Krystexxa® (Pegloticase)

Policy Number: 2023D0082F
Effective Date: December 1, 2023

Instructions for Use

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Community Plan Policy

- Krystexxa® (Pegloticase)

Coverage Rationale

See Benefit Considerations

Krystexxa (Pegloticase) is proven for the treatment of chronic gout refractory to conventional therapy.[1]

Krystexxa (Pegloticase) is medically necessary for the treatment of chronic gout when all of the following criteria are met:[1]

- For **initial therapy**, **all** of the following:
  - Diagnosis of symptomatic gout as defined by **one** of the following:
    - History of at least 2 gout flares in the previous 12 months
    - At least 1 gouty tophus
    - Chronic gouty arthropathy

    and
  - History of contraindication, intolerance, or treatment failure (i.e., failure to normalize uric acid to < 6 mg/dL) after 3 months of therapy (at the maximally medically appropriate dose) with **both** of the following: (For Medicare reviews, refer to the CMS section**)
    - Zyloprim (allopurinol)
    - Uloric (febuxostat)

    and
  - Submission of laboratory values demonstrating baseline serum uric acid level > 6 mg/dL; **and**
  - Prescriber attests that serum uric acid levels will be monitored prior to each infusion and that discontinuation of treatment will be considered if preinfusion levels increase above 6 mg/dL; **and**
  - Prescribed by **one** of the following:
    - Rheumatologist
    - Nephrologist

    and
  - Krystexxa is initiated and titrated according to US FDA labeled dosing for chronic gout; **and**
  - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, **all** of the following:

- Patient has previously received treatment with Krystexxa; **and**
- Patient has experienced a positive clinical response to Krystexxa (e.g., serum uric acid levels < 6mg/dL, tophus reduction, etc); **and**
- Patient has **not** had two consecutive uric acid levels above 6 mg/dL after initiating treatment with Krystexxa; **and**
- Prescribed by **one** of the following:
  - Rheumatologist
  - Nephrologist

  and
- Krystexxa is initiated and titrated according to US FDA labeled dosing for chronic gout; **and**
- Reauthorization will be for no more than 12 months

Krystexxa (Pegloticase) is unproven and not medically necessary for the treatment of asymptomatic hyperuricemia.[1]

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J2507	Injection, Pegloticase, 1mg

Diagnosis Code	Description
M1A.00X0	Idiopathic chronic gout, unspecified site, without tophus (tophi)
M1A.00X1	Idiopathic chronic gout, unspecified site, with tophus (tophi)
M1A.0110	Idiopathic chronic gout, right shoulder, without tophus (tophi)
M1A.0111	Idiopathic chronic gout, right shoulder, with tophus (tophi)
M1A.0120	Idiopathic chronic gout, left shoulder, without tophus (tophi)
M1A.0121	Idiopathic chronic gout, left shoulder, with tophus (tophi)
M1A.0190	Idiopathic chronic gout, unspecified shoulder, without tophus (tophi)
M1A.0191	Idiopathic chronic gout, unspecified shoulder, with tophus (tophi)
M1A.0210	Idiopathic chronic gout, right elbow, without tophus (tophi)
M1A.0211	Idiopathic chronic gout, right elbow, with tophus (tophi)
M1A.0220	Idiopathic chronic gout, left elbow, without tophus (tophi)
M1A.0221	Idiopathic chronic gout, left elbow, with tophus (tophi)
M1A.0290	Idiopathic chronic gout, unspecified elbow, without tophus (tophi)
M1A.0291	Idiopathic chronic gout, unspecified elbow, with tophus (tophi)
M1A.0310	Idiopathic chronic gout, right wrist, without tophus (tophi)
M1A.0311	Idiopathic chronic gout, right wrist, with tophus (tophi)
M1A.0320	Idiopathic chronic gout, left wrist, without tophus (tophi)
M1A.0321	Idiopathic chronic gout, left wrist, with tophus (tophi)
M1A.0390	Idiopathic chronic gout, unspecified wrist, without tophus (tophi)
M1A.0391	Idiopathic chronic gout, unspecified wrist, with tophus (tophi)
M1A.0410	Idiopathic chronic gout, right hand, without tophus (tophi)
M1A.0411	Idiopathic chronic gout, right hand, with tophus (tophi)

Diagnosis Code	Description
M1A.0420	Idiopathic chronic gout, left hand, without tophus (tophi)
M1A.0421	Idiopathic chronic gout, left hand, with tophus (tophi)
M1A.0490	Idiopathic chronic gout, unspecified hand, without tophus (tophi)
M1A.0491	Idiopathic chronic gout, unspecified hand, with tophus (tophi)
M1A.0510	Idiopathic chronic gout, right hip, without tophus (tophi)
M1A.0511	Idiopathic chronic gout, right hip, with tophus (tophi)
M1A.0520	Idiopathic chronic gout, left hip, without tophus (tophi)
M1A.0521	Idiopathic chronic gout, left hip, with tophus (tophi)
M1A.0590	Idiopathic chronic gout, unspecified hip, without tophus (tophi)
M1A.0591	Idiopathic chronic gout, unspecified hip, with tophus (tophi)
M1A.0610	Idiopathic chronic gout, right knee, without tophus (tophi)
M1A.0611	Idiopathic chronic gout, right knee, with tophus (tophi)
M1A.0620	Idiopathic chronic gout, left knee, without tophus (tophi)
M1A.0621	Idiopathic chronic gout, left knee, with tophus (tophi)
M1A.0690	Idiopathic chronic gout, unspecified knee, without tophus (tophi)
M1A.0691	Idiopathic chronic gout, unspecified knee, with tophus (tophi)
M1A.0710	Idiopathic chronic gout, right ankle and foot, without tophus (tophi)
M1A.0711	Idiopathic chronic gout, right ankle and foot, with tophus (tophi)
M1A.0720	Idiopathic chronic gout, left ankle and foot, without tophus (tophi)
M1A.0721	Idiopathic chronic gout, left ankle and foot, with tophus (tophi)
M1A.0790	Idiopathic chronic gout, unspecified ankle and foot, without tophus (tophi)
M1A.0791	Idiopathic chronic gout, unspecified ankle and foot, with tophus (tophi)
M1A.08X0	Idiopathic chronic gout, vertebrae, without tophus (tophi)
M1A.08X1	Idiopathic chronic gout, vertebrae, with tophus (tophi)
M1A.09X0	Idiopathic chronic gout, multiple sites, without tophus (tophi)
M1A.09X1	Idiopathic chronic gout, multiple sites, with tophus (tophi)
M1A.10X0	Lead-induced chronic gout, unspecified site, without tophus (tophi)
M1A.10X1	Lead-induced chronic gout, unspecified site, with tophus (tophi)
M1A.1110	Lead-induced chronic gout, right shoulder, without tophus (tophi)
M1A.1111	Lead-induced chronic gout, right shoulder, with tophus (tophi)
M1A.1120	Lead-induced chronic gout, left shoulder, without tophus (tophi)
M1A.1121	Lead-induced chronic gout, left shoulder, with tophus (tophi)
M1A.1190	Lead-induced chronic gout, unspecified shoulder, without tophus (tophi)
M1A.1191	Lead-induced chronic gout, unspecified shoulder, with tophus (tophi)
M1A.1210	Lead-induced chronic gout, right elbow, without tophus (tophi)
M1A.1211	Lead-induced chronic gout, right elbow, with tophus (tophi)
M1A.1220	Lead-induced chronic gout, left elbow, without tophus (tophi)
M1A.1221	Lead-induced chronic gout, left elbow, with tophus (tophi)
M1A.1290	Lead-induced chronic gout, unspecified elbow, without tophus (tophi)
M1A.1291	Lead-induced chronic gout, unspecified elbow, with tophus (tophi)
M1A.1310	Lead-induced chronic gout, right wrist, without tophus (tophi)
M1A.1311	Lead-induced chronic gout, right wrist, with tophus (tophi)

Diagnosis Code	Description
M1A.1320	Lead-induced chronic gout, left wrist, without tophus (tophi)
M1A.1321	Lead-induced chronic gout, left wrist, with tophus (tophi)
M1A.1390	Lead-induced chronic gout, unspecified wrist, without tophus (tophi)
M1A.1391	Lead-induced chronic gout, unspecified wrist, with tophus (tophi)
M1A.1410	Lead-induced chronic gout, right hand, without tophus (tophi)
M1A.1411	Lead-induced chronic gout, right hand, with tophus (tophi)
M1A.1420	Lead-induced chronic gout, left hand, without tophus (tophi)
M1A.1421	Lead-induced chronic gout, left hand, with tophus (tophi)
M1A.1490	Lead-induced chronic gout, unspecified hand, without tophus (tophi)
M1A.1491	Lead-induced chronic gout, unspecified hand, with tophus (tophi)
M1A.1510	Lead-induced chronic gout, right hip, without tophus (tophi)
M1A.1511	Lead-induced chronic gout, right hip, with tophus (tophi)
M1A.1520	Lead-induced chronic gout, left hip, without tophus (tophi)
M1A.1521	Lead-induced chronic gout, left hip, with tophus (tophi)
M1A.1590	Lead-induced chronic gout, unspecified hip, without tophus (tophi)
M1A.1591	Lead-induced chronic gout, unspecified hip, with tophus (tophi)
M1A.1610	Lead-induced chronic gout, right knee, without tophus (tophi)
M1A.1611	Lead-induced chronic gout, right knee, with tophus (tophi)
M1A.1620	Lead-induced chronic gout, left knee, without tophus (tophi)
M1A.1621	Lead-induced chronic gout, left knee, with tophus (tophi)
M1A.1690	Lead-induced chronic gout, unspecified knee, without tophus (tophi)
M1A.1691	Lead-induced chronic gout, unspecified knee, with tophus (tophi)
M1A.1710	Lead-induced chronic gout, right ankle and foot, without tophus (tophi)
M1A.1711	Lead-induced chronic gout, right ankle and foot, with tophus (tophi)
M1A.20X0	Drug-induced chronic gout, unspecified site, without tophus (tophi)
M1A.20X1	Drug-induced chronic gout, unspecified site, with tophus (tophi)
M1A.2110	Drug-induced chronic gout, right shoulder, without tophus (tophi)
M1A.2111	Drug-induced chronic gout, right shoulder, with tophus (tophi
M1A.2120	Drug-induced chronic gout, left shoulder, without tophus (tophi)
M1A.2121	Drug-induced chronic gout, left shoulder, with tophus (tophi)
M1A.2190	Drug-induced chronic gout, unspecified shoulder, without tophus (tophi)
M1A.2191	Drug-induced chronic gout, unspecified shoulder, with tophus (tophi)
M1A.2210	Drug-induced chronic gout, right elbow, without tophus (tophi)
M1A.2211	Drug-induced chronic gout, right elbow, with tophus (tophi)
M1A.2220	Drug-induced chronic gout, left elbow, without tophus (tophi)
M1A.2221	Drug-induced chronic gout, left elbow, with tophus (tophi)
M1A.2290	Drug-induced chronic gout, unspecified elbow, without tophus (tophi)
M1A.2291	Drug-induced chronic gout, unspecified elbow, with tophus (tophi)
M1A.2310	Drug-induced chronic gout, right wrist, without tophus (tophi)
M1A.2311	Drug-induced chronic gout, right wrist, with tophus (tophi)
M1A.2320	Drug-induced chronic gout, left wrist, without tophus (tophi)
M1A.2321	Drug-induced chronic gout, left wrist, with tophus (tophi)

Diagnosis Code	Description
M1A.2390	Drug-induced chronic gout, unspecified wrist, without tophus (tophi)
M1A.2391	Drug-induced chronic gout, unspecified wrist, with tophus (tophi)
M1A.2410	Drug-induced chronic gout, right hand, without tophus (tophi)
M1A.2411	Drug-induced chronic gout, right hand, with tophus (tophi)
M1A.2420	Drug-induced chronic gout, left hand, without tophus (tophi)
M1A.2421	Drug-induced chronic gout, left hand, with tophus (tophi)
M1A.2490	Drug-induced chronic gout, unspecified hand, without tophus (tophi)
M1A.2491	Drug-induced chronic gout, unspecified hand, with tophus (tophi)
M1A.2510	Drug-induced chronic gout, right hip, without tophus (tophi)
M1A.2511	Drug-induced chronic gout, right hip, with tophus (tophi)
M1A.2520	Drug-induced chronic gout, left hip, without tophus (tophi)
M1A.2521	Drug-induced chronic gout, left hip, with tophus (tophi)
M1A.2590	Drug-induced chronic gout, unspecified hip, without tophus (tophi)
M1A.2591	Drug-induced chronic gout, unspecified hip, with tophus (tophi)
M1A.2610	Drug-induced chronic gout, right knee, without tophus (tophi)
M1A.2611	Drug-induced chronic gout, right knee, with tophus (tophi)
M1A.2620	Drug-induced chronic gout, left knee, without tophus (tophi)
M1A.2621	Drug-induced chronic gout, left knee, with tophus (tophi)
M1A.2690	Drug-induced chronic gout, unspecified knee, without tophus (tophi)
M1A.2691	Drug-induced chronic gout, unspecified knee, with tophus (tophi)
M1A.2710	Drug-induced chronic gout, right ankle and foot, without tophus (tophi)
M1A.2711	Drug-induced chronic gout, right ankle and foot, with tophus (tophi)
M1A.2720	Drug-induced chronic gout, left ankle and foot, without tophus (tophi)
M1A.2721	Drug-induced chronic gout, left ankle and foot, with tophus (tophi)
M1A.2790	Drug-induced chronic gout, unspecified ankle and foot, without tophus (tophi)
M1A.2791	Drug-induced chronic gout, unspecified ankle and foot, with tophus (tophi)
M1A.28X0	Drug-induced chronic gout, vertebrae, without tophus (tophi)
M1A.28X1	Drug-induced chronic gout, vertebrae, with tophus (tophi)
M1A.29X0	Drug-induced chronic gout, multiple sites, without tophus (tophi)
M1A.29X1	Drug-induced chronic gout, multiple sites, with tophus (tophi)
M1A.30X0	Chronic gout due to renal impairment, unspecified site, without tophus (tophi)
M1A.30X1	Chronic gout due to renal impairment, unspecified site, with tophus (tophi)
M1A.3110	Chronic gout due to renal impairment, right shoulder, without tophus (tophi)
M1A.3111	Chronic gout due to renal impairment, right shoulder, with tophus (tophi)
M1A.3120	Chronic gout due to renal impairment, left shoulder, without tophus (tophi)
M1A.3121	Chronic gout due to renal impairment, left shoulder, with tophus (tophi)
M1A.3190	Chronic gout due to renal impairment, unspecified shoulder, without tophus (tophi)
M1A.3191	Chronic gout due to renal impairment, unspecified shoulder, with tophus (tophi)
M1A.3210	Chronic gout due to renal impairment, right elbow, without tophus (tophi)
M1A.3211	Chronic gout due to renal impairment, right elbow, with tophus (tophi)
M1A.3220	Chronic gout due to renal impairment, left elbow, without tophus (tophi)
M1A.3221	Chronic gout due to renal impairment, left elbow, with tophus (tophi)

Diagnosis Code	Description
M1A.3290	Chronic gout due to renal impairment, unspecified elbow, without tophus (tophi)
M1A.3291	Chronic gout due to renal impairment, unspecified elbow, with tophus (tophi)
M1A.3310	Chronic gout due to renal impairment, right wrist, without tophus (tophi)
M1A.3311	Chronic gout due to renal impairment, right wrist, with tophus (tophi)
M1A.3320	Chronic gout due to renal impairment, left wrist, without tophus (tophi)
M1A.3321	Chronic gout due to renal impairment, left wrist, with tophus (tophi)
M1A.3390	Chronic gout due to renal impairment, unspecified wrist, without tophus (tophi)
M1A.3391	Chronic gout due to renal impairment, unspecified wrist, with tophus (tophi)
M1A.3410	Chronic gout due to renal impairment, right hand, without tophus (tophi)
M1A.3411	Chronic gout due to renal impairment, right hand, with tophus (tophi)
M1A.3420	Chronic gout due to renal impairment, left hand, without tophus (tophi)
M1A.3421	Chronic gout due to renal impairment, left hand, with tophus (tophi)
M1A.3490	Chronic gout due to renal impairment, unspecified hand, without tophus (tophi)
M1A.3491	Chronic gout due to renal impairment, unspecified hand, with tophus (tophi)
M1A.3510	Chronic gout due to renal impairment, right hip, without tophus (tophi)
M1A.3511	Chronic gout due to renal impairment, right hip, with tophus (tophi)
M1A.3520	Chronic gout due to renal impairment, left hip, without tophus (tophi)
M1A.3521	Chronic gout due to renal impairment, left hip, with tophus (tophi)
M1A.3590	Chronic gout due to renal impairment, unspecified hip, without tophus (tophi)
M1A.3591	Chronic gout due to renal impairment, unspecified hip, with tophus (tophi)
M1A.3610	Chronic gout due to renal impairment, right knee, without tophus (tophi)
M1A.3611	Chronic gout due to renal impairment, right knee, with tophus (tophi)
M1A.3620	Chronic gout due to renal impairment, left knee, without tophus (tophi)
M1A.3621	Chronic gout due to renal impairment, left knee, with tophus (tophi)
M1A.3690	Chronic gout due to renal impairment, unspecified knee, without tophus (tophi)
M1A.3691	Chronic gout due to renal impairment, unspecified knee, with tophus (tophi)
M1A.3710	Chronic gout due to renal impairment, right ankle and foot, without tophus (tophi)
M1A.3711	Chronic gout due to renal impairment, right ankle and foot, with tophus (tophi)
M1A.3720	Chronic gout due to renal impairment, left ankle and foot, without tophus (tophi)
M1A.3721	Chronic gout due to renal impairment, left ankle and foot, with tophus (tophi)
M1A.3790	Chronic gout due to renal impairment, unspecified ankle and foot, without tophus (tophi)
M1A.3791	Chronic gout due to renal impairment, unspecified ankle and foot, with tophus (tophi)
M1A.38X0	Chronic gout due to renal impairment, vertebrae, without tophus (tophi)
M1A.38X1	Chronic gout due to renal impairment, vertebrae, with tophus (tophi)
M1A.39X0	Chronic gout due to renal impairment, multiple sites, without tophus (tophi)
M1A.39X1	Chronic gout due to renal impairment, multiple sites, with tophus (tophi)
M1A.40X0	Other secondary chronic gout, unspecified site, without tophus (tophi)
M1A.40X1	Other secondary chronic gout, unspecified site, with tophus (tophi)
M1A.4110	Other secondary chronic gout, right shoulder, without tophus (tophi)
M1A.4111	Other secondary chronic gout, right shoulder, with tophus (tophi)
M1A.4120	Other secondary chronic gout, left shoulder, without tophus (tophi)
M1A.4121	Other secondary chronic gout, left shoulder, with tophus (tophi)

Diagnosis Code	Description
M1A.4190	Other secondary chronic gout, unspecified shoulder, without tophus (tophi)
M1A.4191	Other secondary chronic gout, unspecified shoulder, with tophus (tophi)
M1A.4210	Other secondary chronic gout, right elbow, without tophus (tophi)
M1A.4211	Other secondary chronic gout, right elbow, with tophus (tophi)
M1A.4220	Other secondary chronic gout, left elbow, without tophus (tophi)
M1A.4221	Other secondary chronic gout, left elbow, with tophus (tophi)
M1A.4290	Other secondary chronic gout, unspecified elbow, without tophus (tophi)
M1A.4291	Other secondary chronic gout, unspecified elbow, with tophus (tophi
M1A.4310	Other secondary chronic gout, right wrist, without tophus (tophi)
M1A.4311	Other secondary chronic gout, right wrist, with tophus (tophi)
M1A.4320	Other secondary chronic gout, left wrist, without tophus (tophi)
M1A.4321	Other secondary chronic gout, left wrist, with tophus (tophi)
M1A.4390	Other secondary chronic gout, unspecified wrist, without tophus (tophi)
M1A.4391	Other secondary chronic gout, unspecified wrist, with tophus (tophi)
M1A.4410	Other secondary chronic gout, right hand, without tophus (tophi)
M1A.4411	Other secondary chronic gout, right hand, with tophus (tophi)
M1A.4420	Other secondary chronic gout, left hand, without tophus (tophi)
M1A.4421	Other secondary chronic gout, left hand, with tophus (tophi)
M1A.4490	Other secondary chronic gout, unspecified hand, without tophus (tophi)
M1A.4491	Other secondary chronic gout, unspecified hand, with tophus (tophi)
M1A.4510	Other secondary chronic gout, right hip, without tophus (tophi)
M1A.4511	Other secondary chronic gout, right hip, with tophus (tophi)
M1A.4520	Other secondary chronic gout, left hip, without tophus (tophi)
M1A.4521	Other secondary chronic gout, left hip, with tophus (tophi)
M1A.4590	Other secondary chronic gout, unspecified hip, without tophus (tophi)
M1A.4591	Other secondary chronic gout, unspecified hip, with tophus (tophi)
M1A.4610	Other secondary chronic gout, right knee, without tophus (tophi)
M1A.4611	Other secondary chronic gout, right knee, with tophus (tophi)
M1A.4620	Other secondary chronic gout, left knee, without tophus (tophi)
M1A.4621	Other secondary chronic gout, left knee, with tophus (tophi)
M1A.4690	Other secondary chronic gout, unspecified knee, without tophus (tophi)
M1A.4691	Other secondary chronic gout, unspecified knee, with tophus (tophi)
M1A.4710	Other secondary chronic gout, right ankle and foot, without tophus (tophi)
M1A.4711	Other secondary chronic gout, right ankle and foot, with tophus (tophi)
M1A.4720	Other secondary chronic gout, left ankle and foot, without tophus (tophi)
M1A.4721	Other secondary chronic gout, left ankle and foot, with tophus (tophi)
M1A.4790	Other secondary chronic gout, unspecified ankle and foot, without tophus (tophi)
M1A.4791	Other secondary chronic gout, unspecified ankle and foot, with tophus (tophi
M1A.48X0	Other secondary chronic gout, vertebrae, without tophus (tophi)
M1A.48X1	Other secondary chronic gout, vertebrae, with tophus (tophi)
M1A.49X0	Other secondary chronic gout, multiple sites, without tophus (tophi)
M1A.49X1	Other secondary chronic gout, multiple sites, with tophus (tophi)

Diagnosis Code	Description
M1A.9XX0	Chronic gout, unspecified, without tophus (tophi)
M1A.9XX1	Chronic gout, unspecified, with tophus (tophi)

Background

Pegloticase is a uric acid specific enzyme which is a PEGylated product that consists of recombinant modified mammalian urate oxidase (uricase) and achieves its therapeutic effect by catalyzing the oxidation of uric acid to allantoin, thereby lowering serum uric acid. Allantoin is an inert and water-soluble purine metabolite.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Proven

Chronic Gout

Pegloticase is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patient's refractory to conventional therapy.

Professional Societies

European League Against Rheu Matism (EULAR) 2016

In 2017 EULAR published their updated recommendations, representing a systematic review and update of the 2006 recommendations. The guidelines include the following recommendations:

- Recommended first-line options for acute flare are colchicine (within 12 hours of flare onset) and/or an NSAID (plus a proton pump inhibitor if appropriate), oral corticosteroids or articular aspiration and injection of corticosteroids.
- In patients with frequent flares and contraindications to colchicine, NSAIDs and corticosteroids (oral and injectable), interleukin-1 (IL-1) blockers should be considered for treating flares. Urate-lowering therapy (ULT) should be adjusted to achieve the uricemia target following IL-1 blocker treatment for flare.
- Prophylaxis is recommended during the first 6 months of ULT. Recommended prophylactic treatment is colchicine, If colchicine is not tolerated or is contraindicated, prophylaxis with NSAIDs at low dosage should be considered.
- ULT is indicated in all patients with recurrent flares, tophi, urate arthropathy and/or renal stones. Initiation of ULT is recommended close to the time of first diagnosis in patients presenting at a young age (< 40 years) or with a very high serum uric acid (SUA) level (> 8.0 mg/dL; 480 µmol/L) and/or comorbidities (renal impairment, hypertension, ischemic heart disease, heart failure).
- In patients with normal kidney function, allopurinol is recommended for first-line ULT, starting at a low dose (100 mg/day) and increasing by 100 mg increments every 2–4 weeks if required, to reach the uricemia target. If the SUA target cannot be reached by an appropriate dose of allopurinol, allopurinol should be switched to febuxostat or a uricosuric or combined with a uricosuric. Febuxostat or a uricosuric are also indicated if allopurinol cannot be tolerated.
- In patients with crystal-proven, severe debilitating chronic tophaceous gout and poor quality of life, in whom the SUA target cannot be reached with any other available drug at the maximal dosage (including combinations), Pegloticase is indicated.

American College of Physicians (ACP) 2016

The American College of Physicians published their clinical practice guideline for the management of acute and recurrent gout. These guidelines do not address the place in therapy for Pegloticase. The guidelines recommend:

- Clinicians choose corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or colchicine to treat patients with acute gout. (Grade: strong recommendation, high-quality evidence).
- Clinicians use low-dose colchicine when using colchicine to treat acute gout. (Grade: strong recommendation, moderate-quality evidence).
- Against initiating long-term urate-lowering therapy in most patients after a first gout attack or in patients with infrequent attacks. (Grade: strong recommendation, moderate-quality evidence).
- Clinicians discuss benefits, harms, costs, and individual preferences with patients before initiating urate-lowering therapy, including concomitant prophylaxis, in patients with recurrent gout attacks. (Grade: strong recommendation, moderate-quality evidence).

American College of Rheumatology (ACR) 2020

In 2020 the ACR published their updated clinical guidelines for the management of gout. ACR recommends:
Recommendations for choice of initial ULT for patients with gout:

- Treatment with allopurinol as the preferred first-line agent, over all other ULTs, is strongly recommended for all patients, including those with moderate-to-severe CKD (stage ≥ 3).
- The choice of either allopurinol or febuxostat over probenecid is strongly recommended for patients with moderate-to-severe CKD (stage ≥ 3).
- The choice of pegloticase as a first-line therapy is strongly recommended against.
- Starting treatment with low-dose allopurinol (≤ 100 mg/day and lower in patients with CKD [stage ≥ 3]) and febuxostat (≤ 40 mg/day) with subsequent dose titration over starting at a higher dose is strongly recommended.
- Starting treatment with low-dose probenecid (500 mg once to twice daily) with subsequent dose titration over starting at a higher dose is conditionally recommended.
- Administering concomitant anti-inflammatory prophylaxis therapy (e.g., colchicine, nonsteroidal anti-inflammatory drugs [NSAIDs], prednisone/ prednisolone) over no anti-inflammatory prophylaxis therapy is strongly recommended.

When to consider changing ULT strategy:

- Switching to pegloticase over continuing current ULT is strongly recommended for patients with gout for whom XOI treatment, uricosurics, and other interventions have failed to achieve the SU target, and who continue to have frequent gout flares (≥ 2 flares/year) OR who have nonresolving subcutaneous tophi.
- Switching to pegloticase over continuing current ULT is strongly recommended against for patients with gout for whom XOI treatment, uricosurics, and other interventions have failed to achieve the SU target, but who have infrequent gout flares (< 2 flares/year) AND no tophi.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Krystexxa® (Pegloticase) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.[1]

Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Limitations of Use: Krystexxa is not recommended for the treatment of asymptomatic hyperuricemia.

Centers for Medicare and Medicaid Services

Medicare does not have a National Coverage Determination (NCD) for Krystexxa® (pegloticase). Local Coverage Determinations/Articles (LCDs)/LCAs) do not exist.

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals.

**Preferred therapy criteria for Medicare Advantage members, refer to Medicare Part B Step Therapy Programs.

References

1. Krystexa [prescribing information]. Deerfield, IL: Horizon Therapeutics USA, Inc. November 2022.
2. Sundy JS, Baraf HS, Yood RA, et al. Efficacy and tolerability of Pegloticase for the treatment of chronic gout in patient's refractory to conventional treatment: two randomized controlled trials. JAMA 2011; 306:711–720.
3. Baraf HS, Becker MA, Gutierrez-Urena SR, et al. Tophus burden reduction with Pegloticase: results from phase 3 randomized trials and open-label extension in patients with chronic gout refractory to conventional therapy. Arthritis Res Ther. 2013 Sep 26;15(5): R137.
4. Qaseem A, Harris RP, Forclea MA. Management of acute and recurrent gout: A clinical practice guideline from the American College of Physicians. Ann Intern Med. 2017;166(1):58-68.
5. Richette P et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017 Jan;76(1):29-42.
6. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout [published correction appears in Arthritis Care Res (Hoboken). 2020 Aug;72(8):1187]. Arthritis Care Res (Hoboken). 2020;72(6):744-760.
7. Becker MA, Perez-Ruiz F. Pharmacologic urate-lowering therapy and treatment of tophi in patients with gout. Dalbeth N, ed. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com. Accessed on September 10, 2023.
8. Richette P, Doherty M, Pascual E, et al. 2018 updated European League Against Rheumatism evidence-based recommendations for the diagnosis of gout. Ann Rheum Dis. 2020;79(1):31-38. doi:10.1136/annrheumdis-2019-215315.

Policy History/Revision Information

Date	Summary of Changes
12/01/2023	**Coverage Rationale** • Revised medical necessity criteria: ***Initial Therapy*** ○ Added criterion requiring: ▪ Submission of laboratory values demonstrating baseline serum uric acid level > 6 mg/dL ▪ Prescriber attests that serum uric acid levels will be monitored prior to each infusion and that discontinuation of treatment will be considered if pre-infusion levels increase above 6 mg/dL ○ Replaced criterion requiring: ▪ "One of the following: history of at least 2 gout flares in the previous 12 months, at least 1 gouty tophus, or chronic gouty arthropathy" with "*diagnosis of symptomatic gout as defined by* one of the following: history of at least 2 gout flares in the previous 12 months, at least 1 gouty tophus, or chronic gouty arthropathy" ▪ "History of contraindication, intolerance, or treatment failure after 3 months of therapy (at the maximally medically appropriate dose) with Zyloprim (allopurinol) and Uloric (febuxostat)" with "history of contraindication, intolerance, or treatment failure *(i.e., failure to normalize uric acid to < 6 mg/dL)* after 3 months of therapy (at the maximally medically appropriate dose) with Zyloprim (allopurinol) and Uloric (febuxostat)" ▪ "Krystexxa (pegloticase) is prescribed by, *or in consultation with*, a rheumatologist or nephrologist" with "Krystexxa (pegloticase) is prescribed by a rheumatologist or nephrologist"

Date	Summary of Changes
	Continuation of Therapy ○ Added criterion requiring the patient has not had two consecutive uric acid levels above 6 mg/dL after initiating treatment with Krystexxa ○ Replaced criterion requiring "Krystexxa (pegloticase) is prescribed by, *or in consultation with*, a rheumatologist or nephrologist" with "Krystexxa (pegloticase) is prescribed by a rheumatologist or nephrologist" **Supporting Information** • Updated *References* section to reflect the most current information • Archived previous policy version 2022D0082E

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.