Clinical Policy: Ruxolitinib (Jakafi, Opzelura)

Reference Number: CP.PHAR.98
Effective Date: 03.01.12
Last Review Date: 02.24
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ruxolitinib (Jakafi®, Opzelura™) is a Janus kinase (JAK) inhibitor.

FDA Approved Indication(s)

Jakafi is indicated for the treatment of:

- Intermediate or high-risk myelofibrosis (MF) in adults, including:
  - Primary MF
  - Post-polycythemia vera MF (post-PV MF)
  - Post-essential thrombocythemia MF (post-ET MF)
- Polycythemia vera (PCV) in adults who have had an inadequate response to or are intolerant to hydroxyurea
- Steroid-refractory acute graft-versus-host disease (GVHD) in adults and pediatric patients 12 years and older
- Chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.

Opzelura is indicated for the:

- Topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older, whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- Topical treatment of nonsegmental vitiligo (NVS) in adult and pediatric patients 12 years of age and older.

Limitation(s) of use: Use of Opzelura in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

Policy/Criteria

Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Jakafi and Opzelura are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Myelofibrosis (must meet all)**:**

1. Diagnosis of MF (includes primary MF, post-PV MF, post-ET MF);
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 18 years;
5. Documentation of a recent (within the last 30 days) platelet count of ≥ 50×10^9/L;
6. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 50 mg per day;
      ii. 2 tablets per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Polycythemia Vera (must meet all)**:**

1. Diagnosis of PCV;
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 18 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of hydroxyurea, peginterferon, or interferon *(see Appendix B),* unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for hydroxyurea, peginterferon, and interferon*
7. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 50 mg per day;
      ii. 2 tablets per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Graft-Versus-Host Disease (must meet all)**:**

1. Diagnosis of steroid-refractory acute or chronic GVHD post hematopoietic cell transplantation;
2. Request is for Jakafi;

3. Prescribed by or in consultation with an oncologist, hematologist, or bone marrow transplant specialist;
4. Age ≥ 12 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. For acute GVHD, failure of a systemic corticosteroid (e.g., oral prednisone or intravenous methylprednisolone dose equivalent) as defined in *Appendix D*, unless contraindicated or clinically significant adverse effects are experienced;
7. For chronic GVHD, member meets one of the following (a or b):
   a. Failure of a systemic corticosteroid (*see Appendix B)* at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Failure of a systemic immunosuppressant (*see Appendix B)* at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
8. Jakafi is not prescribed concurrently with Imbruvica® or Rezurock®;
9. Request meets one of the following (a or b):*
   a. Dose does not exceed both of the following (i and ii):
      i. 20 mg per day;
      ii. 2 tablets per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Chronic Myelomonocytic Leukemia and Myelodysplastic/Myeloproliferative Neoplasms (MDS/MPN) (off-label use) (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Chronic myelomonocytic leukemia;
   b. MDS/MPN;
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 18 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).**

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

E. Pediatric B-Cell Acute Lymphoblastic Leukemia (off-label use) (must meet all)**:**
1. Diagnosis of pediatric "Ph-like" B-cell acute lymphoblastic leukemia:
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age < 18 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Prescribed in combination with an induction or consolidation regimen;
7. Positive for a JAK-STAT pathway mutation, JAK2 fusion, EPOR rearrangement, SH2B3 alteration, or IL7R insertion/deletion;
8. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).**
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

F. Myeloid/Lymphoid Neoplasm with Eosinophilia (off-label use) (must meet all)**:**
1. Diagnosis of a lymphoid, myeloid, or mixed lineage neoplasm with eosinophilia;
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 18 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Positive for a JAK2 mutation;
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).**
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

G. Essential Thrombocythemia (off-label) (must meet all)**:**
1. Diagnosis of essential thrombocythemia;
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 18 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of hydroxyurea, peginterferon, interferon, or anagrelide (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for hydroxyurea, peginterferon, interferon, or anagrelide*

7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).**
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

H. Atopic Dermatitis (must meet all)**:**
1. Diagnosis of AD;
2. Member has ≤ 20% body surface area (BSA) involvement;
3. Request is for Opzelura;
4. Age ≥ 12 years;
5. Prescribed by or in consultation with a dermatologist or allergist;
6. Member does not have an immunocompromised status;
7. Member meets one of the following (a or b):
   a. Failure of two formulary medium-to-very high potency topical corticosteroids, each used for ≥ 2 weeks, unless contraindicated or clinically adverse effects are experienced (*see Appendix B)*;
   b. For face or intertriginous areas use (e.g., genitals, armpits, forearms, and groin);
8. Failure of a topical calcineurin inhibitor* used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
   **Prior authorization may be required for topical calcineurin inhibitors*
9. Failure of Eucrisa®* used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Eucrisa*
10. Opzelura is not prescribed concurrently with biologic medications (e.g., Dupixent®, Adbry®), biologic disease-modifying antirheumatic drugs (e.g., Humira®, Enbrel®, Taltz®, Stelara®), JAK inhibitors (e.g., Xeljanz®, Rinvoq®, Olumiant®), or potent immunosuppressants (e.g., azathioprine, cyclosporine);
11. Dose does not exceed one of the following (a or b):
    a. One 60-gram tube per week;
    b. One 100-gram tube per 2 weeks.

Approval duration: 8 weeks

I. Nonsegmental Vitiligo (must meet all):
1. Diagnosis of NSV;
2. Documentation of member's total vitiligo involvement is ≤ 10% BSA;
3. Request is for Opzelura;
4. Prescribed by or in consultation with a dermatologist or allergist;
5. Age ≥ 12 years;
6. Member meets one of the following (a or b):
   a. Two formulary medium-to-very high potency topical corticosteroids in the previous 6 months, unless contraindicated or clinically adverse effects are experienced (*see Appendix B)*;
   b. For face or intertriginous areas use (e.g., genitals, armpits, forearms, and groin);

7. Failure of a topical calcineurin inhibitor* used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
   **Prior authorization may be required for topical calcineurin inhibitors*
8. Opzelura is not prescribed concurrently with biologic medications (e.g., Dupixent, Adbry), biologic disease-modifying antirheumatic drugs (e.g., Humira, Enbrel, Taltz, Stelara), JAK inhibitors (e.g., Xeljanz, Rinvoq, Olumiant), or potent immunosuppressants (e.g., azathioprine, cyclosporine);
9. Dose does not exceed one of the following (a or b):
   a. One 60-gram tube per week;
   b. One 100-gram tube per 2 weeks.

Approval duration: 6 months

J. CAR T-Cell Related Toxicities (off-label) (must meet all)**:**
1. Diagnosis of grade 4 cytokine release syndrome (CRS) (*see Appendix E)*;
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;
4. Age ≥ 18 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of both high-dose systemic corticosteroids and anti-IL-6 therapy* (*see Appendix B*), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for anti-IL-6 therapy*
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).**
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 1 month

K. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Atopic Dermatitis or Nonsegmental Vitiligo (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by, including but not limited to, reduction in itching and scratching;
3. Member meets one of the following (a or b):
   a. For AD: Member is responding positively to therapy as evidenced by, including but not limited to, reduction in itching and scratching;
   b. For NSV: Member is responding positively to therapy as evidence by, including, but not limited to, reduction in lesions;
4. Request is for Opzelura;
5. Opzelura is not prescribed concurrently with biologic medications (e.g., Dupixent, Adbry), biologic disease-modifying antirheumatic drugs (e.g., Humira, Enbrel, Taltz, Stelara), JAK inhibitors (e.g., Xeljanz, Rinvoq, Olumiant), or potent immunosuppressants (e.g., azathioprine, cyclosporine);
6. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. One 60-gram tube per week;
   b. One 100-gram tube per 2 weeks.

Approval duration:
AD – 8 weeks
NSV – 6 months

B. CAR T-Cell Related Toxicities

1. Re-authorization is not permitted. CAR-T therapy is indicated to be dosed one time only.

Approval duration: Not applicable

C. All Other Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Jakafi for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Request is for Jakafi;
4. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. For GVHD, Jakafi is not prescribed concurrently with Imbruvica or Rezurock;
6. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For MF, PCV: New dose does not exceed 50 mg (2 tablets) per day;

b. For acute GVHD, cGVHD: New dose does not exceed 20 mg (2 tablets) per day;
c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months (12 months for MF)
Commercial – 12 months or duration of request, whichever is less

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BSA: body surface area
CRS: cytokine release syndrome
FDA: Food and Drug Administration
GVHD: graft-versus-host disease
cGVHD: chronic graft-versus-host disease
JAK: Janus kinase
MDS/MPN: myelodysplastic/myeloproliferative neoplasms
MF: myelofibrosis
NCCN: National Comprehensive Cancer Network
NSV: nonsegmental vitiligo
PCV: polycythemia vera
post-ET MF: post-essential thrombocythemia myelofibrosis
post-PV MF: post-polycythemia vera myelofibrosis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
PCV, Essential Thrombocythemia, and cGVHD		
hydroxyurea (Droxia®, Hydrea®)	PCV, essential thrombocythemia: Varies	Varies
Intron A® (interferon alfa-2b)		
Pegasys®, Pegasys ProClick® (peginterferon alfa-2a)		
PegIntron®, Sylatron® (peginterferon alfa-2b)		
anagrelide (Agrylin®)	Essential thrombocythemia: Varies	Varies
Systemic corticosteroids (e.g., methylprednisolone, prednisone)	cGVHD: Varies	Varies
mycophenolate mofetil (Cellcept®)		
cyclosporine (Gengraf®, Neoral®, Sandimmune®)		
tacrolimus (Prograf®)		
sirolimus (Rapamune®)		
imatinib (Gleevec®)		
Imbruvica® (ibrutinib)		
Rezurock® (belumosudil)		
Atopic Dermatitis		
Very High Potency Topical Corticosteroids		
augmented betamethasone 0.05% (Diprolene® AF) cream, ointment, gel, lotion	Apply topically to the affected area(s) BID	Varies
clobetasol propionate 0.05% (Temovate®) cream, ointment, gel, solution		
diflorasone diacetate 0.05% (Maxiflor®, Psorcon E®) cream, ointment		
halobetasol propionate 0.05% (Ultravate®) cream, ointment		
High Potency Topical Corticosteroids		
augmented betamethasone 0.05% (Diprolene® AF) cream, ointment, gel, lotion	Apply topically to the affected area(s) BID	Varies
diflorasone 0.05% (Florone®, Florone E®, Maxiflor®,Psorcon E®) cream		
fluocinonide acetonide 0.05% (Lidex®, Lidex E®) cream, ointment, gel, solution		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
triamcinolone acetonide 0.5% (Aristocort®, Kenalog®) cream, ointment		
Medium Potency Topical Corticosteroids		
desoximetasone 0.05% (Topicort ®) cream, ointment, gel	Apply topically to the affected area(s) BID	Varies
fluocinolone acetonide 0.025% (Synalar®) cream, ointment		
mometasone 0.1% (Elocon®) cream, ointment, lotion		
triamcinolone acetonide 0.025%, 0.1% (Aristocort®, Kenalog®) cream, ointment		
Low Potency Topical Corticosteroids		
alclometasone 0.05% (Aclovate®) cream, ointment	Apply topically to the affected area(s) BID	Varies
desonide 0.05% (Desowen®) cream, ointment, lotion		
fluocinolone acetonide 0.01% (Synalar®) solution		
hydrocortisone 2.5% (Hytone®) cream, ointment		
Topical Calcineurin Inhibitors		
tacrolimus (Protopic®), pimecrolimus (Elidel®)	Children ≥ 2 years and adults: Apply a thin layer topically to affected skin BID. Treatment should be discontinued if resolution of disease occurs.	Varies
Topical Phosphodiesterase-4 Inhibitor		
Eucrisa® (crisaborole)	Apply to the affected areas BID	Varies
CAR T-Cell Related Toxicities		
Actemra® (tocilizumab)	8 mg /kg IV over 1 hour (not to exceed 800 mg/dose). Repeat in 8 hours if no improvement; no more than 3 doses in 24 hours with a maximum of 4 doses total.	800 mg per dose (max 4 doses total)
dexamethasone (Decadron®, Dexasone®)	10 mg IV every 6 hours	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
methylprednisolone (Solumedrol®, Medrol®)	1000 mg IV every 12-24 hours	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindications: none reported
- Boxed warnings:
  - Jakafi: none reported
  - Opzelura: serious infections, mortality, malignancy, major adverse cardiovascular events (MACE), and thrombosis
    - Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving JAK inhibitors for inflammatory conditions.
    - Higher rate of all-cause mortality, including sudden cardiovascular death have been observed in patients treated with JAK inhibitors for inflammatory conditions.
    - Lymphoma and other malignancies have been observed in patients treated with JAK inhibitors for inflammatory conditions.
    - Higher rate of major adverse cardiovascular events (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with JAK inhibitors for inflammatory conditions.
    - Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, some fatal, have occurred in patients treated with JAK inhibitors for inflammatory conditions.

Appendix D: Steroid Refractoriness or Resistance: Acute and Chronic GVHD (NCCN)

- Acute GVHD
  - Progression of acute GVHD within 3-5 days of therapy onset with ≥ 2 mg/kg/day of prednisone* OR failure to improve within 5-7 days of treatment initiation OR incomplete response after more than 28 days of immunosuppressive treatment including steroids.
- Chronic GVHD
  - Chronic GVHD progression* while on prednisone* at ≥ 1 mg/kg/day for 1-2 weeks OR stable GVHD disease while on ≥ 0.5 mg/kg/day (or 1 mg/kg every other day) of prednisone* for 1-2 months.

**Oral prednisone or IV methylprednisolone dose equivalent.*

Hematopoietic Cell Transplantation (HCT): Graft-Versus-Host-Disease Version 2.2022. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed November 16, 2022.

Appendix E: CRS Grade (NCCN)

- Grade 1: fever ≥ 38º C
- Grade 2: fever with hypotension not requiring vasopressors and/or hypoxia requiring low-flow nasal cannula* or blow-by
- Grade 3: fever with hypotension requiring vasopressors with or without vasopressin and/or hypoxia requiring high-flow cannula*, face mask, nonrebreather mask, or Venturi mask
- Grade 4: fever with hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring positive pressure (e.g., CPAP, BiPAP, intubation, mechanical ventilation)

**Low-flow cannula is defined as oxygen delivered at ≤6 L/min. Low flow also includes blow-by oxygen delivery, sometimes used in pediatrics. High-flow nasal cannula is defined as oxygen delivered at >6 L/min*
Management of Immunotherapy-Related Toxicities Version 1.2022. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed November 16, 2022

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ruxolitinib (Jakafi)	MF	Starting dose is based on patient's baseline platelet count: • Greater than 200 × 10^9/L: 20 mg PO BID • 100 × 10^9/L to 200 × 10^9/L: 15 mg PO BID • 50 × 10^9/L to less than 100 × 10^9/L: 5 mg PO BID Range: 5 mg to 25 mg PO BID	50 mg/day
	PCV	Starting dose: 10mg PO BID Range: 5 mg to 25 mg PO BID	50 mg/day
	acute GVHD	Starting dose: 5mg PO BID Range: 5 mg to 10 mg PO BID	20 mg/day
	cGVHD	Starting dose: 10mg PO BID Range: 5 mg to 10 mg PO BID	20 mg/day
Ruxolitinib (Opzelura)	AD	Apply a thin layer twice daily to affected areas of up to 20% body surface area	60 grams/week or 100 gm per 2 weeks
	NSV	Apply a thin layer twice daily to affected areas of up to 10% body surface area	

VI. Product Availability

Drug Name	Availability
Ruxolitinib (Jakafi)	Tablets: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg
Ruxolitinib (Opzelura)	Cream (tube of 60 grams, 100 grams): 1.5%

VII. References

1. Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation; January 2023. Available at: http://www.jakafi.com. Accessed October 16, 2023.

2. Opzelura Prescribing Information. Wilmington, DE: Incyte Corporation: September 2023. Available at https://www.opzelura.com/prescribing-information.pdf. Accessed April 15, 2024.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalkey.com/pharmacology/.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 15, 2023.
5. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 15, 2023.
6. National Comprehensive Cancer Network. Myeloproliferative Neoplasms Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed November 7, 2023.
7. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation (HCT) Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed November 22, 2023.
8. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed November 22, 2023.
9. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 3.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed November 22, 2023.
10. National Comprehensive Cancer Network. Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes Version 2.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf. Accessed November 22, 2023.
11. National Comprehensive Cancer Network. Management of Immunotherapy-Related Toxicities Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Accessed November 22, 2023.

Atopic Dermatitis

12. Eichenfield F, Tom WL, Chamlin SL et al. Guidelines of Care for the Management of Atopic Dermatitis. *J Am Acad Dermatol*. 2014; 70(2): 116-32.
13. Wong JTY, Tsuyuki RT, Cresswell-Melville A, et al. Guidelines for the management of atopic dermatitis (eczema) for pharmacists. *Can Pharm J (Ott)*. 2017;150(5):285-297.
14. Ference JD and Last AR. Choosing topical corticosteroids. *American Family Physician* Journal. 2009; 79(2):135-140.
15. Sidbury R, Alikhan A, Bercovitch L, et al. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. J Am Acad Dermatol. 2023; 89(1):e1-e20.

CAR T-Cell Related Toxicities

16. Pan J, Deng B, Ling Z, et al. Ruxolitinib mitigates steroid-refractory CRS during CAR T therapy. J Cell Mol Med 2021;25:1089-1099. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33314568.

Vitiligo
17. Eleftheriadou V, Atkar R, and Batchelor J et al. British Association of Dermatologists guidelines for the management of people with vitiligo. British Journal of Dermatology. 2021; 186 (1): 18-29.
18. Taieb A, Alomar A, and Bohm M et al. Guidelines for the management of vitiligo: the European Dermatology Forum Consensus. British Journal of Dermatology. 2012; 168 (1): 5-19.
19. ClinicalTrials.gov. Topical Ruxolitinib Evaluation in Vitiligo Study 1 (TruE-V1). Available at: https://clinicaltrials.gov/ct2/show/NCT04052425. Accessed August 9, 2022.
20. ClinicalTrials.gov. Topical Ruxolitinib Evaluation in Vitiligo Study 2 (TruE-V2). Available at: https://clinicaltrials.gov/ct2/show/NCT04057573. Accessed August 9, 2022.
21. van Geel N, Speeckaert R, Taieb A, et al. Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the International Vitiligo Task Force Part 1: towards a new management algorithm. J Eur Acad Dermatol Venereol. 2023;37:2173-2184.
22. Seneschal J, Speeckaert R, Taieb A, et al. Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the International Vitiligo Task Force – Part 2: Specific treatment recommendations. J Eur Acad Dermatol Venereol. 2023;37:2185-2195.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Criteria added for new FDA indication: steroid-refractory acute graft-versus-host disease; references reviewed and updated.	07.16.19	11.19
1Q 2020 annual review: removed HIM disclaimer for HIM NF drugs; NCCN recommended use for chronic GVHD added with new NCCN guideline update to steroid refractory definitions at Appendix D; additional NCCN uses added for chronic myelomonocytic leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia; references reviewed and updated; continuation approval duration increased to 12 months; references reviewed and updated.	11.19.19	02.20
1Q 2021 annual review: oral oncology generic redirection language added; for pediatric ALL, consolidation therapy and additional mutations added per NCCN; new myeloid/lymphoid and essential thrombocytopenia indications added per NCCN; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.06.20	02.21
Added language for Imbruvica, Rezurock and Jafaki not to be used concurrently since all are used for cGVHD; added legacy WCG auth durations (WCG.CP.PHAR.98 to retire); RT4: updated FDA-approved indication section for cGVHD (previously allowed via off-label use); added newly approved drug, Opzelura, to criteria.	08.24.21	11.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.18.21	02.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revised maximum dose of Opzelura from 60 g per month to 60 g per week per PI.	03.16.22	
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	04.26.22	05.22
RT4: criteria added for new Opzelura indication of NSV; consolidated Legacy WellCare initial approval durations from 12 months to 6 months consistent with standard Medicaid approval durations; for myelofibrosis, added criterion for recent documentation of a platelet count of $\geq 50 \times 10^9$/L per PI and to align with other myelofibrosis policies.	08.09.22	11.22
1Q 2023 annual review: for cGVHD, added option for failure of systemic immunosuppressants; per PI for Opzelura added additional max dose of one 100-gram tube per 2 weeks; per NCCN compendium, removal of chronic myeloid leukoma and addition MDS/MPN and management of CAR T-cell-related toxicities; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	11.16.22	02.23
1Q 2024 annual review: for AD, added criterion member has ≤ 20% BSA involvement per guidelines; for NSV, clarified affected BSA is "≤."; for both AD and NSV, added bypass of medium-to-very high potency topical corticosteroids if use is for face or intertriginous areas; references reviewed and updated.	10.16.23	02.24
For AD and NSV, updated concurrent use criteria by adding "Opzelura is not prescribed concurrently with biologic medications (e.g., Dupixent, Adbry)" in initial and continued therapy sections per FDA labeling.	04.15.24	
For GVHD, revised tablet quantity limit to 2 due to twice daily regimen.	09.04.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.