DRUG DETERMINATION POLICY

Title: DDP-15 Chemotherapy-Induced Myelosuppression Agents

Effective Date: 05/02/2022

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve Benefits. Coverage depends on the specific Benefit plan. Pharmacy Benefit Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Granulocyte colony-stimulating factor (G-CSF) and Cyclin-Dependent Kinase (CDK) Inhibitor agents are specialty drugs indicated for a number of diagnoses and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Granulocyte colony-stimulating factor (GCS-F agents).

A. Filgrastim subcutaneous (Nivestym SQ).

1. Prescription drug benefit coverage:

a. Preferred specialty agent: Nivestym.

b. Excluded filgrastim products: Neupogen, Zarxio, Granix.

- All preferred products contraindicated, inadequate response or had significant adverse effects.

2. Medical benefit coverage: billing through the outpatient prescription drug benefit only.

3. Quantity limits:

a. Covered without prior authorization: ten syringes per 24 days.

b. Prior authorization required: above ten syringes per 24 days.

B. Pegfilgrastim subcutaneous (Ziextenzo SQ).

1. Prescription drug benefit coverage:

a. Preferred specialty agent: Ziextenzo.

b. Excluded specialty agent: Fulphilia, Udenyca, Neulasta, Neulasta Onpro.

- All preferred products contraindicated, inadequate response or had significant adverse effects.

2. Medical benefit coverage: billing through the outpatient prescription drug benefit only.

3. Quantity limits.

a. Covered without prior authorization: one syringe per 24 days.

b. Prior authorization required: above one syringe per 24 days.

C. Approval.

1. Initial and re-approval: six months or less depending on the number of cycles requested.

II. Cyclin-Dependent Kinase (CDK) Inhibitor: Cosela intravenous (trilaciclib IV).

A. Age: at least 18 years.

B. Diagnosis and severity [must meet all listed below]:

1. Extensive stage small cell lung cancer.

2. Used to decrease the incidence of chemo-induced myelosuppression.

3. Chemo regimen: platinum/etoposide-containing regimen or topotecan containing regimen.

C. Other therapies: none.

D. Dosage regimen:

1. Cosela intravenous (trilaciclib IV): 240mg per m^2 per dose given four hours prior to the specifically indicated chemo regimen; repeat on each day chemotherapy is given.

2. Timing: the interval between sequential trilaciclib doses should not be above 28 hours; if discontinued, allow 96 hours after the last trilaciclib dose before resuming chemotherapy.

E. Approval.

1. Initial and re-approval: six months or less depending on the number of cycles requested.

F. Exclusions.

1. Concomitant medications: use in conjunction with granulocyte colony-stimulating factor agents or erythropoiesis-stimulating agents.

III. Appropriate medication use [must meet one listed below]:

A. Food and Drug Administration (FDA) approval status [must meet one listed below]:

1. FDA approved: product, indication, and/or dosage regimen.

2. Non-FDA approved: compendium support (Lexicomp™) for use of a drug for a non-FDA approved indication or dosage regimen.

B. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

4.0 Coding:

Filgrastim and pegfilgrastim products are covered under the outpatient prescription drug benefit only.

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; filgrastim, perfilgrastim and Cosela accessed June 2021.
2. Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; pegfilgrastim, accessed March 2021.
3. Amgen https://www.neulastahcp.com/febrile-neutropenia/?febrile+neutropenia+informationUNB_HCP_Awareness_General_PHM_05.2020FN+General_PHM&utm_source=bing&utm_medium=cpc&utm_campaign=UNB_HCP_Awareness_General_PHM_05.2020&utm_term=febrile%20neutropenia%20information&utm_content=FN%20General_PHM&gclid=CL3u76_-yuwCFZqPxQId6EwCuQ&gclsrc=ds. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology accessed October 20 (NCCN Guidelines®) for Myeloid Growth Factors V.2.2018. ©National Comprehensive Cancer Network, Inc. 2018. All rights reserved. Accessed August 3, 2018. To view the most recent and complete version of the guideline, go online to NCCN.org. ©NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

6.0 Appendices:

See pages 5-7.

7.0 Revision History:

Original Effective Date: 12/14/2005

Next Review Date: 03/24/2023

Revision Date	Reason for Revision
March 2019	Transfer to new format
April 2019	Presented and approved at P & T Workgroup
12/19	Off cycle review; addition of biosimilars; change to consistent verbiage, replace abbreviations.
3/20	Annual review; revised indication, added adult and pediatric dosage regimen
10/20	Off cycle review, clarified preferred agents, non-preferred criteria & criteria instructions; added filgrastim to Monitoring and Patient safety appendix, added D. appropriate medication use, approved at 10/28/20 P&T
2/21	Annual review; updated formulary status, removed diagnosis and severity as well as dosage regimen for pegfilgrastim; approved at 4/28/21 P&T
6/21	Ad hoc review; added drug Cosela, formatting, changed appropriate use section

Revision Date	Reason for Revision
	to included compendium language, changed title from GCS-F agents, modified purpose, corrected typo
02/23/2022	Annual review, formatting

Appendix I: Monitoring and Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Pegfilgrastim SQ (Neulasta, Fulphila, Udenyca, Ziextenzo)	• Musculoskeletal: ostealgia (31%) • Pregnancy Category: C	• Gastrointestinal (GI): abdominal pain • Hematology: monitor for sickle cell crisis, splenomegaly • Hypersensitivity • Musculoskeletal: shoulder pain • Pregnancy: adverse event in animal studies • Renal: glomerulonephritis • Respiratory: pulmonary infiltrates, respiratory distress • Myelosuppressive Chemotherapy: complete blood count (CBC) with difference and platelets prior to and as needed • Hematopoietic Radiation Injury Syndrome: CBC at baseline, established absorbed radiation dose	None needed
Filgrastim SQ (Neupogen, Nivestym , Granix, Zarxio)	• Cardiovascular: chest pain (5-13% • Central Nervous System: fatigue (20%) dizziness (14%), pain (12%) • Dermatologic: skin rash (2%-14%) • Gastrointestinal: nausea (43%) • Hematologic & Oncologic: thrombocytopenia (5%-38%), splenomegaly (≥5%; severe chronic neutropenia: 30%) • Hepatic: increased serum alkaline phosphatase (6%-11%) • Neuromuscular & Skeletal: ostealgia (11%-30%), back pain (2%-15%) • Respiratory: epistaxis (≥5%), cough (14%), dyspnea (13%) • Miscellaneous: fever (8%-48%)	•	
Cosela trilaciclib IV	• Cardiovascular: hypertension (6% to 28%) • Central nervous system: headache (5% to 18%)	• Cardiovascular: blood pressure • Labs: transferrin saturation and serum ferritin (prior and during),	None needed

Drug	Adverse Reactions	Monitoring	REMS
	• Dermatologic: pruritus (16% to 21%), skin rash (2% to 19%) • Gastrointestinal: nausea (35% to 56%), vomiting (19% to 28%) • Local: injection site pain (9% to 13%) • Neuromuscular & Skeletal: arthralgia (10% to 16%) • Respiratory: cough (4% to 26%) • Miscellaneous: fever (10% to 42%)	Hgb (weekly and post dose adjustment • Neurological: monitor signs of seizure	

Appendix II Risk Assessment for chemotherapy-induced Neutropenia

According to the American Society of Clinical Oncology (ASCO) and the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Evaluate the risk of FN and administer primary CSF prophylaxis in first and subsequent cycles for patients at > 20% risk[1,2]

When assessing risk, evaluate both chemotherapy regimen and patient risk factors[2]

Select chemotherapy regimens associated with a HIGH RISK OF FN	Select chemotherapy regimens associated with an INTERMEDIATE RISK OF FN
Breast cancer	**Breast cancer**
• TAC (docetaxel + doxorubicin + cyclophosphamide) Q3W[2,3,*] • TC (docetaxel + cyclophosphamide) Q3W[2,4,*] • TCH*± P† (docetaxel + carboplatin + trastuzumab with or without pertuzumab)[2,5,6]	• AC (doxorubicin + cyclophosphamide) + sequential docetaxel[11,†]
Non-Hodgkin's lymphoma	**Non-small cell lung cancer**
• BR (bendamustine + rituximab)[7,†] • CHOP*,† ± R† (cyclophosphamide + doxorubicin + vincristine + prednisolone with or without rituximab) Q3W[2,8,9]	• Cisplatin + etoposide[2,*] • Cisplatin + docetaxel[2,12,*] • Carboplatin + docetaxel[13,†]
Non-small cell lung cancer	**Prostate cancer**
• Carboplatin + paclitaxel Q3W[10,†]	• Cabazitaxel[2,*] • Docetaxel + prednisone[14,†]
Small cell lung cancer	**Small cell lung cancer**
• Topotecan[2,*]	• Carboplatin + etoposide[2,*]

Even one of these select risk factors can increase risk:[2,§]

- Baseline cytopenias[16,17]
- Poor performance status (ECOG ≥ 2)[18]
- Age ≥ 65 years[17]
- COPD[19,**]
- Chronic immunosuppression in the post-transplant setting, including organ transplant[16]
- Liver disease[20]
- Renal disease[17]
- Cardiovascular disease[17,**]
- Diabetes[21,**]
- Prior chemotherapy[22]
- Prior radiotherapy[16]
- Poor nutritional status[23,**]
- Decreased serum albumin[23,**]
- Open wounds/recent surgery[24]
- Active infections[25,**]
- HIV[20]
- Metastatic[18,**]
- Elevated lactate dehydrogenase[23,**]

§The patient risk factors included here have been identified through published literature and clinical guidelines. This list is not exhaustive. There may be other risk factors that apply based on available research and the clinical judgment of the treating physicians. These risk factors in addition to high or intermediate risk chemotherapy regimens can increase the risk of infection.

**Risk factors not listed by the NCCN.

COPD, chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus.