed 12 mg/m^2 every 3 months (total cumulative lifetime dose of 140 mg/m^2).

Approval duration: 6 months

B. All Other Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or documentation supports that member is currently receiving Novantrone for the oncology indications listed in Section I;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. Prostate cancer: New dose does not exceed 14 mg/m^2 every 21 days;
   b. ANLL: New dose does not exceed 12 mg/m^2 per infusion;
   c. Any indication: New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*);
4. Total cumulative lifetime dose does not exceed 140 mg/m^2.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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.PMN.53 or evidence of coverage documents;

B. Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ANLL: acute nonlymphocytic leukemia
FDA: Food and Drug Administration
MS: multiple sclerosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Avonex®, Rebif® (interferon beta-1a)	*Avonex*: 30 mcg IM Q week *Rebif*: 22 mcg or 44 mcg SC TIW	*Avonex*: 30 mcg/week *Rebif*: 44 mcg TIW
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	*Copaxone*: 20 mg SC QD or 40 mg SC TIW *Glatopa*: 20 mg SC QD	*Copaxone*: 20 mg/day or 40 mg TIW *Glatopa*: 20 mg/day
Gilenya™ (fingolimod)	0.5 mg PO QD	0.5 mg/day
Tecfidera® (dimethyl fumarate)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day

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: General Information

- Disease-modifying therapies for MS are: daclizumab (Zinbryta®), glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), fingolimod (Gilenya™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), and ocreliuzmab (Ocrevus™).
- Mitoxantrone has IIa recommendations from Drugdex for use in anthracycline-resistant breast cancer, liver cancer, and ovarian cancer; however, these indications are not listed by the National Comprehensive Cancer Network (NCCN) guidelines.
- Per the NCCN, prostate cancer that stops responding to traditional androgen deprivation therapy (i.e., hormone therapy) is categorized as castration-recurrent (also known as castration-resistant).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Relapsing MS	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
Hormone-refractory prostate cancer	12 to 14 mg/m^2 given as a short intravenous infusion every 21 days	Cumulative lifetime dose of ≥ 140 mg/m^2
ANLL	Induction: 12 mg/m^2 of mitoxantrone injection (concentrate) daily on Days 1 to 3 given as an intravenous infusion. A second induction course (2 days) may be given if there is an incomplete antileukemic response	Cumulative lifetime dose of ≥ 140 mg/m^2

Indication	Dosing Regimen	Maximum Dose
	Consolidation: 12 mg/m^2 given by intravenous infusion daily on Days 1 and 2	

VI. Product Availability

Multidose vial: 20 mg/10 mL, 25 mg/12.5 mL, 30 mg/15 mL

VII. References

1. Mitoxantrone Prescribing Information. Irvine, CA: Teva Parenteral Medicines, Inc.; June 2012. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4d0f0f1a-31af-40fa-9c64-e90891fa6ce4. Accessed January 5, 2018.
2. 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.
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. March 2017. Accessed January 5, 2018.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 23, 2018.

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
J9293	Injection, mitoxantrone HCl, per 5 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.18 MS Treatments. Criteria: clarified monotherapy restriction, added criteria for re-authorization. Requirement for the trial and failure of at least 2 preferred regimens from different classes added. Removed specific strength requirement from glatiramer.	06.16	08.16
Added age requirement. Removed MRI requirement. Updated preferencing to require at least one of the highly effective DMTs on formulary (Tecfidera or Gilenya). Removed hepatic impairment and hypersensitivity contraindications. Removed reasons to discontinue.	06.17	08.17
2Q 2018 annual review: approval durations modified from 3 months to 6 months and removed LVEF requirement for MS; oncology: criteria added; references reviewed and updated.	01.05.18	05.18

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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