## BACKGROUND

Neulasta is a leukocyte growth factor, sometimes referred to as a colony stimulating factor (CSF). Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. Neulasta is indicated to be administered as a single subcutaneous (SC) injection (6 mg) once per chemotherapy cycle. Neulasta should not be administered in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy. Common adverse events (AEs) noted in placebo-controlled trials with Neulasta include bone pain and extremity pain. Data are available for Neulasta in pediatric patients. However, the Neulasta prescribing information notes that the safety and effectiveness of Neulasta in pediatric patients have not been established.

## REQUIRED REVIEW AND APPROVALS

This policy involves the use of Neulasta. Prior authorization is recommended for medical benefit coverage of Neulasta. Coverage is recommended for those who meet the conditions of coverage in the Criteria, Dosing, Initial/Extended Approval, Duration of Therapy, and Labs/Diagnostics for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. Waste Management applies for all covered conditions. Conditions Not Recommended for Approval are listed following the recommended authorization criteria and Waste Management section.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Neulasta as well as the monitoring required for AEs and long-term efficacy, initial approval requires Neulasta to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is required, a response to therapy is required for continuation of therapy.

## DEFINITIONS

None.
INDICATIONS/Criteria
Coverage of Neulasta is recommended in those who meet one of the following criteria:

FOOD AND DRUG ADMINISTRATION (FDA)-APPROVED INDICATIONS

1. Patients with Cancer (Adults and Children) Receiving Myelosuppressive Chemotherapy.

Criteria. The patient must meet the following criteria (A AND B):

A) The agent is prescribed by, or in consultation with, an oncologist or hematologist; AND

B) The patient meets ONE of the following conditions (i, ii, or iii):

i. The patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (i.e., the risk of febrile neutropenia is at least 20% based on the chemotherapy regimen); OR

ii. The patient is receiving myelosuppressive anti-cancer medications that are associated with a risk of febrile neutropenia but the risk is less than 20% based on the chemotherapy regimen and the patient has one or more risk factors for febrile neutropenia according to the prescribing physician (e.g., older patient [aged ≥ 65 years]; history of previous chemotherapy or radiation therapy; pre-existing neutropenia; open wounds or active infection; poor performance status); OR

iii. The patient has had a neutropenic complication from prior chemotherapy and did not receive prophylaxis with a colony stimulating factor (Leukine® [sargramostim injection], Neulasta, Neupogen® [filgrastim injection], Zarxio™ [filgrastim-sndz injection] and Granix® [tbo-filgrastim]) and a reduced dose or frequency of chemotherapy may compromise treatment outcome.

Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.1-3 The National Comprehensive Cancer Network (NCCN) guidelines for myeloid growth factors (version 2.2014), recommends use of CSF in various scenarios in patients with cancer receiving myelosuppressive chemotherapy.2 Data are also available in children.1,4-7 In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.

Dosing in Patients with Cancer Receiving Myelosuppressive Chemotherapy: Dosing must meet ONE of the following (A OR B):
A) In adults, the dose is a single SC injection of 6 mg administered once per chemotherapy cycle\(^1\); OR

B) In infants, children, and smaller adolescents weighing < 45 kg, a single 100 mcg per kg dose is given once per chemotherapy cycle; maximum dose is 6 mg.\(^1\)\(^2\)\(^4\)\(^7\)

According to the NCCN guidelines for myeloid growth factors (version 2.2014), the majority of trials administered Neulasta the day after chemotherapy but Neulasta can also be administered up to 3 to 4 days after chemotherapy.\(^2\) Limited data suggest that same-day administration of Neulasta may be considered in specific situations. Usually Neulasta is used for chemotherapy regimens given every 3 weeks. Some data demonstrates efficacy for chemotherapy regimens given every 2 weeks. Use of Neulasta with weekly chemotherapy is not recommended.

**Initial Approval/Extended Approval.**

A) *Initial Approval.* Approval is for up to 6 months at one dose per each chemotherapy cycle. Multiple doses in the same cycle are not recommended.

B) *Extended Approval.* Approval is for up to 6-month intervals if the patient continues to receive myelosuppressive chemotherapy.

**Duration of Therapy in Patients with Cancer Receiving Myelosuppressive Chemotherapy.** Therapy may continue as long as the patient is receiving myelosuppressive chemotherapy with one dose per cycle.

**Labs/Diagnostics.** None required.

**Other Uses with Supportive Evidence**

2. **Patients with Cancer Following Peripheral Blood Progenitor Cell (PBPC) Transplantation.**

**Criteria.** *The patient must meet the following criteria:* Neulasta is prescribed by, or in consultation with, an oncologist, a hematologist, or a physician that specializes in transplantation.

Neulasta has been studied in patients with cancer undergoing high dose chemotherapy, followed by infusion of stem cell transplantation, which was usually autologous.\(^8\)\(^-\)\(^20\) Results have been similar to that noted with use of daily Neupogen. Neulasta was usually administered on Day 1 and sometimes up to Day 5 after stem cell transplantation. In the professional opinion of specialist physicians reviewing the data, we have adopted these criteria.
Dosing in Patients with Cancer Following PBPC Transplantation. *Dosing must meet ONE of the following (A OR B)*:8-20
A) The dose in adults is 6 mg SC on Day +1 or up to Day +5 after PBPC transplantation, OR
B) The dose in children is 100 mcg per kg or 200 mcg per kg SC one time.

Initial Approval/Extended Approval.
A) *Initial Approval*. Initial approval is for one dose.
B) *Extended Approval*. Not applicable.

Duration of Therapy in Patients with Cancer Following PBPC Transplantation. Usually only one dose of Neulasta is needed until the absolute neutrophil count (ANC) is adequate.8-20

Labs/Diagnostics. None required.

3. **Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).**

Criteria. *The patient must meet the following criteria*: Neulasta is prescribed by, or in consultation with, a physician with expertise in treating acute radiation syndrome.

The Strategic National Stockpile Radiation Working Group published recommendations for the medical management of acute radiation syndrome in 2004.21 In any adult with a whole body or significant partial body-exposure greater than 3 Grays, therapy with a CSF should be started as soon as biodosimetry results indicate that exposure has occurred or when clinical signs and symptoms indicate a level 3 or 4 degree of hematotoxicity. People at the extremes of age (children aged < 12 years and adults aged > 60 years) may be more susceptible to irradiation and therefore a lower threshold exposure dose (2 Grays) for initiation of CSF therapy is appropriate, as well as in patients who have major trauma injuries or burns.21 The Radiation Injury Treatment Network updated guidelines in September 2010 for the treatment of acute radiation syndrome (injury). CSF therapy is recommended in a variety of clinical scenarios in patients who have experienced radiation injury (syndrome) based on factors such as the radiation dose.22 In the professional opinion of specialist physicians reviewing the data, we have adopted this criterion.

Dosing in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome): The dose of Neulasta in adults and adolescents who weigh > 45 kg is a single SC injection of 6 mg.21

Initial Approval/Extended Approval.
A) *Initial Approval*. Initial approval is for one dose.
B) **Extended Approval.** Not applicable.

**Duration of Therapy in Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).** Usually only one dose of Neulasta is needed until the ANC is adequate.

**Labs/Diagnostics.** None required.

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**Waste Management for All Indications.**
Neulasta is available as a 6 mg syringe. This dose should be sufficient in most situations.

**SPECIAL CONSIDERATIONS**

Neulasta has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.).

1. **Myelodysplastic syndrome (MDS).** Only limited data report use of Neulasta for patients with MDS. Guidelines from the NCCN for MDS (version 1.2016) do not mention use of Neulasta in this patient population.

2. **Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria.** Criteria will be updated as new published data are available.

**LIMITATIONS/EXCLUSIONS**

Please refer to a product line’s certificate of coverage for benefit limitations and exclusions for these services:

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REFERENCES


**OTHER REFERENCES UTILIZED**

**REVISION HISTORY**

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