

## Mitoxantrone (Novantrone)

### Disclaimer

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

### Summary

Mitoxantrone (Brand Name: Novantrone) is a chemotherapy drug approved for the treatment of certain types of multiple sclerosis, advanced prostate cancer, and acute nonlymphocytic leukemia (ANLL). There is also supporting evidence for its use in certain types of cancer or conditions. Mitoxantrone hydrochloride is given by intravenous (IV) infusion, and should not be used via subcutaneous, intramuscular, intra-arterial, or intrathecal injection. The manufacturer states that mitoxantrone hydrochloride for injection concentrate must be diluted prior to IV infusion.

### Definitions

“**Compendia**” are summaries of drug information and medical evidence to support decision-making about the appropriate use of drugs and medical procedures. Examples include, but are not limited to:

1. American Hospital Formulary Service Drug Information
2. Clinical pharmacology
3. National Comprehensive Cancer Network Drugs and Biologics Compendium
4. Thomson Micromedex DrugDex

5. United States Pharmacopeia-National Formulary (USP-NF)

“**FDA**” refers to the federal Food and Drug Administration.

“**Formulary**” refers to the list of medications and products available to members with or without Prior Authorization.

“**Relapse**” refers to an attack or exacerbation of MS (also known as a flare-up) resulting in the occurrence of new symptoms or the worsening of old symptoms.

“**RRMS**” or “**relapsing-remitting MS**” refers to the most common type of MS in which there are clearly defined attacks or relapses of increasing neurologic symptoms followed by periods of partial or complete recovery or remissions.

“**SPMS**” or “**secondary progressive MS**” refers to a version of disease progression that can follow an initial relapsing-remitting course in which there is a worsening of neurologic function and increased disability over time.

### Medical Necessity Criteria for Initial Authorization

The Plan considers mitoxantrone medically necessary when **ALL** the following criteria are met for the applicable indication listed below:

#### For Cancer:

1. The requested medication is prescribed by or in consultation with a hematology and/or oncology specialist; **AND**
2. The member has **ONE** of the following:
  - a. acute nonlymphocytic leukemia (ANLL) [includes myelogenous, promyelocytic, monocytic and erythroid leukemias]; **or**
  - b. advanced hormone-refractory prostate cancer; **or**
  - c. autologous stem cell transplant preparation in patients with relapsed/refractory lymphoma (i.e., in combination with melphalan as a myeloablative conditioning regimen during the transplant phase in patients with relapsed/refractory Hodgkin and non-Hodgkin lymphomas); **or**
  - d. chronic lymphocytic leukemia; **or**
  - e. metastatic hepatocellular cancer; **or**

- f. previously treated metastatic breast cancer; **or**
  - g. relapsed or refractory acute lymphoblastic leukemia; **or**
  - h. relapsed or refractory Hodgkin and non-Hodgkin lymphomas; **or**
  - i. relapsed, refractory, or poor-risk B-cell lymphomas; **or**
  - j. T-cell prolymphocytic leukemia (T-PLL)
3. The member has documentation of quantitative evaluation of left ventricular ejection fraction (LVEF) using appropriate methodology (e.g., echocardiogram, multigated radionuclide angiography (MUGA), or magnetic resonance imagery (MRI)) AND does not have a LVEF less than (<) 50%.

**If the above prior authorization criteria are met, mitoxantrone will be approved for 6-months.**

**For Multiple Sclerosis:**

1. The requested medication is prescribed by or in consultation with a neurologist; **AND**
2. The member has **ONE** of the following forms of multiple sclerosis:
  - a. secondary (chronic) progressive; **or**
  - b. progressive-relapsing; **or**
  - c. worsening or relapsing-remitting multiple sclerosis (RRMS); **AND**
3. The member has documentation of quantitative evaluation of left ventricular ejection fraction (LVEF) using appropriate methodology (e.g., echocardiogram, multigated radionuclide angiography (MUGA), or magnetic resonance imagery (MRI)) **AND** does not have a LVEF less than (<) 50%; **AND**
4. The member is unable to use or has tried and failed ALL appropriate formulary alternative (e.g., Aubagio, Betaseron, Copaxone, dimethyl fumarate, Gilenya, Mayzent, Rebif, Vumerity, Zeposia, Tysabri) for the given diagnosis; **AND**
5. The member has not received a cumulative lifetime dose of  $\geq 140$  mg/m<sup>2</sup>; **AND**
6. The requesting provider has submitted the necessary clinical documentation (e.g., chart notes, laboratory reports, disease progression, previous medications tried and failed, etc) for review.

**If the above prior authorization criteria are met, mitoxantrone will be approved for 3-months.**

## Medical Necessity Criteria for Reauthorization

### For Cancer:

Reauthorization for **six (6)** months will be granted if **BOTH** of the following are met:

1. the member still meets the applicable initial criteria; **AND**
2. recent chart documentation within the last three (3) months shows **ONE** of the following:
  - a. the member has **NOT** developed severe or life-threatening toxicity; **or**
  - b. the member has experienced severe or life-threatening toxicity **AND** the toxicity has been fully resolved

### For Multiple Sclerosis:

Reauthorization for **three (3)** months will be granted if **BOTH** of the following are met:

1. the member still meets the applicable initial criteria; **AND**
2. recent chart documentation within the last three (3) months shows **ONE** of the following:
  - a. The member has shown a clinical improvement (e.g., reduction in neurologic disability and/or the frequency of clinical relapses) in symptoms since starting the requested medication; **or**
  - b. The member has experienced disease stability since starting the requested medication.

**Table 1: Applicable Billing Codes (HCPCS/CPT Codes)**

<b>Code</b>	<b>Description</b>
J9293	Injection, mitoxantrone hydrochloride, per 5 mg

**Table 2: ICD-10-CM (diagnosis) Codes for Labeled and Off-Label use of Mitoxantrone (Novantrone)**

<b>Codes</b>	<b>Description</b>	<b>FDA or Compendia supported use</b>
C61	Malignant neoplasm of prostate	FDA
C92.90	Myeloid leukemia, unspecified, not having achieved remission	FDA
C92.91	Myeloid leukemia, unspecified in remission	FDA
C92.92	Myeloid leukemia, unspecified in relapse	FDA
G35	Multiple sclerosis	FDA

C22.0	Liver cell carcinoma	Compendia
C22.2	Hepatoblastoma	Compendia
C22.3	Angiosarcoma of liver	Compendia
C22.4	Other sarcomas of liver	Compendia
C22.7	Other specified carcinomas of liver	Compendia
C22.8	Malignant neoplasm of liver, primary, unspecified as to type	Compendia
C50.011	Malignant neoplasm of nipple and areola, right female breast	Compendia
C50.012	Malignant neoplasm of nipple and areola, left female breast	Compendia
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast	Compendia
C50.021	Malignant neoplasm of nipple and areola, right male breast	Compendia
C50.022	Malignant neoplasm of nipple and areola, left male breast	Compendia
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast	Compendia
C50.111	Malignant neoplasm of central portion of right female breast	Compendia
C50.112	Malignant neoplasm of central portion of left female breast	Compendia
C50.119	Malignant neoplasm of central portion of unspecified female breast	Compendia
C50.121	Malignant neoplasm of central portion of right male breast	Compendia
C50.122	Malignant neoplasm of central portion of left male breast	Compendia
C50.129	Malignant neoplasm of central portion of unspecified male breast	Compendia
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast	Compendia
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast	Compendia
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast	Compendia
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast	Compendia
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast	Compendia
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast	Compendia
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast	Compendia
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast	Compendia
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast	Compendia
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast	Compendia
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast	Compendia

C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast	Compendia
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast	Compendia
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast	Compendia
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast	Compendia
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast	Compendia
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast	Compendia
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast	Compendia
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast	Compendia
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast	Compendia
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast	Compendia
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast	Compendia
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast	Compendia
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast	Compendia
C50.611	Malignant neoplasm of axillary tail of right female breast	Compendia
C50.612	Malignant neoplasm of axillary tail of left female breast	Compendia
C50.619	Malignant neoplasm of axillary tail of unspecified female breast	Compendia
C50.621	Malignant neoplasm of axillary tail of right male breast	Compendia
C50.622	Malignant neoplasm of axillary tail of left male breast	Compendia
C50.629	Malignant neoplasm of axillary tail of unspecified male breast	Compendia
C50.811	Malignant neoplasm of overlapping sites of right female breast	Compendia
C50.812	Malignant neoplasm of overlapping sites of left female breast	Compendia
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast	Compendia
C50.821	Malignant neoplasm of overlapping sites of right male breast	Compendia
C50.822	Malignant neoplasm of overlapping sites of left male breast	Compendia
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast	Compendia
C50.911	Malignant neoplasm of unspecified site of right female breast	Compendia
C50.912	Malignant neoplasm of unspecified site of left female breast	Compendia
C50.919	Malignant neoplasm of unspecified site of unspecified female breast	Compendia
C50.921	Malignant neoplasm of unspecified site of right male breast	Compendia

C50.922	Malignant neoplasm of unspecified site of left male breast	Compendia
C50.929	Malignant neoplasm of unspecified site of unspecified male breast	Compendia
C79.81	Secondary malignant neoplasm of breast	Compendia
C81.00	Nodular lymphocyte predominant Hodgkin lymphoma, unspecified site	Compendia
C81.01	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of head, face, and neck	Compendia
C81.02	Nodular lymphocyte predominant Hodgkin lymphoma, intrathoracic lymph nodes	Compendia
C81.03	Nodular lymphocyte predominant Hodgkin lymphoma, intra-abdominal lymph nodes	Compendia
C81.04	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of axilla and upper limb	Compendia
C81.05	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C81.06	Nodular lymphocyte predominant Hodgkin lymphoma, intrapelvic lymph nodes	Compendia
C81.07	Nodular lymphocyte predominant Hodgkin lymphoma, spleen	Compendia
C81.08	Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of multiple sites	Compendia
C81.09	Nodular lymphocyte predominant Hodgkin lymphoma, extranodal and solid organ sites	Compendia
C81.20	Mixed cellularity Hodgkin lymphoma, unspecified site	Compendia
C81.21	Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck	Compendia
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes	Compendia
C81.23	Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes	Compendia
C81.24	Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb	Compendia
C81.25	Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C81.26	Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes	Compendia
C81.27	Mixed cellularity Hodgkin lymphoma, spleen	Compendia
C81.28	Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites	Compendia
C81.29	Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites	Compendia

C81.30	Lymphocyte depleted Hodgkin lymphoma, unspecified site	Compendia
C81.31	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck	Compendia
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes	Compendia
C81.33	Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes	Compendia
C81.34	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb	Compendia
C81.35	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C81.36	Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes	Compendia
C81.37	Lymphocyte depleted Hodgkin lymphoma, spleen	Compendia
C81.38	Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites	Compendia
C81.39	Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites	Compendia
C81.40	Lymphocyte-rich Hodgkin lymphoma, unspecified site	Compendia
C81.41	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck	Compendia
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes	Compendia
C81.43	Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes	Compendia
C81.44	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb	Compendia
C81.45	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C81.46	Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes	Compendia
C81.47	Lymphocyte-rich Hodgkin lymphoma, spleen	Compendia
C81.48	Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites	Compendia
C81.49	Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites	Compendia
C81.70	Other Hodgkin lymphoma, unspecified site	Compendia
C81.71	Other Hodgkin lymphoma, lymph nodes of head, face, and neck	Compendia
C81.72	Other Hodgkin lymphoma, intrathoracic lymph nodes	Compendia
C81.73	Other Hodgkin lymphoma, intra-abdominal lymph nodes	Compendia
C81.74	Other Hodgkin lymphoma, lymph nodes of axilla and upper limb	Compendia



C81.75	Other Hodgkin lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C81.76	Other Hodgkin lymphoma, intrapelvic lymph nodes	Compendia
C81.77	Other Hodgkin lymphoma, spleen	Compendia
C81.78	Other Hodgkin lymphoma, lymph nodes of multiple sites	Compendia
C81.79	Other Hodgkin lymphoma, extranodal and solid organ sites	Compendia
C81.90	Hodgkin lymphoma, unspecified, unspecified site	Compendia
C81.91	Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck	Compendia
C81.92	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes	Compendia
C81.93	Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes	Compendia
C81.94	Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb	Compendia
C81.95	Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb	Compendia
C81.96	Hodgkin lymphoma, unspecified, intrapelvic lymph nodes	Compendia
C81.97	Hodgkin lymphoma, unspecified, spleen	Compendia
C81.98	Hodgkin lymphoma, unspecified, lymph nodes of multiple sites	Compendia
C81.99	Hodgkin lymphoma, unspecified, extranodal and solid organ sites	Compendia
C82.50	Diffuse follicle center lymphoma, unspecified site	Compendia
C82.51	Diffuse follicle center lymphoma, lymph nodes of head, face, and neck	Compendia
C82.52	Diffuse follicle center lymphoma, intrathoracic lymph nodes	Compendia
C82.53	Diffuse follicle center lymphoma, intra-abdominal lymph nodes	Compendia
C82.54	Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb	Compendia
C82.55	Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C82.56	Diffuse follicle center lymphoma, intrapelvic lymph nodes	Compendia
C82.57	Diffuse follicle center lymphoma, spleen	Compendia
C82.58	Diffuse follicle center lymphoma, lymph nodes of multiple sites	Compendia
C82.59	Diffuse follicle center lymphoma, extranodal and solid organ sites	Compendia
C84.90	Mature T/NK-cell lymphomas, unspecified, unspecified site	Compendia
C84.91	Mature T/NK-cell lymphomas, unspecified, lymph nodes of head, face, and neck	Compendia

C84.92	Mature T/NK-cell lymphomas, unspecified, intrathoracic lymph nodes	Compendia
C84.93	Mature T/NK-cell lymphomas, unspecified, intra-abdominal lymph nodes	Compendia
C84.94	Mature T/NK-cell lymphomas, unspecified, lymph nodes of axilla and upper limb	Compendia
C84.95	Mature T/NK-cell lymphomas, unspecified, lymph nodes of inguinal region and lower limb	Compendia
C84.96	Mature T/NK-cell lymphomas, unspecified, intrapelvic lymph nodes	Compendia
C84.97	Mature T/NK-cell lymphomas, unspecified, spleen	Compendia
C84.98	Mature T/NK-cell lymphomas, unspecified, lymph nodes of multiple sites	Compendia
C84.99	Mature T/NK-cell lymphomas, unspecified, extranodal and solid organ sites	Compendia
C84.A0	Cutaneous T-cell lymphoma, unspecified, unspecified site	Compendia
C84.A1	Cutaneous T-cell lymphoma, unspecified lymph nodes of head, face, and neck	Compendia
C84.A2	Cutaneous T-cell lymphoma, unspecified, intrathoracic lymph nodes	Compendia
C84.A3	Cutaneous T-cell lymphoma, unspecified, intra-abdominal lymph nodes	Compendia
C84.A4	Cutaneous T-cell lymphoma, unspecified, lymph nodes of axilla and upper limb	Compendia
C84.A5	Cutaneous T-cell lymphoma, unspecified, lymph nodes of inguinal region and lower limb	Compendia
C84.A6	Cutaneous T-cell lymphoma, unspecified, intrapelvic lymph nodes	Compendia
C84.A7	Cutaneous T-cell lymphoma, unspecified, spleen	Compendia
C84.A8	Cutaneous T-cell lymphoma, unspecified, lymph nodes of multiple sites	Compendia
C84.A9	Cutaneous T-cell lymphoma, unspecified, extranodal and solid organ sites	Compendia
C84.Z0	Other mature T/NK-cell lymphomas, unspecified site	Compendia
C84.Z1	Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck	Compendia
C84.Z2	Other mature T/NK-cell lymphomas, intrathoracic lymph nodes	Compendia
C84.Z3	Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes	Compendia
C84.Z4	Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb	Compendia
C84.Z5	Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb	Compendia
C84.Z6	Other mature T/NK-cell lymphomas, intrapelvic lymph nodes	Compendia

C84.Z7	Other mature T/NK-cell lymphomas, spleen	Compendia
C84.Z8	Other mature T/NK-cell lymphomas, lymph nodes of multiple sites	Compendia
C84.Z9	Other mature T/NK-cell lymphomas, extranodal and solid organ sites	Compendia
C85.10	Unspecified B-cell lymphoma, unspecified site	Compendia
C85.11	Unspecified B-cell lymphoma, lymph nodes of head, face, and neck	Compendia
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes	Compendia
C85.13	Unspecified B-cell lymphoma, intra-abdominal lymph nodes	Compendia
C85.14	Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb	Compendia
C85.15	Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C85.16	Unspecified B-cell lymphoma, intrapelvic lymph nodes	Compendia
C85.17	Unspecified B-cell lymphoma, spleen	Compendia
C85.18	Unspecified B-cell lymphoma, lymph nodes of multiple sites	Compendia
C85.19	Unspecified B-cell lymphoma, extranodal and solid organ sites	Compendia
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site	Compendia
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck	Compendia
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes	Compendia
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes	Compendia
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb	Compendia
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes	Compendia
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen	Compendia
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites	Compendia
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites	Compendia
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site	Compendia
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck	Compendia
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph	Compendia

	nodes	
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes	Compendia
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb	Compendia
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb	Compendia
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes	Compendia
C85.87	Other specified types of non-Hodgkin lymphoma, spleen	Compendia
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites	Compendia
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites	Compendia
C85.90	Non-Hodgkin lymphoma, unspecified, unspecified site	Compendia
C85.91	Non-Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck	Compendia
C85.92	Non-Hodgkin lymphoma, unspecified, intrathoracic lymph nodes	Compendia
C85.93	Non-Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes	Compendia
C85.94	Non-Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb	Compendia
C85.95	Non-Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb	Compendia
C85.96	Non-Hodgkin lymphoma, unspecified, intrapelvic lymph nodes	Compendia
C85.97	Non-Hodgkin lymphoma, unspecified, spleen	Compendia
C85.98	Non-Hodgkin lymphoma, unspecified, lymph nodes of multiple sites	Compendia
C85.99	Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites	Compendia
C86.0	Extranodal NK/T-cell lymphoma, nasal type	Compendia
C86.1	Hepatosplenic T-cell lymphoma	Compendia
C86.2	Enteropathy-type (intestinal) T-cell lymphoma	Compendia
C86.3	Subcutaneous panniculitis-like T-cell lymphoma	Compendia
C86.4	Blastic NK-cell lymphoma	Compendia
C91.00	Acute lymphoblastic leukemia not having achieved remission	Compendia

C91.01	Acute lymphoblastic leukemia, in remission	Compendia
C91.02	Acute lymphoblastic leukemia, in relapse	Compendia
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission	Compendia
C91.11	Chronic lymphocytic leukemia of B-cell type in remission	Compendia
C92.00	Acute myeloblastic leukemia, not having achieved remission	Compendia
C92.01	Acute myeloblastic leukemia, in remission	Compendia
C92.02	Acute myeloblastic leukemia, in relapse	Compendia
C92.40	Acute promyelocytic leukemia, not having achieved remission	Compendia
C92.41	Acute promyelocytic leukemia, in remission	Compendia
C92.42	Acute promyelocytic leukemia, in relapse	Compendia
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission	Compendia
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission	Compendia
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse	Compendia
C94.20	Acute megakaryoblastic leukemia not having achieved remission	Compendia
C94.21	Acute megakaryoblastic leukemia, in remission	Compendia
C94.22	Acute megakaryoblastic leukemia, in relapse	Compendia
C94.30	Mast cell leukemia not having achieved remission	Compendia
C94.31	Mast cell leukemia, in remission	Compendia
C94.32	Mast cell leukemia, in relapse	Compendia
C94.40	Acute panmyelosis with myelofibrosis not having achieved remission	Compendia
C94.41	Acute panmyelosis with myelofibrosis, in remission	Compendia
C94.42	Acute panmyelosis with myelofibrosis, in relapse	Compendia
D05.00	Lobular carcinoma in situ of unspecified breast	Compendia
D05.01	Lobular carcinoma in situ of right breast	Compendia
D05.02	Lobular carcinoma in situ of left breast	Compendia
D05.10	Intraductal carcinoma in situ of unspecified breast	Compendia
D05.11	Intraductal carcinoma in situ of right breast	Compendia
D05.12	Intraductal carcinoma in situ of left breast	Compendia

D05.80	Other specified type of carcinoma in situ of unspecified breast	Compendia
D05.81	Other specified type of carcinoma in situ of right breast	Compendia
D05.82	Other specified type of carcinoma in situ of left breast	Compendia
D05.90	Unspecified type of carcinoma in situ of unspecified breast	Compendia
D05.91	Unspecified type of carcinoma in situ of right breast	Compendia
D05.92	Unspecified type of carcinoma in situ of left breast	Compendia

### Experimental or Investigational / Not Medically Necessary

Mitoxantrone (Novantrone) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

### References

1. Basch E, Loblaw DA, Oliver TK, et al. Systemic therapy in men with metastatic castration-resistant prostate cancer: American Society of Clinical Oncology and Cancer Care Ontario clinical practice guideline. *J Clin Oncol*. 2014;32(30):3436-3448.
2. Clinical Pharmacology [online]. Elsevier. 2021. Accessed July 2022. Available at: <http://www.clinicalpharmacology.com>
3. Cooper TM, Franklin J, Gerbing RB, et al. AAML03P1, a pilot study of the safety of gemtuzumab ozogamicin in combination with chemotherapy for newly diagnosed childhood acute myeloid leukemia: a report from the Children's Oncology Group. *Cancer*. 2012;118(3):761-769.
4. Fernandez de Larrea C, Martinez C, Gaya A, et al. Salvage Chemotherapy With Alternating MINE-ESHAP Regimen in Relapsed or Refractory Hodgkin's Lymphoma Followed By Autologous Stem-Cell Transplantation. *Ann Oncol*. 2010;21(6):1211-1216.
5. Griggs JJ, Bohlke K, Balaban EP, et al. Appropriate systemic therapy dosing for obese adult patients with cancer: ASCO guideline update. *J Clin Oncol*. 2021;39(18):2037-2048. doi:10.1200/JCO.21.00471
6. Hopfinger, G., Busch, R., Pflug, N., Weit, N., Westermann, A., Fink, A. M., ... & Herling, M. (2013). Sequential chemoimmunotherapy of fludarabine, mitoxantrone, and cyclophosphamide induction followed by alemtuzumab consolidation is effective in T-cell prolymphocytic leukemia. *Cancer*, 119(12), 2258-2267.
7. Lexicomp Online Database [database on the Internet]. Hudson (OH): Lexicomp Inc.: 2022. Available from: <http://online.lexi.com>. Updated periodically. Accessed: August 2022.
8. Mandelli F, Vignetti M, Suci S, et al, "Daunorubicin versus Mitoxantrone versus Idarubicin as Induction and Consolidation Chemotherapy for Adults With Acute Myeloid Leukemia: The EORTC and GIMEMA Groups Study AML-10," *J Clin Oncol*, 2009, 27(32):5397-403.
9. Mitoxantrone [prescribing information]. Lake Forest, IL: Hospira Inc; April 2021.

10. Peccatori FA, Azim HA Jr, Orecchia R, et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013;24 Suppl 6:vi160-167.
11. Pérez Fidalgo JA, García Fabregat L, Cervantes A, et al. Management of Chemotherapy Extravasation: ESMO-EONS Clinical Practice Guidelines. *Ann Oncol.* 2012;23(suppl 7):167-173.
12. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Published April 2018.
13. Rossato, L. G., Costa, V. M., de Pinho, P. G., Arbo, M. D., de Freitas, V., Vilain, L., ... & Remiao, F. (2013). The metabolic profile of mitoxantrone and its relation with mitoxantrone-induced cardiotoxicity. *Archives of toxicology*, 87(10), 1809-1820.
14. Shaikh, A. Y., Suryadevara, S., Tripathi, A., Ahmed, M., Kane, J. L., Escobar, J., ... & Aurigemma, G. P. (2016). Mitoxantrone-Induced Cardiotoxicity in Acute Myeloid Leukemia—A Velocity Vector Imaging Analysis. *Echocardiography*, 33(8), 1166-1177.
15. Vitolo U, Chiappella A, Angelucci E, et al. Dose-Dense and High-Dose Chemotherapy Plus Rituximab With Autologous Stem Cell Transplantation for Primary Treatment of Diffuse Large B-Cell Lymphoma With a Poor Prognosis: A Phase II Multicenter Study. *Haematologica.* 2009;94(9):1250-1258.

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