



Dear Healthcare Professional,

Thank you for your unsolicited request for information. Accompanying this letter is the following information you requested on Purified Cortrophin® Gel. If we can be of any further assistance, please contact our Medical Information department at (844) CORT-GEL (844-267-8435) between the hours of 9:00 AM to 7:00 PM ET (6:00 AM to 4:00 PM PT), Monday through Friday or via email at [cortrophinmedinfo@anipharma.com](mailto:cortrophinmedinfo@anipharma.com).

Purified Cortrophin Gel is indicated in the following disorders:

1. Rheumatic disorders:

As 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.

Acute gouty arthritis.

2. Collagen diseases:

During an exacerbation or as maintenance therapy in selected cases of:

Systemic lupus erythematosus.

Systemic dermatomyositis (polymyositis).

3. Dermatologic diseases:

Severe erythema multiforme (Stevens-Johnson syndrome).

Severe psoriasis.

4. Allergic states:

Atopic dermatitis

Serum sickness.

5. Ophthalmic diseases:

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.

Anterior segment inflammation.



6. Respiratory diseases:

Symptomatic sarcoidosis.

7. Edematous states:

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.

8. Nervous system:

Acute exacerbations of multiple sclerosis.

Purified Cortrophin Gel is contraindicated for intravenous administration.

Purified Cortrophin Gel is contraindicated in patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive heart failure, hypertension, or sensitivity to proteins derived from porcine sources.

Purified Cortrophin Gel is contraindicated in patients with primary adrenocortical insufficiency or adrenocortical hyperfunction.

Please see the enclosed Purified Cortrophin Gel Prescribing Information (PI) for detailed information including Warnings and Precautions and Adverse Reactions as well as the appropriate use of Purified Cortrophin Gel.

This communication may contain confidential, proprietary, and/or privileged information. It is intended solely for the use of the addressee. If you are not the intended recipient, you are strictly prohibited from disclosing, copying, distributing or using any of this information. If you received this communication in error, please contact the sender immediately and destroy the material in its entirety, whether electronic or hard copy.

Thank you for your inquiry. Sincerely,

Steve Wu, PharmD

A handwritten signature in black ink that reads "Steve Wu". The signature is written in a cursive, flowing style.

ANI Pharmaceuticals Medical Information

# Use of Purified Cortrophin<sup>®</sup> Gel (Repository Corticotropin Injection USP) 80 U/mL in Patients With Systemic Lupus Erythematosus

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## Abstract

- This document provides summary information pertaining to Purified Cortrophin Gel (repository corticotropin injection USP) and its indication for use during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus (SLE).
- The active agent in Purified Cortrophin Gel is porcine-derived adrenocorticotrophic hormone (ACTH peptide, amino acids 1-39), which is biologically similar to endogenous, human ACTH, and of the same class as other natural-product and synthetic formulations of ACTH.
- To date, there are no published clinical data available that directly interrogate the clinical efficacy and safety of Purified Cortrophin Gel in patients with SLE.
- Summarized in this document are the results of a literature search of publicly available, peer-reviewed clinical studies of other natural-product and synthetic formulations of ACTH. Seven studies – including randomized controlled trials, open-label studies, and retrospective medical record reviews – were identified, involving a total of 250 patients treated with ACTH for SLE.

**Note that this document is for information purposes only. Please refer to the Purified Cortrophin Gel (repository corticotropin injection USP) USPI for [full prescribing information](#). ANI Pharmaceuticals does not recommend the use of its products in any manner inconsistent with the FDA-approved labeling.**

**To report an adverse event for any ANI Pharmaceuticals product, please call 1-800-308-6755 or contact the FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

**Email: [drugsafety@anipharmaceuticals.com](mailto:drugsafety@anipharmaceuticals.com).**

## Introduction

### Clinical Background<sup>1</sup>

Purified Cortrophin Gel (Repository Corticotropin Injection USP) is approved by the FDA for the treatment of collagen diseases, during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus (SLE) and systemic dermatomyositis (polymyositis).

### Composition of Cortrophin Gel<sup>1</sup>

Purified Cortrophin Gel is a porcine-derived purified corticotropin (ACTH) in a sterile solution of gelatin. It is made up of a complex mixture of ACTH, ACTH-related peptides, and other porcine pituitary-derived peptides.

The drug product is a sterile preparation containing 80 USP units per mL; it contains 0.5% phenol (as preservative), 15.0% gelatin (for prolonged activity), and water for injection; and the pH is adjusted with hydrochloric acid and sodium hydroxide.

Purified Cortrophin Gel contains the porcine-derived ACTH (1-39) with the following amino acid sequence:



### Purified Cortrophin Gel Clinical Pharmacology

ACTH, the active agent in Purified Cortrophin Gel, is the anterior pituitary hormone that stimulates the functioning adrenal cortex to produce and secrete adrenocortical hormones.<sup>1</sup>

Following administration of a single intramuscular (IM) injection of 80 units of Purified Cortrophin Gel to healthy volunteers (n=20) in an open-label pharmacodynamic study, the median time (range) to reach peak cortisol concentration was 8 (3 to 12) hours. The baseline corrected geometric mean maximum (coefficient of variation [CV%]) cortisol levels were 34.52 µg/dL (28.2%).<sup>1</sup>

The porcine-derived ACTH (1-39) found in Purified Cortrophin Gel is biologically similar to endogenous human ACTH<sup>2</sup>, and of the same class as other natural-product<sup>3</sup> and synthetic ACTH<sup>4</sup> formulations.

ANI conducted a study on the pharmacodynamic effect of Purified Cortrophin Gel, including maximum observed effect (E<sub>max</sub>), area under the effect curve over 24 hours (AUEC<sub>0-24</sub>), and time to achieve maximum observed effect (T<sub>E<sub>max</sub></sub>), and compared it with the response of the same or similar depot structures from published literature.<sup>5,6</sup>

## Select Clinical Data in Support of ACTH in Patients With SLE

### Study Selection

ANI Pharmaceuticals is not aware of any published (or unpublished) randomized clinical trials or adequately designed studies using Purified Cortrophin Gel for the treatment of SLE that directly interrogate its clinical efficacy and safety.

Below is an overview of peer-reviewed publications of clinical studies that use Acthar Gel, which shares the same porcine-derived active agent, ACTH, as Purified Cortrophin Gel; and synthetic ACTH, which is a truncated ACTH derivative comprising amino acids 1 through 24 of ACTH (1-39). The summary below provides an overview of the published clinical evidence of in-class ACTH-based therapies, with references to source material.

### Study Results Summary

A PubMed search was conducted through May 2025 to identify studies assessing the use of ACTH in patients with SLE. The selection included studies with  $\geq 10$  patients, excluding case series and reports. Based on these criteria, seven studies were identified, representing a total of 250 patients who received ACTH for SLE treatment. These studies included randomized controlled trials, open-label studies, and retrospective medical record reviews, and are summarized in Tables 1 and 2 below.

Table 1. Summary of Clinical Data in Support of ACTH Use in Patients With SLE

| Study                             | Objective  | Design  | RCI  | Comparator     | Patient Population   | Study Tx Regimen   | Efficacy  | Safety  |
|-----------------------------------|--|---|--|----------------|--|--|---|---|
| <b>Fiechtner 2014<sup>7</sup></b> | To evaluate the efficacy of Acthar Gel in patients with active SLE receiving underlying conventional maintenance treatments.                         | Prospective single-center, open-label trial.<br><br><b>Duration:</b> 28 days<br><br><b>Primary outcome:</b><br><ul style="list-style-type: none"> <li>Change from baseline in SLEDAI-2K score</li> </ul> <b>Select secondary outcomes:</b> <ul style="list-style-type: none"> <li>Physician and patient global assessments</li> <li>FACIT-Fatigue</li> <li>BILAG scores</li> <li>ESR</li> </ul>                               | N=10   | None           | <b>Key inclusion criteria:</b> <ul style="list-style-type: none"> <li>Ages 18-75 years</li> <li>Met at least 4 of 11 ACR criteria for SLE, including positive history of ANA</li> <li>Presented with chronic, moderate to severe active SLE and a disease flare during standard treatment</li> </ul>   | 80 U SC QD for 10 days, with optional 5-day rescue period for partial or non-responders  | Statistically significant improvements from baseline were observed at all follow-up visits for the following outcomes:<br><b>Primary outcome:</b> <ul style="list-style-type: none"> <li>SLEDAI-2K score improved from 9.60 at baseline to 4.00 at Day 28 (<math>P&lt;0.01</math>)</li> </ul> <b>Secondary outcomes:</b> <ul style="list-style-type: none"> <li>Physician global assessment improved from 2.07 at baseline to 1.09 at Day 28 (<math>P&lt;0.01</math>)</li> <li>Patient global assessment improved from 7.10 at baseline to 3.80 at Day 28 (<math>P\leq 0.01</math>)</li> <li>FACIT-Fatigue improved from 30.70 at baseline to 20.50 at Day 28 (<math>P&lt;0.01</math>)</li> <li>ESR improved from 26.70 at baseline to 18.80 at Day 28 (<math>P\leq 0.03</math>)</li> </ul> | <ul style="list-style-type: none"> <li>No treatment-related serious AEs were observed. <ul style="list-style-type: none"> <li>One patient had bilateral edema in legs and ankles</li> <li>One patient reported a sinus infection</li> </ul> </li> </ul>   |
| <b>Furie 2016<sup>8</sup></b>     | To evaluate the efficacy and safety of RCI added to standard of care in patients with persistent active SLE requiring moderate-dose corticosteroids. | Prospective, randomized, double-blind, phase 4, placebo-controlled pilot study.<br><br><b>Duration:</b> 52 weeks (8 weeks double-blind phase + 44 weeks OLE)<br><br><b>Primary endpoint:</b> <ul style="list-style-type: none"> <li>Treatment response at Week 4, measured by a decrease in hSLEDAI score for arthritis (from 4 to 0) or rash (from 2 to 0), without worsening BILAG scores in other organ systems</li> </ul> | n=26<br><br>40 U SC QD: (n=13)<br><br>80 U SC QD: (n=13) | Placebo (n=12) | Patients with persistently active SLE involving skin and/or joints.<br><br><b>Key inclusion criteria:</b> <ul style="list-style-type: none"> <li>Adults <math>\geq 18</math> years old with SLE meeting <math>\geq 4</math> ACR criteria</li> <li>Active disease with arthritis and/or rash based on the hSLEDAI</li> <li>BILAG score of A or B in the musculoskeletal or mucocutaneous domains</li> <li>Seropositive for ANAs and anti-dsDNA, anti-Smith, or anti-cardiolipin antibodies</li> </ul> | 40 U SC QD or 80 U SC QOD for 8 weeks.<br><br>Dose tapering:<br><ul style="list-style-type: none"> <li>Weeks 1-4: Reduced to 16 U QD and 40 U QD if safety criteria met.</li> <li>Weeks 5-8: Gradually taper to 2x/week by end of double-blind period.</li> </ul><br>In OLE phase, patients received | <b>Primary endpoint:</b> <ul style="list-style-type: none"> <li>No significant difference in treatment response at Week 4 between RCI combined vs placebo (16.0% vs 27.3%, respectively)</li> </ul> <b>Secondary endpoints:</b> <ul style="list-style-type: none"> <li>Proportion of responders at Week 8 was higher in RCI-treated patients (44.0%) vs placebo (27.3%), but not statistically significant</li> <li>Post hoc analysis: Proportion of responders, as defined by the SRI, at Week 8 was statistically significantly higher for the combined RCI group vs placebo</li> </ul>   | In the double-blind phase: <ul style="list-style-type: none"> <li>Similar rates of overall TEAEs were observed in the combined RCI and placebo groups (76.0% vs 81.8%, respectively)</li> <li>Overall incidence of infections was higher in patients treated with RCI (23.1% for both doses) vs placebo (9.1%)</li> </ul> <b>TEAE discontinuations:</b> <ul style="list-style-type: none"> <li>n=4 patients (16.0%) in the combined RCI group vs n=0 placebo</li> </ul> |

| Study                         | Objective   | Design  | RCI                         | Comparator                  | Patient Population  | Study Tx Regimen  | Efficacy  | Safety  |
|-------------------------------|---|---|-----------------------------|-----------------------------|---|---|---|---|
|                               |   | <b>Secondary endpoints:</b> <ul style="list-style-type: none"> <li>Proportion of responders at Week 8</li> <li>Total hSLEDAI</li> <li>BILAG-2004, CLASI, SF-36, KFSS or PGA scores</li> </ul> |                             |                             | <ul style="list-style-type: none"> <li>Persistent disease activity despite moderate-dose corticosteroids for at least 4 weeks prior to screening</li> </ul> | 16, 40, or 80 U RCI 1-3x weekly.<br><br><b>Study visit completion in double-blind phase for RCI vs placebo group:</b> n=22 vs n=11, respectively<br><br><b>52-week study completion for RCI/RCI group vs placebo/RCI group:</b> n=13 vs n=7, respectively | (52.0% vs 9.1%, respectively; $P=0.032$ )<br><br><ul style="list-style-type: none"> <li>hSLEDAI, BILAG, and CLASI-Activity scores: Statistically significant improvements were observed for the following scores in patients treated with combined RCI vs placebo at Week 8:               <ul style="list-style-type: none"> <li>total hSLEDAI: -3.8 vs -0.8, respectively (<math>P=0.008</math>)</li> <li>total BILAG score: -8.6 vs -1.8, respectively (<math>P=0.001</math>)</li> <li>CLASI-Activity: -3.1 vs -0.6, respectively (<math>P=0.047</math>)</li> </ul> </li> </ul>  | <b>Most common AEs:</b> <ul style="list-style-type: none"> <li>Weight gain: (20.0% of patients treated with combined RCI vs 18.2% placebo)</li> <li>Abdominal pain: 8.0% of patients treated with combined RCI vs 0% placebo</li> </ul>   |
| <b>Furie 2017<sup>9</sup></b> | Post hoc analysis of the Furie 2016 <sup>8</sup> study. | See Furie 2016 <sup>8</sup>   | See Furie 2016 <sup>8</sup> | See Furie 2016 <sup>8</sup> | See Furie 2016 <sup>8</sup>   | See Furie 2016 <sup>8</sup>   | <b>Patient response:</b> <ul style="list-style-type: none"> <li>Novel Index: At Week 52, 12.0% of RCI/RCI patients and 36.4% of placebo/RCI patients were responders</li> <li>Revised Novel Responder Index: At Week 52, 48.0% of RCI/RCI-treated patients and 54.5% of placebo/RCI-treated patients, respectively, were responders</li> <li>SRI responders: At Week 52, 40.0% of RCI/RCI-treated patients and 54.5% of placebo/RCI-treated patients, respectively, were responders</li> </ul> <b>Disease Activity Scores:</b> <ul style="list-style-type: none"> <li>hSLEDAI scores decreased in both RCI/RCI (10.0 to 3.5) and placebo/RCI-treated patients (9.1 to 3.3) from baseline to Week 52, respectively</li> <li>BILAG scores decreased in both RCI/RCI (15.7 to 4.6) and placebo/RCI-treated patients</li> </ul> | <b>At 52 weeks:</b> <ul style="list-style-type: none"> <li>Similar rates of overall TEAEs were observed in the RCI/RCI and placebo/RCI groups (92.0% vs 100%, respectively)</li> <li>One death attributed to <i>Klebsiella</i> sepsis and multiorgan failure was reported in the RCI/RCI group</li> <li>Serious TEAEs were reported in n=4 RCI/RCI-treated patients (two of which were treatment-related) and n=4 placebo/RCI-treated patients</li> </ul> |

| Study                             | Objective  | Design  | RCI  | Comparator     | Patient Population   | Study Tx Regimen  | Efficacy  | Safety  |
|-----------------------------------|--|---|------|----------------|--|---|---|---|
|                                   |  |   |      |                |  |   | (15.4 to 2.6) from baseline to Week 52, respectively<br><b>Steroid tapering:</b><br><ul style="list-style-type: none"> <li>By the end of Week 52, 36.0% of patients in the RCI/RCI group reduced their daily prednisone dosage to &lt;7.5 mg</li> </ul>   |   |
| <b>Nelson 2017<sup>10</sup></b>   | To describe real-world patient characteristics, RCI treatment patterns, barriers to RCI use, and compare MRU before and after RCI therapy in patients with RA, PsA, DM/PM, or SLE. | Retrospective medical record review; real-world evidence.   | N=95 | None           | <b>Key inclusion criteria:</b> <ul style="list-style-type: none"> <li>Patients diagnosed with SLE</li> <li>Completed at least one course of RCI treatment in the last 2 years and at least 3 months prior to medical review</li> </ul>   | N/A   | <b>Primary measure, MRU:</b><br>After RCI therapy, there was a reduction in the mean number (per patient) of: <ul style="list-style-type: none"> <li>Hospital admissions: 0.17 (pre-RCI) to 0.03 (post-RCI); <i>P</i>&lt;0.05</li> <li>Hospital days: 0.45 (pre-RCI) to 0.04 (post-RCI); <i>P</i>&lt;0.05</li> <li>Outpatient visits: 2.74 (pre-RCI) to 2.55 (post-RCI)</li> </ul>  | Investigators did not report safety data in the study.  |
| <b>Askanase 2020<sup>11</sup></b> | To assess the efficacy and safety of RCI in patients with persistently active SLE despite treatment with moderate-dose glucocorticoids.  | Multicenter, randomized, double-blind, phase 4, placebo-controlled study.<br><br><b>Duration:</b> 24 weeks<br><br><b>Primary endpoint:</b> <ul style="list-style-type: none"> <li>SRI-4 responders at Week 16, defined by a four-point reduction from baseline in SLEDAI-2K, with no new BILAG A scores, no more than one new BILAG B organ domain score, and ≤10% increase from baseline in PGA</li> </ul><br><b>Secondary endpoints:</b><br>Change from baseline to Week 16 in: <ul style="list-style-type: none"> <li>28 SJC/TJC</li> <li>CLASI-Activity</li> <li>SLEDAI-2K</li> <li>BILAG-2004</li> </ul> | n=86 | Placebo (n=86) | Patients with persistently active SLE.<br><b>Select key inclusion criteria:</b> <ul style="list-style-type: none"> <li>Adults ≥18 years old with SLE meeting ≥4 ACR criteria</li> <li>SLEDAI-2K score ≥6</li> <li>Moderate to severe rash and/or arthritis as indicated by BILAG-2004 scores A or B in the mucocutaneous or musculoskeletal domains</li> <li>Stable glucocorticoid doses (7.5-30 mg/day prednisone equivalent) for ≥4 weeks before screening</li> <li>Stable doses of antimalarials for ≥4 weeks before screening</li> </ul> | 80 U SC QOD through Week 4, then 2x/week through Week 24.<br><br><b>Study visit completion in RCI group vs placebo:</b><br>n=73 vs n=71, respectively | <b>Primary endpoint:</b> <ul style="list-style-type: none"> <li>No significant difference in treatment response at Week 16 between the RCI vs placebo group (47.6% vs 43.5%, respectively; <i>P</i>=0.5762)</li> </ul><br><b>Secondary endpoints:</b><br>Statistically significant reductions were observed in the following scores in RCI-treated patients vs placebo at Week 16: <ul style="list-style-type: none"> <li>28 SJC/TJC: -6.4 vs -4.2, respectively (<i>P</i>=0.0203)</li> <li>CLASI-Activity: -4.5 vs -2.7, respectively (<i>P</i>=0.0423)</li> </ul> There were no statistically significant differences for the following scores at Week 16: <ul style="list-style-type: none"> <li>SLEDAI-2K: -3.8 vs -3.1, respectively (<i>P</i>=0.3520)</li> <li>BILAG-2004: -10.2 vs -8.6, respectively (<i>P</i>=0.0938)</li> </ul> | More patients in the placebo group (n=5) discontinued participation in the study due to disease progression compared to the RCI group (n = 1).<br><br><b>TEAE discontinuations:</b> n=4 patients (4.7%) in RCI group vs n=3 patients in placebo group (3.5%)<br><br><b>Reasons for TEAE discontinuations in RCI group:</b> <ul style="list-style-type: none"> <li>SLE flare (n=2; 2.3%)</li> <li>Drug hypersensitivity (n=1; 1.2%)</li> <li>Nephrotic syndrome (n=1; 1.2%)</li> </ul> |

| Study                             | Objective   | Design                          | RCI                             | Comparator                      | Patient Population              | Study Tx Regimen                | Efficacy   | Safety  |
|-----------------------------------|---|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|--|---|
|                                   |   |                                 |                                 |                                 |                                 |                                 |  | <p><b>Most common AEs</b> (in <math>\geq 3\%</math> of patients in the RCI group):</p> <ul style="list-style-type: none"> <li>• upper respiratory tract infection (n=9; 10.5%)</li> <li>• insomnia (n=7; 8.1%)</li> <li>• headache (n=6; 7.0%)</li> <li>• hypertension (n=6; 7.0%)</li> <li>• urinary tract infection (n=6; 7.0%)</li> <li>• herpes zoster (n=4; 4.7%)</li> <li>• influenza (n=4; 4.7%)</li> <li>• nasopharyngitis (n=3; 3.5%)</li> <li>• urticaria (n=3; 3.5%)</li> <li>• bronchitis (n=3; 3.5%)</li> <li>• hyperglycemia (n=3, 3.5%)</li> </ul> |
| <b>Askanase 2021<sup>12</sup></b> | Post hoc analysis of the Askanase 2020 <sup>11</sup> study to assess QoL and work productivity in SLE patients with high disease activity treated with RCI. | See Askanase 2020 <sup>11</sup> | See Askanase 2020 <sup>11</sup> | See Askanase 2020 <sup>11</sup> | See Askanase 2020 <sup>11</sup> | See Askanase 2020 <sup>11</sup> | <p><b>Patient-reported outcomes</b></p> <p>Lupus QoL Pain and Planning Domains:</p> <ul style="list-style-type: none"> <li>• Statistically significant nominal improvements from baseline were observed in the RCI vs placebo group at Week 16 in the pain domain (mean change: 20.6 vs 12.4, respectively; <math>P &lt; 0.05</math>) and at Week 24 in the planning domain (mean change: 22.4 vs 13.9, respectively; <math>P &lt; 0.05</math>)</li> </ul> <p>WPAI-Lupus Absenteeism:</p> <ul style="list-style-type: none"> <li>• Percentage of work time missed at Week 24 for patients with baseline CLASI-Activity <math>&lt; 11</math> was statistically significantly improved in the RCI group (mean</li> </ul> | None reported   |

| Study                              | Objective   | Design                                 | RCI   | Comparator | Patient Population   | Study Tx Regimen   | Efficacy   | Safety  |
|------------------------------------|---|--|---|------------|--|--|--|---|
|                                    |   |  |   |            |  |  | change: -8.4) vs placebo (mean change: -7.8) ( <i>P</i> =0.0182)   |   |
| <b>Ho-Mahler 2021<sup>13</sup></b> | To understand the practice patterns and outcomes of RCI in patients with SLE. | Retrospective medical record analysis. | N=30 <ul style="list-style-type: none"> <li>40 U BID (n=1)</li> <li>80 U QD (n=2)</li> <li>80 U QW (n=4)</li> <li>80 U BW (n=21)</li> <li>No data on starting dose and frequency (n=2)</li> </ul> | None       | Adults diagnosed with SLE.<br><b>Inclusion criteria:</b> <ul style="list-style-type: none"> <li>Age ≥18 years</li> <li>Physician-reported diagnosis of SLE according to ACR criteria</li> <li>Initiation of RCI between Jan 1, 2011, and Feb 15, 2016</li> <li>Had to have undergone RCI during an exacerbation or as maintenance therapy</li> </ul> | <ul style="list-style-type: none"> <li>40 U BID</li> <li>80 U QD</li> <li>80 U QW</li> <li>80 U BIW</li> </ul> <b>Mean (SD) duration of RCI treatment:</b> 6.5 (±3.3) months | <b>Physician assessment of efficacy:</b> <ul style="list-style-type: none"> <li>94.7% of patients with SLE treated with RCI were reported to be “improved” as per physician’s assessment</li> <li>Mean (SD) time to best impression of change was 4.3 (±2.7) months</li> </ul> | <b>TEAE discontinuations:</b> n=3<br><br><b>Reasons for TEAE discontinuations:</b><br>Specific TEAEs that directly led to discontinuation for each patient were not detailed separately.<br><br><b>Serious AEs</b> were reported in n=4 (13%) patients, including: <ul style="list-style-type: none"> <li>altered musculoskeletal pain</li> <li>dehydration</li> <li>adrenal insufficiency</li> <li>pneumonia</li> <li>renal failure</li> <li>transient ischemic attack</li> </ul> <b>AEs</b> were reported in n=5 (17%) patients including: <ul style="list-style-type: none"> <li>diarrhea</li> <li>gastrointestinal upset</li> <li>edema</li> <li>neuralgia</li> <li>pneumonia</li> <li>weight gain</li> </ul> |

ACR, American College of Rheumatology; ANA, antinuclear antibody; BAFF, B-cell activating factor; BICLA, British Isles Lupus Assessment Group-based Combined Lupus Assessment; BID, twice daily (bi-daily); BIW, bi-weekly; BILAG, British Isles Lupus Assessment Group; CLASI, cutaneous lupus erythematosus disease area and severity index; DM, dermatomyositis; DMARDs, disease-modifying antirheumatic drugs; dsDNA, double-stranded deoxyribonucleic acid; ESR, erythrocyte sedimentation rate; FACIT-Fatigue, functional assessment of chronic illness therapy-fatigue; hSLEDAI, hybrid SLE disease activity index; KFSS, Krupp Fatigue Severity Scale; MRU, medical resource use; OLE, open-label extension; PGA, physician’s global assessment; PM, polymyositis; PsA, psoriatic arthritis; QD, once daily; QOD, once every other day; QoL, quality of life; QW, once weekly; RA, rheumatoid arthritis; RCI, repository corticotropin injection; SC, subcutaneous; SF-36, medical outcomes survey short form-36; SD, standard deviation; SJC/TJC, swollen joint count/tender joint count; SLE, systemic lupus erythematosus; SLEDAI-2K, systemic lupus erythematosus disease activity Index-2000; SLICC, Systemic Lupus International Collaborating Clinics; SRI, SLE responder index; TEAE, treatment-emergent adverse event; U, units; WPAl, work productivity and activity impairment.

**Table 2. Prior and Concomitant Medications**

| Study                                    | Prior Therapy   | Concurrent Therapy to RCI  |
|--|---|--|
| <p><b>Fiechtner 2014<sup>7</sup></b></p> | <p>All patients received a stable dose of prednisone (or equivalent) 20 mg/day from at least 4 weeks prior to signing the informed consent.</p> <p>Previous treatments included:</p> <ul style="list-style-type: none"> <li>• methylprednisolone (70%)</li> <li>• prednisone (60%)</li> <li>• methotrexate (40%)</li> <li>• mycophenolate mofetil (30%)</li> <li>• thalidomide (20%)</li> </ul> | <ul style="list-style-type: none"> <li>• Belimumab (90%)</li> <li>• Meloxicam, prednisone, hydroxychloroquine (50%)</li> <li>• Tramadol, methotrexate (40%)</li> <li>• Folic acid (30%)</li> <li>• Diclofenac cream (20%)</li> <li>• Ibuprofen, sulfasalazine, celecoxib, diclofenac sodium, hydrocortisone (10%)</li> </ul> |

| Study                             | Prior Therapy   | Concurrent Therapy to RCI  |
|-----------------------------------|---|--|
|                                   | <ul style="list-style-type: none"> <li>hydroxychloroquine (40%)</li> </ul>  |  |
| <b>Furie 2016<sup>8</sup></b>     | <ul style="list-style-type: none"> <li>All patients received stable, moderate-dose corticosteroids for at least 4 weeks before screening (prednisone 7.5-30 mg/day or equivalent)</li> <li>The average daily prednisone dosage was 10.8 g/day and 9.2 g/day in the RCI 40 U and 80 U groups, respectively, and 16.4 mg/day in the combined placebo group</li> </ul> | <p><b>Combined RCI group:</b></p> <ul style="list-style-type: none"> <li>antimalarials (72%)</li> <li>immunosuppressants (24%)</li> <li>mycophenolate mofetil (12%)</li> <li>methotrexate (12%)</li> <li>azathioprine (12%)</li> </ul> <p><b>Combined placebo group</b></p> <ul style="list-style-type: none"> <li>antimalarials (72.7%)</li> <li>immunosuppressants (54.5%)</li> <li>mycophenolate mofetil (36.4%)</li> <li>methotrexate (27.3%)</li> </ul> |
| <b>Furie 2017<sup>9</sup></b>     | See Furie 2016 <sup>8</sup>   | <p>During the 52-week study period:</p> <ul style="list-style-type: none"> <li>immunosuppressants (azathioprine, methotrexate, or mycophenolate mofetil) (33.3%)</li> <li>antimalarials (72.2%)</li> </ul> <p>The average prednisone daily dosage was 10.0 mg/day and 16.4 mg/day in the RCI/RCI and placebo/RCI groups, respectively.</p>   |
| <b>Nelson 2017<sup>10</sup></b>   | Patients with SLE had received a mean of 3.6 medications prior to the study.  | Concurrent therapies were not reported.  |
| <b>Askanase 2020<sup>11</sup></b> | <p>Patients were enrolled if they received glucocorticoids for ≥8 weeks before screening and had been receiving stable glucocorticoid dosages of 7.5-30 mg of daily prednisone equivalents for ≥4 weeks prior to screening.</p> <p>At baseline, patients were treated with the following therapy:</p>   | Topical and/or inhaled glucocorticoids were allowed during the study period.   |

| Study                               | Prior Therapy   | Concurrent Therapy to RCI  |
|-------------------------------------|---|--|
|                                     | <ul style="list-style-type: none"> <li>• Prednisone ≤20 mg/day: RCI group, n=82 (97.6%); placebo, n=79 (92.9%)</li> <li>• Prednisone &gt;20 mg/day: RCI group, n=2 (2.4%); placebo, n=6 (7.1%)</li> <li>• Antimalarials: RCI group, n=65 (77.4%); placebo, n=69 (81.2%)</li> <li>• Immunosuppressants: RCI group, n=62 (73.8%); placebo, n=47 (55.3%)</li> </ul>  |  |
| <b>Askase 2021</b> <sup>12</sup>    | <p>The average baseline prednisone (range: 7.5-30 mg) or equivalent glucocorticoid dosage was 11.1 mg—95.3% of patients were receiving ≤20 mg/day. Some of the prior medications used by the patients include:</p> <ul style="list-style-type: none"> <li>• Azathioprine: RCI, n=27 (32.1%); placebo, n=20 (23.5%)</li> <li>• Methotrexate: RCI, n=27 (32.1%); placebo, n=22 (25.9%)</li> <li>• Mycophenolate mofetil: RCI, n=8 (9.5); placebo, n=9 (10.6%)</li> <li>• Mycophenolic acid: RCI, n=14 (16.7%); placebo, n=10 (11.8%)</li> </ul> | Antimalarials, NSAIDs, and immunosuppressants were allowed throughout the study. |
| <b>Ho-Mahler 2021</b> <sup>13</sup> | <ul style="list-style-type: none"> <li>• Corticosteroids, n=24 (80%)</li> <li>• Immunosuppressive drug, n=17 (57%)</li> <li>• Monoclonal antibodies, n=14 (47%)</li> <li>• Nonbiologic DMARDs, n=22 (73%)</li> </ul>  | None reported.   |

DMARDs, disease-modifying antirheumatic drugs; NSAIDs, nonsteroidal anti-inflammatory drugs; RCI, repository corticotropin injection; SLE, systemic lupus erythematosus.

## Citations

1. Purified Cortrophin® Gel (Repository Corticotropin Injection USP). Package insert. Published online 2025. Accessed April 15, 2025. <https://www.cortrophin.com/pdfs/purified-cortrophin-gel-prescribing-information.pdf>
2. Upton GV, Hollingsworth DR, Lande S, et al. Comparison of purified human and porcine ACTH in man. *J Clin Endocrinol Metab*. 1970;30(2):190-195. doi:10.1210/jcem-30-2-190
3. Acthar® Gel (Repository Corticotropin Injection). Package insert. Mallinkrodt ARD LLC; 2024. Accessed April 15, 2025. <https://acthar.com/Static/pdf/Acthar-PI.pdf>
4. Atnahs Pharma UK Ltd. Synacthen Depot Ampoules 1 mg/ml. Summary of Product Characteristics (SmPC). July 2, 2021. Accessed April 15, 2025. <https://www.medicines.org.uk/emc/product/10823/smpc/>
5. ANI Pharmaceuticals, Inc. Data on file. Clinical Monograph. 2021.
6. ANI Pharmaceuticals, Inc. Data on file. Study CA28049. 2020.
7. Fiechtner J, Montroy T. Treatment of moderately to severely active systemic lupus erythematosus with adrenocorticotrophic hormone: a single-site, open-label trial. *Lupus*. 2014;23(9):905-912.
8. Furie R, Mitrane M, Zhao E, Das M, Li D, Becker PM. Efficacy and tolerability of repository corticotropin injection in patients with persistently active SLE: results of a phase 4, randomised, controlled pilot study. *Lupus Sci Med*. 2016;3(1):e000180.
9. Furie RA, Mitrane M, Zhao E, Becker PM. Repository corticotropin injection in patients with persistently active SLE requiring corticosteroids: post hoc analysis of results from a two-part, 52-week pilot study. *Lupus Sci Med*. 2017;4(1):e000240.
10. Nelson WW, Philbin MJ, Gallagher JR, Heap K, Carroll S, Wan GJ. A retrospective medical record review of utilization patterns and medical resource use associated with repository corticotropin injection among patients with rheumatologic diseases in the United States. *Rheumatol Ther*. 2017;4(2):465-474. doi:10.1007/s40744-017-0087-x
11. Askanase AD, Zhao E, Zhu J, Bilyk R, Furie RA. Repository corticotropin injection for persistently active systemic lupus erythematosus: results from a phase 4, multicenter, randomized, double-blind, placebo-controlled trial. *Rheumatol Ther*. 2020;7:893-908.
12. Askanase AD, Wan GJ, Panaccio MP, et al. Patient-reported outcomes from a phase 4, multicenter, randomized, double-blind, placebo-controlled trial of repository corticotropin injection (Acthar® Gel) for persistently active systemic lupus erythematosus. *Rheumatol Ther*. 2021;8:573-584.
13. Ho-Mahler N, Turner B, Eaddy M, Hanke ML, Nelson WW. Treatment with repository corticotropin injection in patients with rheumatoid arthritis, systemic lupus erythematosus, and dermatomyositis/polymyositis. *Open Access Rheumatol Res Rev*. Published online. 2020:21-28