Mitoxantrone
Policy Number: C10292-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
11/1/2013	12/4/2019	12/4/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J9293-injection, mitoxantrone hydrochloride, per 5mg	RxPA	Q1 2020 20200122C10292-A

PRODUCTS AFFECTED:
mitoxantrone

DRUG CLASS:
antineoplastic antibiotics

ROUTE OF ADMINISTRATION:
Intravenous infusion

PLACE OF SERVICE:
Buy and bill, specialty pharmacy
The recommendation is that medications in this policy will be for medical benefit coverage and the product is administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center)

AVAILABLE DOSAGE FORMS:
mitoxantrone vial 2mg/ml, mitoxantrone Inj 2mg/ml

FDA-APPROVED USES:
acute myeloid leukemia in combination with other approved agents, secondary progressive, progressive relapsing or worsening relapsing-remitting multiple sclerosis, advanced hormone-refractory prostate cancer in combination with corticosteroids

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
acute myeloid leukemia in combination with other approved agents, secondary progressive, progressive relapsing or worsening relapsing-remitting multiple sclerosis, advanced hormone-refractory prostate cancer in combination with corticosteroids, acute lymphoid leukemia, bone marrow transplant, breast cancer, head and neck cancer, liver carcinoma, indolent malignant lymphoma non-Hodgkin's lymphoma, ovarian cancer, or solid tumor

REQUIRED MEDICAL INFORMATION:
A. MULTIPLE SCLEROSIS:
1. Documentation of diagnosis of a relapsing form of multiple sclerosis as defined bythe

McDonald criteria (relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS)
NOTE: Mitoxantrone is not indicated in the treatment of patients with primary progressive multiple sclerosis.
AND

2. Documented inadequate response (6 months of therapy), intolerance or FDA labeled contraindication to ALL preferred formulary disease modify therapies- Inadequate response is defined as increase frequency, severity and/or sequelae of relapses, changes in MRI or increase in disability progression.
   AND
3. Documentation that mitoxantrone will not be used concurrently with any other disease modifying therapy OR leflunomide
   AND
4. Documentation of Tuberculin skin test that indicates NO evidence of active, latent or inadequately treated tuberculosis infection within the recent 3 months
   AND
5. Documentation of baseline MRI, normal complete blood count, transaminase and bilirubin levels within 6 months prior to initiation
   AND
6. If member is female and of child bearing potential: A documented negative pregnancy test prior to initiating therapy is required.
   AND
7. Documentation of left ventricular ejection fraction (LVEF) > 50% demonstrated by a recent echocardiogram or multigated radionuclide angiography (MUGA)
   AND
8. Documentation of normal liver function and normal liver enzymes AND
9. Documentation that prescriber has verified patient has not reach the maximum lifetime dose of 140mg/m2

B. ALL OTHER INDICATIONS:

1. (a) Documentation of a diagnosis of pain related to advanced hormone-refractory (castration-resistant) prostate cancer
   AND
   (b) patient will use the medication in combination with corticosteroids
   (c) AND
   (d) the patient has a neutrophil count 1500 cell/mm3 or higher
   OR
2. (a) Patient has a diagnosis of acute nonlymphocytic leukemia (e.g., myelogenous, promyelocytic, monocytic, and erythroid)
   AND
   (b) the medication will be used in combination with other medications used for the treatment of ANLL

DURATION OF APPROVAL:
Multiple Sclerosis- Initial authorization: 6 months. Continuation of therapy: up to 12 months
All other indications- Initial authorization: 3 months, Continuation of therapy: 6 months or maximum duration per FDA label or NCCN guideline, whichever is shorter

QUANTITY:
12 mg/m2 per 3 months

PRESCRIBER REQUIREMENTS:
Multiple Sclerosis: Prescribed by or in consultation with a board-certified neurologist or a multiple sclerosis physician specialist, all other indications: Prescribed by or in consultation with a board- certified oncologist.

AGE RESTRICTIONS:
18 years of age and older

CONTINUATION OF THERAPY:
A. ALL ONCOLOGY INDICATIONS:
1. Documentation patient has not experienced disease progression and has a neutrophil count 1500cell/mm3 or higher

B. MULTIPLE SCLEROSIS:
1. Patient has had an objective response to therapy (i.e. no or slowed progression of disease) AND
2. Patient's neutrophil count is 1500 cell/mm3 or higher AND
3. LVEF is 50% or higher AND
4. Patient has not experienced a clinically significant reduction in LVEF AND
5. Patient's cumulative lifetime dose of mitoxantrone is <140 mg/m2

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
non-FDA approved supported indications, hypersensitivity to any component of the formulation, hepatic impairment, left ventricular ejection fraction (LVEF) less than 50 percent or clinically significant decrease in LVEF (greater than 10 percent decrease from baseline), or patients cumulative dose is more than 140 mg per meter squared (if patient has received drug in the past)

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:
None

APPENDIX:
Table. Kurtzke Expanded Disability Status Scale
0 Normal neurological exam (all grade 0 in Functional Systems (FS); cerebral grade 1 acceptable).
1 No disability, minimal signs in one FS (i.e., one grade 1 excluding cerebral grade 1).
1.5 No disability, minimal signs in more than one FS (more than one grade 1 excluding cerebral grade 1).
2.0 Minimal disability in one FS (one FS grade 2, others 0 or 1).
2.5 Minimal disability in two FS (two FS grade 2, others 0 or 1).
3.0 Moderate disability in one FS (one FS grade 3, others 0 or 1), or mild disability in three or four FS (three-four FS grade 2, others 0 or 1).
3.5 Fully ambulatory but with moderate disability in one FS (one grade 3 and one or two FS grade 2) or two FS grade 3, others 0 or 1, or five FS grade 2, others 0 or 1.

4.0 Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability consisting of one FS grade 4 (others 0 or 1), or combinations of lesser grades exceeding limits of previous steps. Able to walk without aid or rest some 500 meters (0.3 miles).
4.5 Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability. (Usually consisting of one FS grade 4 (others 0 or 1) or combinations of lesser grades exceeding limits of previous steps. Able to walk without aid or rest for some 300 meters (975 ft.).)

5.0 Ambulatory without aid or rest for about 200 meters (650 ft.); disability severe enough to impair full daily activities (e.g., to work full day without special provisions). (Usual FS equivalents are one grade 5 alone (others
0 or 1); or combinations of lesser grades usually exceeding specifications for step 4.0.)
5.5 Ambulatory without aid or rest for about 100 meters (325 ft); disability severe enough to impair full daily activities. (Usual FS equivalents are one grade 5 alone (others 0 or 1); or combinations of lesser grades usually exceeding specifications for step 4.0.)
6.0 Intermittent or constant unilateral assistance (cane, crutch, or brace) required to walk about 100 meters (325 ft.) with or without resting. (Usual FS equivalents are combinations with more than two FS grade 3+.)
6.5 Constant bilateral assistance (canes, crutches, or braces) required to walk about 20 meters (65 ft.). (Usual FS equivalents are combinations with more than two FS grade 3+.)
7.0 Unable to walk beyond about 5 meters (16 ft.) event with aid, essentially restricted to wheelchair, wheels self in standard wheelchair a full day and transfers alone; up and about in wheelchair some 12 hours a day. (Usual FS equivalents are combinations with more than one FS grade 4+; very rarely pyramidal grade 5 alone.)
7.5 Unable to take more than a few steps; restricted to wheelchair; may need aid in transfers, wheels self but cannot carry on in standard wheelchair a full day; may require motorized wheelchair. (Usual FS equivalents are combinations with more than one FS grade 4+.)
8.0 Essentially restricted to bed or chair or perambulated in wheelchair; but may be out of bed much of the day; retains may self-care functions; generally has effective use of arms. (Usual FS equivalents are combinations, generally grade 4+ in several systems.)
8.5 Essentially restricted to bed for much of the day; has some effective use of arm(s); retains some self-care functions. (Usual FS equivalents are combinations, generally grade 4+ in several systems.)
9.0 Helpless bed patient; can communicate and eat. (Usual FS equivalents are combinations, mostly grade 4.)
9.5 Totally helpless bed patient; unable to communicate or effectively eat/swallow. (Usual FS equivalents are combinations, almost all grade 4+.)
10 Death due to MS

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES:

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5. Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS
6. Council for Clinical Practice Guidelines. Neurology. 2002 Jan;58(2):169-78.
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8. McDonald criteria. Annals of Neurology. 2011;69(2):292-302. doi:10.1002/ana.22366.