

UTILIZATION MANAGEMENT MEDICAL POLICY

- POLICY:** Repository Corticotropin – Cortrophin Gel Utilization Management Medical Policy
- Purified Cortrophin™ Gel (repository corticotropin subcutaneous and intramuscular injection – ANI)

REVIEW DATE: 05/01/2024

OVERVIEW

Cortrophin Gel, a porcine derived purified corticotropin (adrenocorticotrophic hormone [ACTH] {1-39}) product, is indicated in the following disorders:¹

- **Allergic states**, such as atopic dermatitis and serum sickness.
- **Collagen diseases**, during an exacerbation or as a maintenance therapy in selected cases of systemic lupus erythematosus and systemic dermatomyositis (polymyositis).
- **Dermatologic diseases**, such as severe erythema multiforme (Stevens-Johnson syndrome) and severe psoriasis.
- **Edematous state** including to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.
- **Nervous system**, acute exacerbations of multiple sclerosis.
- **Respiratory diseases** such as symptomatic sarcoidosis.
- **Rheumatoid disorders**, as an adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in psoriatic arthritis, rheumatoid arthritis (including juvenile rheumatoid arthritis) [selected cases may require low-dose maintenance therapy], ankylosing spondylitis, and acute gouty arthritis.
- **Ophthalmic diseases** including severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as allergic conjunctivitis, keratitis, iritis and iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, and anterior segment inflammation.

Clinical Efficacy

A recent review regarding repository corticotropin found few randomized controlled trials supporting the clinical benefit of repository corticotropin or ACTH for various conditions (e.g., use in rheumatoid arthritis, ankylosing spondylitis, optic neuritis, systemic lupus erythematosus, and nephrotic syndrome).² Most data suggest that repository corticotropin or ACTH was not superior to corticosteroids for treating relapses in patients with multiple sclerosis.

Guidelines

Several guidelines discuss repository corticotropin or ACTH.

- **Kidney Disease Improving Global Outcomes (KDIGO)** published clinical practice guidelines for the management of glomerular disease (2021).³ This includes diagnoses such as nephrotic syndrome, membranous nephropathy, immunoglobulin A nephropathy, minimal change disease, infection-related glomerulonephritis, focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, and lupus nephritis. ACTH is not prominent in the guidelines and there is a lack of quality evidence regarding ACTH. Updated KDIGO guidelines were published regarding the management of lupus nephritis (2024), as well as for the management of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (2024).^{20,21} ACTH is not mentioned in the guidelines.

- The **National Multiple Sclerosis Society** has recommendations regarding corticosteroids in the management of multiple sclerosis relapses or exacerbations.⁴ High-dose corticosteroids are the accepted standard of care short-term. The most common regimen is 500 to 1,000 mg of intravenous methylprednisolone given daily for 3 to 5 days, with or without an oral steroid tapering regimen (most often prednisone) for 1 to 3 weeks. ACTH and high-dose intravenous methylprednisolone have been shown to possess similar efficacy in the management of multiple sclerosis relapses.⁵
- The **American College of Rheumatology** has many guidelines regarding use in rheumatoid-type conditions.⁶ ACTH does not have a prominent role and is generally not recommended for use in any of the related American College of Rheumatology guidelines.
- The **American College of Rheumatology** has guidelines for the management of gout (2020).⁷ For gout flare management, using colchicine, non-steroidal anti-inflammatory drugs, or glucocorticoids (oral, intraarticular, or intramuscular) are appropriate first-line therapy for gout flare over interleukin-1 inhibitors or ACTH.
- The **European Respiratory Society** published guidelines on the treatment of sarcoidosis (2021).⁸ Repository corticotropin use should be reserved for patients who have failed prior treatments (e.g., steroids, antimetabolites). Only limited data are available. Repository corticotropin should be considered in a case by case basis only when other therapies are not effective or tolerated.

POLICY STATEMENT

Due to the lack of updated clinical efficacy data and potential safety concerns with long-term use, **approval is not recommended** for Cortrophin Gel. The current Cortrophin Gel efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits beyond those provided by other available therapies.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

None.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Cortrophin Gel is not recommended in the following situations:

1. **Ankylosing Spondylitis.** The American College of Rheumatology guidelines for the treatment of ankylosing spondylitis do not convey a role for ACTH in this condition.^{9,10}
2. **Dermatomyositis or Polymyositis.** British Society for Rheumatology guidelines on the management of pediatric, adolescent, and adult patients with idiopathic inflammatory myopathy (2022) do not cite ACTH as an agent to utilize in patients with such conditions.¹¹
3. **Diabetic Nephropathy.** ACTH is not a cited therapy or the standard of care for the management of chronic kidney disease in patients with diabetes.^{3,12}
4. **Glomerular Kidney Diseases.**
Note: Diagnoses can include nephrotic syndrome, membranous nephropathy, immunoglobulin A nephropathy, minimal change disease, infection-related glomerulonephritis, focal segmental glomerulosclerosis, and membranoproliferative glomerulonephritis. ACTH is not prominent in related

guidelines from KDIGO (2021) and there is a lack of quality evidence regarding ACTH to supports its use.³ KDIGO guidelines for the management of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (2024) do not mention ACTH.²¹

5. **Gout.** American College of Rheumatology guidelines for gout (2020) recommend other therapies beside ACTH for gout flare management (e.g., colchicine, non-steroidal anti-inflammatory drugs, or glucocorticoids).⁷
6. **Infantile Spasms, Treatment.** Purified Cortrophin Gel is not FDA-approved for this use.¹
7. **Juvenile Idiopathic Arthritis.** Related guidelines from the American College of Rheumatology regarding the treatment of juvenile idiopathic arthritis (2021) do not mention ACTH as having a role for this disease.¹³
8. **Lupus Nephritis.** The KDIGO guidelines for the management of glomerular disease (2021) cite many other agents besides ACTH for the management of this condition.³ The European League Against Rheumatism-European Renal Association-European Dialysis and Transplantation Association joint recommendations on the management of lupus nephritis do not cite ACTH as a therapy to use in this condition.¹⁴ Updated KDIGO guidelines were published regarding the management of lupus nephritis (2024) and do not mention ACTH.²⁰
9. **Multiple Sclerosis, Acute Exacerbations.** High-dose corticosteroids, usually intravenous methylprednisolone, are the accepted standard of care short-term for acute relapses or exacerbations.⁴
10. **Ophthalmic Conditions.** Only limited data describes the use of ACTH in ophthalmic-related conditions (e.g., acute optic neuritis, keratitis, retinal vasculitis).^{2,15-17} Prospective data are needed to more rigorously define the efficacy and safety of ACTH in ocular disease.
11. **Psoriatic Arthritis.** The American College of Rheumatology/National Psoriasis Foundation guidelines for the treatment of psoriatic arthritis (2018) do not mention a role for ACTH in this condition.¹⁸
12. **Rheumatoid Arthritis.** The American College of Rheumatology guidelines for the treatment of rheumatoid arthritis (2021) do not mention a role for ACTH in this disease state.¹⁹
13. **Sarcoidosis.** The European Respiratory Society published guidelines on the treatment of sarcoidosis (2021).⁸ Repository corticotropin use should be reserved for patients who have failed prior treatments (e.g., steroids, antimetabolites). Only limited data are available. Repository corticotropin should be considered in a case by case basis only when other therapies are not effective or tolerated.
14. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Purified Cortrophin™ Gel subcutaneous and intramuscular injection [prescribing information]. Baudette, MN: ANI; October 2023.
2. Tran KA, Harrod C, Bourdette DN, et al. Characterization of the clinical evidence supporting repository corticotropin injection for FDA-approved indications. A scoping review. *JAMA Intern Med.* 2022;182(2):206-217.
3. Kidney Disease: Improving Global Outcomes Glomerular Diseases Working Group. KDIGO 2021 clinical practice guidelines for the management of glomerular diseases. *Kidney Int.* 2021;100:S1-S276.

4. National Multiple Sclerosis Society. Expert Opinion Paper. National Clinical Advisory Board of the National Multiple Sclerosis Society. Treatment Recommendations for Physicians. Recommendations Regarding Corticosteroids in the Management of Multiple Sclerosis. Available at: http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ExpOp_Steroids.pdf. Accessed on April 19, 2024.
5. Thompson AJ, Kennard C, Swash M, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapses in MS. *Neurology*. 1989;39:969-971.
6. American College of Rheumatology. Clinical Practice Guidelines. Available at: <https://rheumatology.org/clinical-practice-guidelines>. Accessed on April 19, 2024.
7. Fitzgerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology guideline for the management of gout. *Arthritis Care Res (Hoboken)*. 2020;72(6):744-760.
8. Baughman RP, Valeyre D, Korsten P, et al. ERS clinical practice guidelines on treatment of sarcoidosis. *Eur Respir J*. 2021;58(6):2004079.
9. Ward MM, Deodhar A, Gensler LS, et al. 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol*. 2019;71(10):1599-1613.
10. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Care Res*. 2016;68:151-166.
11. Oldroyd AGS, Lilleker JB, Amin T, et al. British Society for Rheumatology guideline on management of paediatric, adolescent and adult patients with idiopathic inflammatory myopathy. *Rheumatology*. 2022;61(5):1760-1768.
12. American Diabetes Association Professional Practice Committee. Chronic Kidney Disease and Risk Management: Standards of Medical Care in Diabetes-2024. *Diabetes Care*. 2024;47(1):S219-S230.
13. Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology Guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for oligoarthritis, temporomandibular joint arthritis, and systemic juvenile idiopathic arthritis. *Arthritis Rheumatol*. 2022;74(4):553-569.
14. Fanouriakis A, Kostopoulou M, Cheema K, et al. 2019 Update of the Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDT) recommendations for the management of lupus nephritis. *Ann Rheum Dis*. 2020;79:713-732.
15. Crane AB, Sharon Y, Chu DS. Use of adrenocorticotrophic hormone in ophthalmology. *J Ocul Pharmacol Ther*. 2020;36(9):661-667.
16. Wirta D, McLaurin E, Ousler G, et al. Repository corticotropin injection (Acthar® gel) for refractory severe noninfectious keratitis: efficacy and safety from a phase 4, multicenter, open-label study. *Ophthalmol Ther*. 2021;10:1077-1092.
17. Anesi SD, Chang PY, Maleki A, et al. Treatment of noninfectious retinal vasculitis using subcutaneous repository corticotropin injection. *J Ophthalmic Vis Res*. 2021;16:219-233.
18. Singh JA, Guyatt G, Ordie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheumatol*. 2019;71(1):5-32.
19. Fraenkiel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res (Hoboken)*. 2021;73(7):924-939.
20. Kidney Disease Improving Global Outcomes lupus nephritis work group. KDIGO 2024 clinical practice guidelines for the management of lupus nephritis. *Kidney Int*. 2024;105(Suppl 1S):S1-S69.
21. Kidney Disease Improving Global Outcomes ANCA Vasculitis Work Group. KDIGO 2024 clinical practice guideline for the management of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. *Kidney Int*. 2024;105(Suppl 3S):S71-S116.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	04/19/2023
Annual Revision	No criteria changes.	05/01/2024