Clinical Policy: Mitoxantrone
Reference Number: ERX.SPMN.163
Effective Date: 10/16
Last Review Date: 09/16

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that mitoxantrone is medically necessary for the following indications:

I. Initial Approval Criteria
   A. Multiple Sclerosis (must meet all):
      1. Prescribed by or in consultation with a neurologist;
      2. MRI features consistent with multiple sclerosis (MS) and diagnosis of (a or b):
         a. Relapsing-remitting MS (RRMS), and
            i. Member has a contraindication to or failed (a or b):
               a) Betaseron or Rebif AND at least one of the following agents:
                  glatiramer acetate (Copaxone, Glatopa), Tecfidera, Gilenya, or Aubagio;
               b) Any 2 of the following agents: glatiramer acetate (Copaxone, Glatopa), Tecfidera, Gilenya, or Aubagio;
            b. Secondary-progressive MS (SPMS);
      3. Prescribed dose does not exceed cumulative lifetime dose of 140 mg/m²;
      4. Member will not use other disease modifying therapies for MS concurrently.

   Approval duration: 3 months (1 dose)

   B. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy

II. Continued Approval
   A. Multiple Sclerosis (must meet all):
      1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
      2. Responding positively to therapy;
      3. Prescribed dose does not exceed cumulative lifetime dose of 140 mg/m²;
      4. Member will not use other DMTs for MS concurrently.

   Approval duration: 3 months (1 dose)

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
      2. Refer to ERX.SPMN.16 - Global Biopharm Policy.
Background

Description/Mechanism of Action:
Mitoxantrone, a DNA-reactive agent that intercalates into DNA through hydrogen bonding, causes crosslinks and strand breaks. Mitoxantrone also interferes with RNA and is a potent inhibitor of topoisomerase II, an enzyme responsible for uncoiling and repairing damaged DNA. It has a cytotoxic effect on both proliferating and nonproliferating cultured human cells, suggesting lack of cell cycle phase specificity. Mitoxantrone injection has been shown in vitro to inhibit B cell, T cell, and macrophage proliferation and impair antigen presentation, as well as the secretion of interferon gamma, TNFα, and IL-2.

Formulations:
Mitoxantrone is a sterile aqueous solution containing mitoxantrone hydrochloride at a concentration equivalent to 2 mg mitoxantrone free base per mL supplied in vials for multidose use (10 mL, 12.5 mL, and 15 mL).

FDA Approved Indication(s):
Mitoxantrone is an anthracenedione/intravenous infusion 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 (i.e., patients whose neurologic status is significantly abnormal between relapses).
• Initial chemotherapy in combination with corticosteroids for the treatment of patients with pain related to advanced hormone-refractory prostate cancer.
• Initial therapy in combination with other approved drug(s) for the treatment of acute nonlymphocytic leukemia in adults, including myelogenous, promyelocytic, monocytic, and erythroid acute leukemias.

Limitations of use:
• Mitoxantrone is not indicated in the treatment of patients with primary progressive multiple sclerosis.

Appendices

Appendix A: Abbreviation Key
DNA: deoxyribonucleic acid
MRI: magnetic resonance imaging
MS: multiple sclerosis
RNA: ribonucleic acid
RRMS: relapsing-remitting multiple sclerosis
SPMS: secondary-progressive multiple sclerosis

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
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J9293 | Injection, mitoxantrone HCl, per 5 mg

### Reviews, Revisions, and Approvals

| Policy split from USS.SPMN.36 Multiple Sclerosis (MS) Treatments and converted to new template. Removed safety criteria, clarified monotherapy restriction, modified trial/failure criteria to require trial/failure of 2 agents from different classes, and added criteria for re-authorization. | Date | Approval Date |
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 | 08/16 | 09/16 |

### References


### 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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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