Evolent Clinical Guideline 3072 for Pegasys™ (peginterferon alfa-2a)

Guideline Number:	Applicable Codes	
Evolent_CG_3072		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. 		
Original Date:	**Last Revised Date:**	**Implementation Date:**
April 2024	April 2025	April 2025

TABLE OF CONTENTS

STATEMENT

Purpose

To define and describe the accepted indications for Pegasys (peginterferon alfa-2a) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Myelofibrosis (PMF)

- Pegasys (peginterferon alfa-2a) may be used as first line or subsequent therapy for members with low-risk myelofibrosis.

Prognostic models for patients with PMF

Prognostic model	Risk groups and clinical relevance
IPSS[80]	
Risk factors (weight):	Low risk: 0 (median survival, 11.3 y)
• Age >65 y (1 point)	Intermediate-1 risk: 1 point (7.9 y)
• Constitutional symptoms (1 point)	Intermediate-2 risk: 2 points (4.0 y)
• Hemoglobin <10 g/dL (1 point)	High risk: ≥3 points (2.3 y)
• WBC count >25 × 10^9/L (1 point)	IPSS estimates survival at the time of diagnosis
• Circulating blasts ≥1% (1 point)	
DIPSS[81]	
Risk factors (weight):	Low risk: 0 (median survival, >20 y)
• Age >65 y (1 point)	Intermediate-1 risk: 1-2 points (14.2 y)
• Constitutional symptoms (1 point)	Intermediate-2 risk: 3-4 points (4.0 y)
• Hemoglobin <10 g/dL (2 points)	High risk: 5-6 points (1.5 y)
• WBC count >25 × 10^9/L (1 point)	DIPSS can be applied anytime during clinical course
• Circulating blasts ≥ 1% (1 point)	
DIPSS-plus[83]	
Risk factors (weight):	Low risk: 0 (median survival, 15 y)
• DIPSS score (DIPPS low = 0, DIPPS int-1 = 1 point, DIPPS int-2 = 2 points, DIPSS high = 3 points)	Intermediate-1 risk: 1 point (6.6 y)
• RBC transfusion need (1 point)	Intermediate-2 risk: 2-3 points (2.9 y)
• PLT count <100 × 10^9/L (1 point)	High risk: 4-6 points (1.3 y)
• Unfavorable karyotype* (1 point)	DIPSS-plus can be applied anytime during clinical course

Polycythemia Vera (PV)

- Pegasys (peginterferon alfa-2a) may be used as first line or subsequent therapy for members with symptomatic low-risk polycythemia vera or high-risk polycythemia vera.

Table 5. Prognostic models for patients with PV

Prognostic model	Risk groups and clinical relevance
Conventional thrombosis score (European LeukemiaNet recommendations)[70]	
At least 1 of the following risk factors:	Low risk: age <60 y AND no history of thrombosis, that is, no risk factors
• Age ≥60 y	High risk: age ≥60 y AND/OR history of thrombosis, that is, at least 1 risk factor
• Previous thrombosis	Low-risk patients are given low-dose aspirin and undergo regular phlebotomy to keep hematocrit <45%; high-risk patients are given also a cytoreductive treatment
IPSS for overall survival in PV[78]	
Risk factors (weight):	Low risk: 0 (median survival, 28 y)
• Age ≥67 y (5 point)	Intermediate risk: 1-2 points (median survival, 19 y)
• Age 57-66 y (2 points)	High risk: ≥3 points (median survival, 11 y)
• Leukocyte count ≥15 × 10^9/L (1 point)	
• Previous venous thrombosis (1 point)	

Essential Thrombocythemia (ET)

- Pegasys (peginterferon alfa-2a) may be used as subsequent therapy for members with intermediate/high-risk essential thrombocythemia.

Table 4. Prognostic models for patients with ET

Prognostic model	Risk groups and clinical relevance
Conventional score for prediction of vascular complications (European LeukemiaNet recommendations)[70]	
At least 1 of the following risk factors:	
• Age ≥60 y	Low risk: age <60 y AND no history of thrombosis or major bleeding AND PLT count <1500 × 10^9/L, that is, none of the 3 major risk factors
• Previous thrombosis or major bleeding	High risk: age ≥60 y AND/OR history of thrombosis or major bleeding AND/OR PLT count ≥1500 × 10^9/L, that is, at least 1 of the 3 major risk factors
• PLT count ≥1500 × 10^9/L	While low-risk patients are just followed (observation alone) or given low-dose aspirin, high-risk patients are given a cytoreductive treatment plus low-dose aspirin
IPSET-thrombosis (International Prognostic Score for ET: estimates the risk of thrombosis)[71]	
Risk factors (weight):	Low risk: 0-1 point (probability of thrombotic events: 1.03% of patients/year)
• Age ≥60 y (1 point)	Intermediate risk: 2 points (2.35% of patients/year)
• Previous thrombosis (2 points)	High risk: ≥3 points (3.56% of patients/year)
• Cardiovascular risk factors* (1 point) • *JAK2* (V617F) mutation (2 points)	Potential therapeutic implications: (1) observation alone may be adequate in patients with no risk factors; (2) low-dose aspirin should be used in all patients with *JAK2* (V617F) and/or cardiovascular risk factors; (3) older patients (≥60 y) without additional risk factors may not need a cytoreductive treatment; (4) conversely, a cytoreductive treatment may be considered in younger patients (<60 y) with *JAK2*-mutant ET and concomitant cardiovascular risk factors, even in the absence of previous thrombosis
IPSET (International Prognostic Score for ET: predicts survival)[73]	
Risk factors (weight):	Low risk: 0 (median survival not reached)
• Age ≥60 y (2 points)	Intermediate risk: 1-2 points (median survival, 24.5 y)
• Previous thrombosis (1 point)	High risk: 3-4 points (median survival, 13.8 y)
• Leukocyte count >11 × 10^9/L (1 point)	

*Cardiovascular risk factors include hypertension, diabetes, and active tobacco use.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Autoimmune hepatitis
  - Hepatic decompensation in patients with cirrhosis
  - Use in neonates/infants
  - Known hypersensitivity reactions such as urticaria, angioedema, bronchoconstriction and anaphylaxis to alpha interferons or any component of the product
- US Boxed Warning
  - Risk of Serious Disorders
    - May cause or aggravate fatal or life-threatening neuropsychiatric,

autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders.

EXCLUSION CRITERIA

- Disease progression while taking Pegasys (peginterferon alfa-2a).
- Concurrent use with other anticancer therapies.
- Dosing exceeds single dose limit of 180 mcg.
- Investigational use of Pegasys (peginterferon alfa-2a) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
    - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
    - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
    - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
    - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J3590 - peginterferon alfa-2a

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
April 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1497 Pegasys (peginterferon alfa-2a)
April 2024	• Guideline created

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

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