PHARMACY POLICY STATEMENT **Indiana Medicaid**	
DRUG NAME	Zarxio (filgrastim-sndz)
BILLING CODE	For medical - Q5101 For Rx - must use valid NDC
BENEFIT TYPE	Medical or Pharmacy
SITE OF SERVICE ALLOWED	Home/Office/Outpatient Hospital
COVERAGE REQUIREMENTS	Prior Authorization Required (Preferred Product) QUANTITY LIMIT— N/A
LIST OF DIAGNOSES CONSIDERED **NOT** MEDICALLY NECESSARY	Click Here

Zarxio (filgrastim-sndz) is a **preferred** product and will only be considered for coverage under the **medical or pharmacy** benefit when the following criteria are met:

Members must be clinically diagnosed with one of the following disease states and meet their individual criteria as stated.

ACUTE MYELOID LEUKEMIA

For **initial** authorization:

1. Member has diagnosis of AML documented in chart notes; AND
2. Medication is being used to reduce the time to neutrophil recovery and the duration of fever following induction or consolidation chemotherapy treatment; AND
3. Medication is being administered 24 hours after the last dose of chemotherapy until neutrophil recovery (ANC ≥ 1000/mm^3 for 3 consecutive days or ≥ 10,000/mm^3 for 1 day) or for a maximum of 35 days; AND
4. Chart notes with the length of chemotherapy cycle, the days of the cycle on which chemotherapy will be administered, and the days of the cycle on which Zarxio will be administered are submitted with the prior authorization request.
5. **Dosage allowed:** 5 mcg/kg/day subcutaneous injection, short intravenous infusion (15 to 30 minutes), or continuous intravenous infusion.

If member meets all the requirements listed above, the medication will be approved for 3 months.

For **reauthorization**:

1. Member must be in compliance with all initial criteria; AND
2. Chart notes have been provided that show the member is stable or has shown improvement on Zarxio therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

AUTOLOGOUS BONE MARROW TRANSPLANT (BMT)

For **initial** authorization:

1. Member has diagnosis of non-myeloid malignancy and is undergoing myeloablative chemotherapy followed by autologous BMT; AND
2. Medication is being used to reduce duration of neutropenia following autologous BMT.
3. **Dosage allowed:** 10 mcg/kg/day beginning at least 24 hours after cytotoxic chemotherapy and 24 hours after bone marrow infusion.

If member meets all the requirements listed above, the medication will be approved for 3 months.

For **reauthorization**:

1. Member must be in compliance with all initial criteria; AND
2. Chart notes have been provided that show the member is stable or has shown improvement on Zarxio therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

AUTOLOGOUS PERIPHERAL BLOOD PROGENITOR CELL (PBPC) MOBILIZATION

For **initial** authorization:

1. Medication is being used to mobilize autologous peripheral blood progenitor cells for collection by leukapheresis; AND
2. Medication is being administered for at least 4 days before first leukapheresis and continued until the last leukapheresis (until a sustainable ANC (≥ 1000/mm^3) is reached).
3. **Dosage allowed:** 10 mcg/kg/day subcutaneous injection.

If member meets all the requirements listed above, the medication will be approved for 3 months.

For **reauthorization**:

1. Member must be in compliance with all initial criteria; AND
2. Chart notes have been provided that show the member is stable or has shown improvement on Zarxio therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

PREVENTION OF FEBRILE NEUTROPENIA

For **initial** authorization:

1. Member has a non-myeloid malignancy; AND
2. Medication will not be administered within 24 hours before or after chemotherapy; AND
3. Chart notes with the length of chemotherapy cycle, the days of the cycle on which chemotherapy will be administered, and the days of the cycle on which Zarxio will be administered are submitted with the prior authorization request; AND
4. Member is receiving myelosuppressive chemotherapy and has a history of febrile neutropenia (defined as an ANC < 1000/mm^3 and temperature > 38.2°C) following a previous course of chemotherapy; OR
5. Member is receiving a myelosuppressive chemotherapy regimen that is associated with a high risk (>20%) of febrile neutropenia; OR
6. Member is receiving a myelosuppressive chemotherapy regimen that is associated with an intermediate risk (10-20%) of febrile neutropenia AND has at least **one** of the following risk factors:
   a) Prior chemotherapy or radiation therapy;
   b) Persistent neutropenia;
   c) Tumor involving the bone marrow;
   d) Recent surgery and/or open wounds;
   e) Liver dysfunction (i.e. documented bilirubin >2.0);
   f) Renal dysfunction (i.e. documented creatinine clearance <50 mL/min);
   g) Age >65 years receiving full intensity dose of chemotherapy.
7. **Dosage allowed:** 5 mcg/kg per day.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:
1. Member must be in compliance with all initial criteria; AND
2. Chart notes have been provided that show the member is stable or has shown improvement on Zarxio therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

SEVERE CHRONIC NEUTROPENIA

For **initial** authorization:
1. Member has a history of SCN (i.e. congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia) with chart notes confirming **both** of the following:
   a) Absolute neutrophil count (ANC) < 500/mm^3 on three occasions during a 6 month period (or for cyclic neutropenia 5 consecutive days of ANC < 500/mm^3 per cycle); AND
   b) Member must have experienced a clinically significant infection during the previous 12 months.
2. **Dosage allowed:** Idiopathic neutropenia: 5 mcg/kg per day as a single dose; Cyclic neutropenia: 5 mcg/kg per day as a single dose; Congenital neutropenia: 6 mcg/kg per day in 2 divided doses.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:
1. Member must be in compliance with all initial criteria; AND
2. Chart notes have been provided that show the member is stable or has shown improvement on Zarxio therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

CareSource considers Zarxio (filgrastim-sndz) not medically necessary for the treatment of the following disease states based on a lack of robust clinical controlled trials showing superior efficacy compared to currently available treatments:

- Agranulocytosis
- AIDS - Neutropenia
- Aplastic anemia
- Febrile neutropenia
- Febrile neutropenia, In myeloid malignancies following bone marrow transplant; Prophylaxis
- Hematopoietic Syndrome of Acute Radiation Syndrome
- Infectious disease; Prophylaxis
- Leukemia
- Myelodysplastic syndrome
- Neutropenia - Pre-eclampsia

DATE	ACTION/DESCRIPTION
10/19/2017	New policy for Zarxio created. Age limits and degree of hematotoxicity was removed; radiation exposure level requirement was decreased. Criteria coverage for Prevention of Febrile Neutropenia was expanded. Chemotherapy regimens with high and intermediate risk of febrile neutropenia were added to the policy's appendix. List of not covered diagnoses was added.

References:

1. Zarxio (filgrastim-sndz) [prescribing information]. Princeton, NJ: Sandoz Inc; March 2016.
2. Schmitz N, Linch DC. Randomised trial of filgrastim-mobilized peripheral blood progenitor cell transplantation versus autologous bone-marrow transplantation in lymphoma patients. Lancet. 1996;347(8998): 353-358. Doi: 10.1016/S0140-6736(96)90536-X.
3. Blackwell K, Semiglazov V, Krasnozhon D, et al. Comparison of EP2006, a filgrastim biosimilar, to the reference: a phase III, randomized, double-blind clinical study in the prevention of severe neutropenia in patients with breast cancer receiving myelosuppressive chemotherapy. Ann Oncol. 2015;26:1948-1953. Doi: 10.1093/annonc/mdv281.
4. Dale DC, Bonilla MA, Davis MW, et al. A randomized controlled phase III trial of recombinant human granulocyte colony-stimulating factor (filgrastim) for treatment of severe chronic neutropenia. 1993;81(10):2496-2502.
5. Crawford J, Becker PS, Armitage JO, et al. Myeloid growth factors. NCCN Clinical Practice Guidelines in Oncology. Available from www.nccn.org. Published April 28, 2017. Accessed July 27, 2017.
6. Harada K, Yamada Y, Konishi T, et al. Comparison of transplant outcomes and economic costs between biosimilar and originator filgrastim in allogeneic hematopoietic stem cell transplantation. Int J Hematol. 2016;104:709-719. Doi: 10.1007/s/12185-016-2085-0.
7. Radiation Emergency Medical Management. Myeloid cytokines for acute exposure to myelosuppressive doses of radiation (hematopoietic subsyndrome of ARS). U.S. Department of Health and Human Services. Available from https://www.remm.nlm.gov/cytokines.htm. Updated February 22, 2017. Accessed July 27, 2017.
8. Filgrastim-sndz. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: http://www.micromedexsolutions.com. Accessed March 15, 2017.

Effective date: 01/01/2018
Revised date: 10/19/2017

CareSource

Appendix

Chemotherapy Regimens with a High Risk for Febrile Neutropenia (>20%)

Cancer Type	Regimen
Acute Lymphoblastic Leukemia (ALL)	ALL induction regimens (see NCCN guidelines)
Bladder Cancer	MVAC (methotrexate, vinblastine, doxorubicin, cisplatin) (neoadjuvant, adjuvant, metastatic)
Breast Cancer	Docetaxel + trastuzumab (metastatic or relapsed)
	Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel) (adjuvant)
	TAC (docetaxel, doxorubicin, cyclophosphamide) (adjuvant)
Esophageal and Gastric Cancers	Docetaxel/cisplatin/fluorouracil
Hodgkin Lymphoma	BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
Kidney Cancer	Doxorubicin/gemcitabine
Non-Hodgkin's Lymphoma	ICE (ifosfamide, carboplatin, etoposide) (diffuse large B-cell lymphoma [DLBCL], peripheral T-cell lymphomas [PTCL], 2nd line)
	RICE (rituximab, ifosfamide, carboplatin, etoposide)
	CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
	MINE (mesna, ifosfamide, novantrone, etoposide) (DLBCL, 2nd line, refractory)
	DHAP (dexamethasone, cisplatin, cytarabine)
	ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C)) (DLBCL, PTCL, 2nd line, recurrent)
	HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
Melanoma	Dacarbazine-based combination (dacarbazine, cisplatin, vinblastine) (advanced, metastatic, or recurrent)
	Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha) (advanced, metastatic, or recurrent)
Ovarian Cancer	Topotecan
	Paclitaxel
	Docetaxel
Soft Tissue Sarcoma	MAID (mesna, doxorubicin, ifosfammide, dacarbazine)
	Doxorubicin
	Ifosfamide/doxorubicin
Small Cell Lung Cancer	topotecan
Testicular cancer	VelP (vinblastine, ifosfamide, cisplatin)
	VIP (etoposide, ifosfamide, cisplatin)
	BEP (bleomycin, etoposide, cisplatin)

	TIP (paclitaxel, ifosfamide, cisplatin)

National Comprehensive Cancer Network (NCCN): Myeloid Growth Factors, 2016.

Chemotherapy Regimens with an Intermediate Risk of Febrile Neutropenia (10% to 19%)

Cancer Histology	**Regimen**
Occult primary - adenocarcinoma	Gemcitabine/docetaxel
Breast cancer	Docetaxel every 21 days
	CMF classic (cyclophosphamide, methotrexate, fluorouracil) (adjuvant)
	AC (doxorubicin, cyclophosphamide) + sequential docetaxel (adjuvant) (taxane portion only)
	AC + sequential docetaxel + trastuzumab (adjuvant)
	FEC (fluorouracil, epirubicin, cyclophosphamide) + sequential docetaxel
	TC (docetaxel, cyclophosphamide)
Cervical Cancer	Cisplatin/topotecan (recurrent or metastatic)
	Paclitaxel/cisplatin
	Topotecan (recurrent or metastatic)
	Irinotecan (recurrent or metastatic)
Colorectal	FOLFOX (fluorouracil, leucovorin, oxaliplatin)
Esophageal and Gastric Cancers	Irinotecan/cisplatin
	Epirubicin/cisplatin/5-fluorouracil
	Epirubicin/cisplatin/capecitabine
Multiple myeloma	DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophoaphamide/etoposide)
	DT-PACE + bortezomib (VTD-PACE)
Non-Hodgkin's lymphomas	EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) (AIDS-related NHL, Burkitt lymphoma, recurrent, otherr NHL subtypes)
	EPOCH-IT chemotherapy (AIDS-related NHL, DLBCL, recurrent)
	GDP (gemcitabine, dexamethasone, cisplatin) (DLBCL, PTCL, 2nd line)
	GDP (gemcitabine, dexamethasone, cisplatin) + rituximab (DLBCL, 2nd line, Burkitt lymphoma, other NHL subtypes)
	FMR (fludarabine, mitoxantrone, rituximab)
	CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin or mitoxantrone substituted for doxorubicin
Non-Small Cell Lung Cancer	Cisplatin/paclitaxel (advanced/metastatic)
	Cisplatin/vinorelbine (adjuvant, advanced/metastatic)
	Cisplatin/docetaxel (adjuvant, advanced/metastatic)
	Cisplatin/etoposide (adjuvant, advanced/metastatic)

	Carboplatin/paclitaxel (adjuvant, advanced/metastatic)
	Docetaxel (advanced/metastatic)
Ovarian Cancer	Carboplatin/docetaxel
Pancreatic Cancer	FOLFIRINOX
Prostate Cancer	Cabazitaxel
Small Cell Lung Cancer	Etoposide/carboplatin
Testicular Cancer	Etoposide/cisplatin
Uterine Sarcoma	Docetaxel (advanced or metastatic)

National Comprehensive Cancer Network (NCCN): Myeloid Growth Factors, 2016.