Mitoxantrone (Novantrone®) **Policy Number: M-0017**
Revision: 2 **Last Update: 6/4/2014**

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

When appropriate compendia references the use of one of the chemotherapeutic agents listed in this Article as part of a 'combination therapy', the drug is only approved for use in such 'combinations', and the documentation should reflect, and be specific about, the use of the additional 'combination therapy' drugs.

Coverage Guidelines:

FDA:

- Acute myeloid leukemia, In combination with other approved agents
- Multiple sclerosis, Secondary progressive, progressive relapsing, or worsening relapsing-remitting; to reduce neurologic disability and/or frequency of clinical relapses
- Prostate cancer, In combination with corticosteroids, for pain related to advanced hormone-refractory prostate cancer

Off Label:

- Acute lymphoid leukemia
- Bone marrow transplant
- Breast cancer
- Head and neck cancer
- Liver carcinoma
- Malignant lymphoma, Indolent
- Non-Hodgkin's lymphoma
- Ovarian cancer

- Solid tumor configuration

Coding Information:

HCPCS Code(s)

J9293	INJECTION, MITOXANTRONE HYDROCHLORIDE, PER 5 MG

ICD-9 Code(s)

155.0-155.2	MALIGNANT NEOPLASM OF LIVER PRIMARY - MALIGNANT NEOPLASM OF LIVER NOT SPECIFIED AS PRIMARY OR SECONDARY
174.0-174.9	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA OF FEMALE BREAST - MALIGNANT NEOPLASM OF BREAST (FEMALE) UNSPECIFIED SITE
175.0-175.9	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA OF MALE BREAST - MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED SITES OF MALE BREAST
185	MALIGNANT NEOPLASM OF PROSTATE
200.00-200.88	RETICULOSARCOMA UNSPECIFIED SITE - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
202.00-202.98	NODULAR LYMPHOMA UNSPECIFIED SITE - OTHER AND UNSPECIFIED MALIGNANT NEOPLASMS OF LYMPHOID AND HISTIOCYTIC TISSUE INVOLVING LYMPH NODES OF MULTIPLE SITES
204.00-204.02	ACUTE LYMPHOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION - ACUTE LYMPHOID LEUKEMIA, IN RELAPSE
204.80-204.82	OTHER LYMPHOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION - OTHER LYMPHOID LEUKEMIA, IN RELAPSE
204.90-204.92	UNSPECIFIED LYMPHOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION - UNSPECIFIED LYMPHOID LEUKEMIA, IN RELAPSE
205.00-205.02	ACUTE MYELOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION - ACUTE MYELOID LEUKEMIA, IN RELAPSE
205.10	CHRONIC MYELOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
205.12	CHRONIC MYELOID LEUKEMIA, IN RELAPSE
205.20	SUBACUTE MYELOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
205.22	SUBACUTE MYELOID LEUKEMIA, IN RELAPSE

205.30	MYELOID SARCOMA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
205.32	MYELOID SARCOMA, IN RELAPSE
205.80	OTHER MYELOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
205.82	OTHER MYELOID LEUKEMIA, IN RELAPSE
205.90	UNSPECIFIED MYELOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
205.92	UNSPECIFIED MYELOID LEUKEMIA, IN RELAPSE
206.00	ACUTE MONOCYTIC LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
206.02	ACUTE MONOCYTIC LEUKEMIA, IN RELAPSE
206.10	CHRONIC MONOCYTIC LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
206.12	CHRONIC MONOCYTIC LEUKEMIA, IN RELAPSE
206.20	SUBACUTE MONOCYTIC LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
206.22	SUBACUTE MONOCYTIC LEUKEMIA, IN RELAPSE
206.80	OTHER MONOCYTIC LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
206.82	OTHER MONOCYTIC LEUKEMIA, IN RELAPSE
206.90	UNSPECIFIED MONOCYTIC LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
206.92	UNSPECIFIED MONOCYTIC LEUKEMIA, IN RELAPSE
207.00	ACUTE ERYTHREMIA AND ERYTHROLEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
207.02	ACUTE ERYTHREMIA AND ERYTHROLEUKEMIA, IN RELAPSE
340	MULTIPLE SCLEROSIS

Background:

NOVANTRONE belongs to the general group of medicines called antineoplastics. Mitoxantrone, a DNA-reactive agent that intercalates into deoxyribonucleic acid (DNA) through hydrogen bonding, causes crosslinks and strand breaks. Mitoxantrone also interferes with ribonucleic acid (RNA) and is a potent inhibitor of topoisomerase II, an

enzyme responsible for uncoiling and repairing damaged DNA. It has a cytocidal effect on both proliferating and nonproliferating cultured human cells, suggesting lack of cell cycle phase specificity. NOVANTRONE 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.

Black Box Warning:

WARNING

Novantrone® (mitoxantrone for injection concentrate) should be administered under the supervision of a physician experienced in the use of cytotoxic chemotherapy agents.

Novantrone® should be given slowly into a freely flowing intravenous infusion. It must *never* be given subcutaneously, intramuscularly, or intra-arterially. Severe local tissue damage may occur if there is extravasation during administration.

NOT FOR INTRATHECAL USE. Severe injury with permanent sequelae can result from intrathecal administration.

Except for the treatment of acute nonlymphocytic leukemia, Novantrone® therapy generally should not be given to patients with baseline neutrophil counts of less than 1,500 cells/mm3. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving Novantrone®.

Cardiotoxicity:

Congestive heart failure (CHF), potentially fatal, may occur either during therapy with Novantrone® or months to years after termination of therapy. Cardiotoxicity risk increases with cumulative Novantrone dose and may occur whether or not cardiac risk factors are present. Presence or history of cardiovascular disease, radiotherapy to the mediastinal/pericardial area, previous therapy with other anthracyclines or anthracenediones, or use of other cardiotoxic drugs may increase this risk. In cancer patients, the risk of symptomatic CHF was estimated to be 2.6% for patients receiving up to a cumulative dose of 140 mg/m2. To mitigate the cardiotoxicity risk with Novantrone, prescribers should consider the following:

All Patients:

– All patients should be assessed for cardiac signs and symptoms by history, physical examination, and ECG prior to start of Novantrone® therapy.

– All patients should have baseline quantitative evaluation of left ventricular ejection fraction (LVEF) using appropriate methodology (ex. Echocardiogram, multi-gated radionuclide angiography (MUGA), MRI, etc.).

Multiple Sclerosis Patients:

– MS patients with a baseline LVEF below the lower limit of normal should not be treated with Novantrone®.

– MS patients should be assessed for cardiac signs and symptoms by history, physical examination and ECG prior to each dose.

– MS patients should undergo quantitative reevaluation of LVEF prior to each dose using the same methodology that was used to assess baseline LVEF. Additional doses of Novantrone® should not be administered to multiple sclerosis patients who have experienced either a drop in LVEF to below the lower limit of normal or a clinically significant reduction in LVEF during Novantrone® therapy.

– MS patients should not receive a cumulative Novantrone dose greater than 140 mg/m2.

– MS patients should undergo yearly quantitative LVEF evaluation after stopping Novantrone to monitor for late occurring cardiotoxicity.

Definitions:

HCPCS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.

ICD-9 Code—International Classification of Disease, 9th edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

References:

1. Novantrone [package insert]. Rockland, MA: EMD Serono; March 2012. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/019297s035lbl.pdf.. June 6, 2012.
2. The NCCN Drugs & Biologics Compendium™ © 2010 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 23, 2012.
3. Local Coverage Article for Drugs and Biologicals – Chemotherapeutic Agents (A48896) (R4). Available at: http://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=48896&ver=89&ContrId=213&ContrVer=1&CntrctrSelected=213*1&Date=01%2f01%2f2013&DocID=A48896&bc=hAAAAAgAEAAAAA%3d%3d&. Accessed June 4, 2014.
4. Micromedex® 2.0 Novantrone. Available at: http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/3D2222/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/FC09A0/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.IntermediateToDocumentLink?docId=379240&contentSetId=100&title=Mitoxantrone+Hydrochloride&servicesTitle=Mitoxantrone+Hydrochloride. Accessed 6-6-12

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For the Archived Policy, please go to http://www.vivaprovider.com/Resources/CoveragePolicies.aspx and click on the Archived Policies Link.