

## Clinical Policy: Ruxolitinib (Jakafi, Opzelura)

Reference Number: ERX.SPA.18

Effective Date: 07.01.16

Last Review Date: 11.22

Line of Business: Commercial, Medicaid

[Revision Log](#)

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

### Description

Ruxolitinib (Jakafi<sup>®</sup>, Opzelura<sup>™</sup>) 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 (post-PV MF)
  - Post-essential thrombocythemia (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 (cGVHD) 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 (AD) 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 (NSV) 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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions<sup>TM</sup> 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  $\geq$  18 years;
5. Documentation of a recent (within the last 30 days) platelet count of  $\geq 50 \times 10^9/L$ ;
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 50 mg 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:****Commercial – Length of Benefit****Medicaid – 6 months****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  $\geq$  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*

8. Request meets one of the following (a or b):\*

- a. Dose does not exceed 50 mg 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:****Commercial – Length of Benefit****Medicaid – 6 months****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  $\geq$  12 years;
5. For Jakafi requests, member must use ruxolitinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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. Jakafi is not prescribed concurrently with Imbruvica® or Rezurock™;
8. Request meets one of the following (a or b):\*

- a. Dose does not exceed 20 mg 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:****Commercial – Length of Benefit****Medicaid – 6 months****D. Chronic Myelomonocytic Leukemia and Chronic Myeloid Leukemia (off-label use) (must meet all):**

1. Diagnosis of one of the following (a or b):
  - a. Chronic myelomonocytic leukemia;
  - b. BCR-ABL negative atypical chronic myeloid leukemia;
2. Request is for Jakafi;
3. Prescribed by or in consultation with a hematologist or oncologist;

4. Age  $\geq$  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:**

**Commercial** – Length of Benefit

**Medicaid** – 6 months

**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:**

**Commercial** – Length of Benefit

**Medicaid** – 6 months

**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  $\geq$  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:**

**Commercial** – Length of Benefit

**Medicaid** – 6 months

**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  $\geq$  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:**

**Commercial** – Length of Benefit

**Medicaid** – 6 months

**H. Atopic Dermatitis** (must meet all):

1. Diagnosis of AD;
2. Request is for Opzelura;
3. Prescribed by or in consultation with a dermatologist or allergist;
4. Age ≥ 12 years;
5. Member does not have an immunocompromised status;
6. Failure of all of the following (a, b, and c), unless contraindicated or clinically significant adverse effects are experienced:
  - a. Two formulary medium to very high potency topical corticosteroids, each used for ≥ 2 weeks;
  - b. Topical calcineurin inhibitor\* (e.g., tacrolimus 0.03% ointment, pimecrolimus 1% cream) used for ≥ 4 weeks;  
*\*Topical tacrolimus and pimecrolimus may require prior authorization*
  - c. Eucrisa® used for ≥ 4 weeks;  
*\*Eucrisa may require prior authorization*
7. Opzelura is not prescribed concurrently with 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);
8. Dose does not exceed one 60-gram tube per week.

**Approval duration: 8 weeks**

**I. Nonsegmental Vitiligo** (must meet all):

1. Diagnosis of nonsegmental vitiligo (NSV);
2. Documentation of less than 10% of the member's total vitiligo body surface area affected;
3. Request is for Opzelura;
4. Prescribed by or in consultation with a dermatologist or allergist;
5. Age ≥ 12 years;
6. Failure of both of the following (a and b), unless contraindicated or clinically significant adverse effects are experienced:
  - a. Two formulary medium to very high potency topical corticosteroids in the past 6 months;
  - b. Topical calcineurin inhibitor\* used for ≥ 4 weeks (e.g., tacrolimus 0.03% ointment, pimecrolimus 1% cream);  
*\*Topical tacrolimus and pimecrolimus may require prior authorization*
7. Opzelura is not prescribed concurrently with 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);
8. Dose does not exceed one 60-gram tube per week.

**Approval duration: 6 months**

**J. Other diagnoses/indications**

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**II. Continued Therapy**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. 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 evidenced by, including but not limited to, reduction in lesions;
- 3. Request is for Opzelura;
- 4. Opzelura is not prescribed concurrently with 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);
- 5. Dose does not exceed one 60-gram tube per week.

**Approval duration:****AD – 8 weeks****NSV – 6 months****B. All Other Indications in Section I (must meet all):**

- 1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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 per day;
  - b. For acute GVHD, cGVHD: New dose does not exceed 20 mg 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:****Commercial – Length of Benefit****Medicaid – 6 months (12 months for MF)****C. Other diagnoses/indications (must meet 1 or 2):**

- 1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
- 2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 policy – ERX.PA.01 or evidence of coverage documents.

**IV. Appendices/General Information****Appendix A: Abbreviation/Acronym Key**

AD: atopic dermatitis

NSV: nonsegmental vitiligo

FDA: Food and Drug Administration

PCV: polycythemia vera

GVHD: graft-versus-host disease

post-ET MF: post-essential thrombocythemia

cGVHD: chronic graft-versus-host disease

myelofibrosis

MF: 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
<b>PCV, Essential Thrombocythemia, and cGVHD</b>		
hydroxyurea (Droxia®, Hydrea®)	PCV, essential thrombocythemia: Varies	Varies
Intron A® (interferon alfa-2b)		
Pegasys®, Pegasys ProClick® (peginterferon alfa-2a)		
PeglIntron®, 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® (imbrutinib)		
Rezurock™ (belumosudil)		
<b>Atopic Dermatitis and NSV</b>		
<b>Very High Potency Topical Corticosteroids</b>		
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% (Maxiflор®, Psorcon E®) cream, ointment		
halobetasol propionate 0.05% (Ultravate®) cream, ointment		
<b>High Potency Topical Corticosteroids</b>		
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®, Maxiflор®, Psorcon E®) cream		
fluocinonide acetonide 0.05% (Lidex®, Lidex E®) cream, ointment, gel, solution		
triamcinolone acetonide 0.5% (Aristocort®, Kenalog®) cream, ointment		
<b>Medium Potency Topical Corticosteroids</b>		
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		
<b>Low Potency Topical Corticosteroids</b>		
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		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<b>Topical Calcineurin Inhibitors</b>		
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
<b>Atopic Dermatitis</b>		
<b>Topical Phosphodiesterase-4 Inhibitor</b>		
Eucrisa® (crisaborole)	Apply to the affected areas BID	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

- Jakafi: none reported
- Opzelura:
  - Contraindications: none reported
  - Boxed warnings:
    - 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): Pre-Transplant Recipient Evaluation and Management of Graft-Versus-Host Disease Version 1.2020. National Comprehensive Cancer Network Guidelines. Available at [www.nccn.org](http://www.nccn.org). Accessed November 6, 2019.

#### 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 $200 \times 10^9/L$ : 20 mg PO BID	50 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		<ul style="list-style-type: none"> <li>• <math>100 \times 10^9/\text{L}</math> to <math>200 \times 10^9/\text{L}</math>: 15 mg PO BID</li> <li>• <math>50 \times 10^9/\text{L}</math> to less than <math>100 \times 10^9/\text{L}</math>: 5 mg PO BID</li> </ul> <p>Range: 5 mg to 25 mg PO BID</p>	
	PCV	<p>Starting dose: 10 mg PO BID</p> <p>Range: 5 mg to 25 mg PO BID</p>	50 mg/day
	Acute GVHD	<p>Starting dose: 5 mg PO BID</p> <p>Range: 5 mg to 10 mg PO BID</p>	20 mg/day
	cGVHD	<p>Starting dose: 10 mg PO BID</p> <p>Range: 5 mg to 10 mg PO BID</p>	20 mg/day
Ruxolitinib (Opzelura)	AD	Apply a thin layer twice daily to affected areas of up to 20% body surface area	60 gram tube/week or 100 gram tube/2 weeks
	NSV	Apply a thin layer twice daily to affected areas of up to 10% body surface area	60 gram tube/week or 100 gram tube/2 weeks

## 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

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Removed request for bloodwork. Removed NCCN off-label use for myelofibrosis. References updated.	11.22.17	02.18
1Q 2019 annual review: intermediate or high-risk MF is removed to accommodate additional NCCN recommendations; interferons are added to PCV as a failed trial choice per NCCN; references reviewed and updated.	11.13.18	02.19
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: 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 thrombocytophenia indications added per NCCN; 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 GVHD; 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.	11.16.21	02.22
Revised maximum dose of Opzelura from 60 g per month to 60 g per week per PI.	03.16.22	
RT4: criteria added for new Opzelura indication of NSV; 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

#### **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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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