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@anipharmaceuticals.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.



Thank you for your inquiry.

Sincerely,

Steve Wu, PharmD
ANI Pharmaceuticals Medical Information

# Use of Purified Cortrophin® Gel (Repository Corticotropin Injection USP) 80U/mL in Patients With Proteinuria Due to Nephrotic Syndrome


## Abstract

- This document provides summary information pertaining to Purified Cortrophin Gel (repository corticotropin injection USP) and its indication to induce a diuresis or a remission of proteinuria in nephrotic syndrome (NS) without uremia of the idiopathic type of that due to lupus erythematosus.
- The active agent in Purified Cortrophin Gel is porcine-derived adrenocorticotropic hormone (ACTH peptide, amino acids 1-39), which is biologically similar to endogenous human ACTH, and of the same class as other, FDA-approved natural-product and synthetic ACTH formulations.
- To date, there are no published clinical data available that directly interrogate the clinical efficacy and safety of Purified Cortrophin Gel in patients with proteinuria due to NS.
- 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.
- The included selection of studies is limited to retrospective or prospective studies in 5 or more patients with focal segmental glomerulosclerosis (FSGS) or membranous nephropathy (MN) as primary causes of NS published in January 2011 or later. In aggregate, the 15 included studies represent a total of 222 patients with proteinuria due to either FSGS or MN, presenting with NS.


**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.**

**Email: drugsafety@anipharmaceuticals.com.**

# Introduction

## Clinical Background

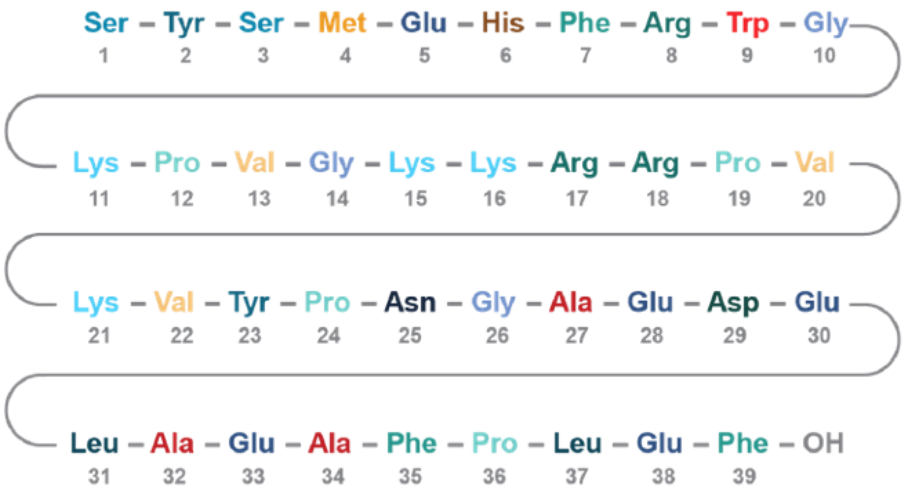
Purified Cortrophin Gel™ (repository corticotropin injection USP) is approved by the FDA for use in edematous states to induce a diuresis or a remission of proteinuria in nephrotic syndrome (NS) without uremia of the idiopathic type or that due to lupus erythematosus.[1]

## Composition of Purified Cortrophin Gel

Purified Cortrophin Gel is a porcine derived purified corticotropin, adrenocorticotropic hormone (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.[1]

The drug product is a sterile preparation containing 80 USP units per mL and it contains 0.5% phenol (as preservative), 15.0% gelatin (for prolonged activity), water for injection, and the pH is adjusted with hydrochloric acid and sodium hydroxide.[1]

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




## Purified Cortrophin Gel Clinical Pharmacology

ACTH, the active agent in Purified Cortrophin Gel, is the anterior pituitary hormone which stimulates the functioning adrenal cortex to produce and secrete adrenocortical hormones.[1]

Following administration of a single intramuscular 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 plasma cortisol concentration was 8 (3 to 12) hours. The baseline corrected geometric mean maximum (CV%) cortisol levels were 34.52 µg/dL (28.2%).[1]

The porcine-derived ACTH (1-39) found in Purified Cortrophin Gel is biologically similar to endogenous human ACTH,[2] and of the same class as other, FDA-approved natural-product and synthetic ACTH formulations.[3–5]

ANI conducted a study on the pharmacodynamic effect of Purified Cortrophin Gel, including $E_{max}$, $AUEC_{0-24}$, and $TE_{max}$, and compared it with the response of the same or similar depot structures from published literature.[6]

## Select Clinical Data in Support of ACTH in Patients with Proteinuria Due to Nephrotic Syndrome

### 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 proteinuria due to nephrotic syndrome (NS) that directly interrogate its clinical efficacy and safety.

Below is a selection 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 available clinical evidence of in-class ACTH-based therapies, with references to source material.

Based on results of a PubMed search (performed September 2023), the selection is limited to retrospective or prospective studies including 5 or more patients with the most prevalent primary causes of NS: focal segmental glomerulosclerosis (FSGS) or membranous nephropathy (MN), to align with the indication as labeled. Selection was further limited to publications from January 2011 to October 2023.

### Background and Definitions

Proteinuria is the passing of plasma protein into the urine due to abnormalities in the kidneys including NS. NS is a constellation of symptoms that indicate kidney dysfunction. According to Hull and Goldsmith, NS in adults is defined by the following criteria[7]:

- Proteinuria >3-3.5 g/24 hours OR spot urine protein:creatinine ratio of >300-350 mg/mmol
- Clinical evidence of edema
- Serum albumin <25 g/L
- Hyperlipidemia

There are 4 known pathologies that are thought to have a direct, or *primary*, relationship to NS, which can be diagnosed by exclusion of secondary causes and identification of specific pathologic features and which can cause nephrotic range proteinuria[7]:

- IgA nephropathy
- Minimal change disease (MCD)
- FSGS
- MN

The clinical data compiled here were limited to FSGS and MN, the 2 most prevalent causes of NS, which together account for approximately 70% of all cases of NS and were the 2 types of primary NS for which published clinical trial data were available and met search criteria.[7] MCD, IgA nephropathy, or other, secondary causes of NS were not considered in this compilation.

## Selected Study Results Summary: FSGS

The summary includes 7 studies (Table 1) totaling 97 patients with FSGS, 6 of which included 87 patients who received Acthar Gel, and 1 of which included 10 patients who received a synthetic ACTH derivative.[8–14]

While the specific dosing regimens varied among the included studies, in general, Acthar Gel was administered at 40 to 80 U twice a week for 6 months or longer. A weekly or biweekly dose of 1 mg was administered for a median of 18 months in the single synthetic ACTH study (see Table 1 for individual study dosing regimens).[8–14]

### Outcome Measures

Clinical responses were based on predetermined statistical methods, timepoints and standard clinical methods for monitoring proteinuria (total protein in 24-hour urine collection sample), although exact thresholds that defined complete (CR) and partial responses (PR) varied among the included studies (see Table 1 for details).[8–14] Five of the 7 studies used a standard threshold of <500 mg proteinuria to define CR and at least a 50% decrease to <3500 mg for PR.[8–12] Of the remaining 2 studies, 1 had less strict criteria (<1000 mg for CR),[13] and the other, stricter (the single synthetic ACTH study had <200 mg and <2000 mg for CR and PR, respectively).[14] Additionally, in 1 study, a limited response, defined as a 30% to 50% decrease in proteinuria but not to less than 3500 mg, was met by 4 further patients (note that this was not tallied as a response in summary Table 1).[11]

### Patient Demographics

Of the 97 patients with FSGS included in the selected studies who received either Acthar Gel or a synthetic ACTH derivative, the mean number of prior therapies ranged from 1.7 to >3 across the selected studies; in aggregate, 92.8% (90/97) of all patients with FSGS observed across studies received prior immunosuppressive therapy (see Table 1 for individual study results).[8–14] With the exception of 1 study that did not report,[14] all patients had either an implied or explicitly reported poor response to prior immunosuppressive therapy.[8–13]

### Efficacy and Safety Profile Summary

Partial remissions were more common (38.1% [37/97] in aggregate; ranging from 20% to 62% across studies) than complete remissions (12.4% [12/97] in aggregate; ranging from 0% to 30% across studies) (see Table 1 for individual study results).[8–14]

Full proteinuria data were available for 87 patients from 6 of the 7 selected studies, of whom 64 (74%) showed at least some decline in proteinuria following treatment (with a smaller proportion achieving CR or PR based on defined criteria as noted above).

Generally, Acthar Gel or synthetic ACTH derivative had the following adverse events, the frequencies of which are enumerated per study in Table 1[8–14]:

- Weight gain
- Hypertension
- Hyperglycemia
- Edema
- Insomnia
- Skin pigmentation

In aggregate, 8.9% (6/97) experienced weight gain, 8.2% (8/97) experienced hypertension, 12.3% (12/97) experienced hyperglycemia, 10.3% (10/97) experienced edema, 8.9% (6/97) experienced insomnia, and 4.1% (4/97) experienced skin pigmentation.

### Patient Follow-Up

Included studies in patients with FSGS had follow-up times ranging from 0 to 48 months.[8–14]

## Select Study Results Summary: MN

This summary includes 10 studies of 125 patients with MN (Table 2), including 5 studies of 56 patients who received Acthar Gel[8,11,12,15,16] and 5 studies of 69 patients who received a synthetic ACTH derivative.[17–21] While Acthar Gel treatment regimens varied with regard to dosage, frequency and duration across (and within) the 5 included studies, the majority of patients received 40 U or 80 U, 2 to 3 times weekly for 3 to 12 months. Similarly, the dosage, frequency and duration of synthetic ACTH varied across (and within) the 5 studies with most frequently 1 to 2 mg being administered weekly for up to a year (see Table 2 for individual study dosing regimens).[8,11,12,15–21]

### Outcome Measures

Clinical responses were based on predetermined statistical methods, timepoints and standard clinical methods for monitoring proteinuria (total albumin in 24-hour urine collection sample), although exact thresholds for CR and PR varied across studies (see Table 2 for individual study details). Five studies used <500 mg proteinuria to define CR and a ≥50% decrease to below 3500 mg for PR.[8,11,12,15,16] In 2 studies where CR and PR thresholds were not applied by the authors to the proteinuria data (Berg, 1999[17]; and Berg, 2004,[18] in Table 2), the thresholds defined by Chakraborty, et al., (<300 mg proteinuria for CR and a ≥50% decrease to below 3500 mg for PR) were applied to normalize

these data for the purposes of this summary.[22] Two other studies used the Chakraborty criteria,[19,20] and 1 additional study had stricter thresholds of ≤200 mg for CR and below 3000 mg for PR.[21]

### Patient Demographics

In aggregate, these 10 studies included 125 patients with MN who received either Acthar Gel or a synthetic ACTH derivative.[7,15]Of 109 patients with MN, 61% (66/109) had a poor response to prior immunosuppressive therapy.[8,11,12,15–18,20,21] One study excluded patients with prior immunosuppressive therapy (Table 2).[19]

### Efficacy and Safety Profile Summary

Patients achieved both PR (49% [61/125] in aggregate, ranging from 25% to 93% across studies) and CR(23.2% [29/125] in aggregate, ranging from 0% to 62.5% across studies) (see Table 2 for individual study details).[8,11,12,15–21] One study reported a clinical response in 2 patients, defined as a 30% to 50% decrease in proteinuria and not falling below 3500 mg (this was not tallied as a response as in summary Table 2).[11] Another study saw 1 patient with a >50% reduction in proteinuria, but it did not fall below 3500 mg.[15] Additionally, 101 (81%) showed at least some decline in proteinuria following treatment (with a smaller proportion achieving CR or PR based on defined criteria as noted above).[8,11,12,15–21]

Generally, Acthar Gel or synthetic ACTH derivative appeared to be well tolerated across studies, with manageable adverse events that included the following, the frequencies of which are enumerated per study in Table 2:

- Weight gain
- Hypertension
- Hyperglycemia
- Edema
- Insomnia
- Skin pigmentation

In aggregate, 11.2% (14/125) experienced weight gain, 4.0% (5/125) experienced hypertension, 22.4% (28/125) experienced hyperglycemia, 15.2% (19/125) experienced edema, 17.6% (22/125) experienced insomnia, and 12.8% (16/125) experienced skin pigmentation.

### Patient Follow-Up

Included studies in patients with MN had follow-up times ranging from 3 to 61 months.

## Table 1: Summary of Select Clinical Data on Use of ACTH in Patients With FSGS as the Primary Cause of Nephrotic Syndrome

| Study | Study Type | Patients With FSGS, N | Baseline proteinuria | Prior Therapies, Mean (SD) | Prior Immuno-Suppressive Therapy, n/N (%) | Treatment and Duration | Efficacy, Total Response (CR+PR) Rate | CR Rate | PR Rate | Safety |
|---|---|---|---|---|---|---|---|---|---|---|
| **Repository Corticotropin Injection (Brand Name: Acthar Gel)** | | | | | | | | | | |
| **Bomback 2012**[8] | Prospective open label | 5[a] | Median: 1.96 mg/g (range 1.65-4.76) | 3 (1) | 5/5 (100%) | 40 U 2× per week for 2 weeks + 80 U 2× per week for 22 weeks; 24 weeks total | 2/5 (40%) | 0/5 (0%; final proteinuria <500 mg) | 2/5 (40%; ≥50% reduction and final proteinuria 500-3500 mg) | In all patients (N=15), insomnia (n=4), skin pigmentation (n=2) |
| **Hogan 2013**[9] | Pilot study/ retrospective | 24 | Median: 4595 mg/g (IQR 2200-8020) | 2.2 (1.2) | 22/24 (92%) | 12 patients receiving 40 U weekly for 2 weeks, followed by 80 U weekly for 2 weeks then 2× a week for 12 weeks (2160 U total); 7 received 40 U 2× for 2 weeks followed by 22 weeks of 80 U 2× (3840 U total); 5 remaining had a median of 80 U 2×/week for 12 to 56 weeks | 7/24 (29%) | 2/24 (8%; final proteinuria <500 mg) | 5/24 (22%; ≥50% reduction and final proteinuria 500-3500 mg) | AEs occurring in ≥3 patients: edema (n=5), increased energy (n=4), mood alteration (n=4), upper respiratory tract symptoms (n=4), muscle cramps (n=4), elevated blood pressure (n=3) |
| **Filippone 2016**[10] | Retrospective | 10 | 3100 mg/g to 36,000 mg/g | 2.4 (1.8) | 8/10 (80%) | 40 U (n=2) weekly to 80 U (n=8) 2× a week for 1 to 10 months | 4/10 (40%) | 2/10 (20%; final proteinuria <500 mg) | 2/10 (20%; ≥50% reduction and final proteinuria 500-3500 mg) | Weight gain (n=4), myalgia (n=2), worsening diabetes (n=2), hypertension (n=2), skin hyperpigmentation (n=2), edema (n=1), fatigue (n=1), weakness (n=1), Cushingoid features (n=1) |
| **Madan 2016**[11] | Retrospective | 15 | 2500 mg/d to 9306 mg/d | 1.7 (1.4) | 12/15 (80%) | 80 U 2× per week for ≥6 months | 9/15 (60%) | 0/15 (0%; final proteinuria <500 mg/d) | 9/15 (60%; ≥50% reduction and final proteinuria 500-3500 mg) | Treatment-related AEs occurred in 20% of patients, including two AEs (edema and unknown) that led to early termination. Increased swelling (n=1), hyperglycemia (n=2), hypertension (n=1), weight gain (n=1), upper respiratory infection (n=1) |
| **Tumlin 2017**[12] | Prospective study of ACTH monotherapy and ACTH + TAC | 13 | Median: 6.47 g/g ± 1.2 (95% CI) | ≥2 | 13/13 (100%) | 40 U to 80 U 2 to 3× a week[b] for a median of 7.3 (1.0) months; those with no response or PR received ACTH + TAC for another 6 months | ACTH monotherapy: 9/13 (69%)<br><br>ACTH + TAC: 10/12 (83%) | ACTH monotherapy: 1/13 (8%; final proteinuria <500 mg)<br>ACTH + TAC: 2/12 (17%; final proteinuria <500 mg) | ACTH monotherapy: 8/13 (62%; ≥50% reduction and final proteinuria 500-3500 mg<br>ACTH + TAC: 8/12 (67%; ≥50% reduction and final proteinuria 500-3500 mg) | Out of all patients (N=22; 13 FSGS and 9 MN): hyperglycemia (n=5, 22%), edema (n=3, 14%), insomnia (n=2, 9%), dysgeusia (n=1, 4.5%) |
| **Alhamad 2019**[13] | Retrospective | 20 | Mean (SD): 8.6 g/g (7.6) | >3 | 20/20 (100%) | 80 U 2× a week for up to 96 weeks | 10/20 (50%) | 4/20 (20%; final proteinuria <1000 mg) | 6/20 (30%; ≥50% reduction and final proteinuria 1000-3500 mg) | Allograft failure (n=8): recurrent or de novo FSGS despite the use of ACTH gel (n=5), cytomegalovirus disease (n=1), and JC virus nephropathy (n=1)<br><br>3 patient deaths during the follow-up due to aortic dissection (while on ACTH gel), hemorrhagic stroke (off ACTH gel) and related to infection 10 months after initiating of dialysis (off ACTH gel). |
| **Synthetic ACTH** | | | | | | | | | | |
| **Berg 2013**[14] | Prospective study of ACTH in combination with secondary immunosuppressive therapy | 10 | Not reported | ≥2 | 10/10 (100%) | 1 mg/week to 2 × 1 mg/week for 7 to 48 months (median 18) while continuing secondary immuno-suppressive therapy | 8/10 (80%) | 3/10 (30%; final proteinuria <200 mg) | 5/10 (50%; ≥50% reduction and final proteinuria 200-2000 mg) | Not reported |

ACTH, adrenocorticotropic hormone; AE, adverse event; CR, complete response; JC, human polyomavirus 2; PR, partial response; TAC, tacrolimus.

[a]Includes patients with FSGS and minimal change disease. [b]Patients with diabetes received 16 U of Acthar Gel daily.



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## Table 2: Summary of Select Clinical Data on Use of ACTH in Patients With MN as the Primary Cause of Nephrotic Syndrome

| Study | Study Type | Patients With MN, N | Baseline proteinuria | Median prior regimens, n | Prior Immuno-suppressive Therapy, n/N (%) | Treatment Duration | Efficacy, Total Response (CR+PR) Rate | CR Rate | PR Rate | Safety |
|---|---|---|---|---|---|---|---|---|---|---|
| **Repository Corticotropin Injection (Brand Name: Acthar Gel)** | | | | | | | | | | |
| **Bomback 2011**[16] | Retrospective case series | 11 | 2625 mg/d to 11,911 mg/d | 2 | 10/11 (91%) | 40 U to 80 U, 2× to 3× a week for 6-12 months | 9/11 (82%) | 3/11 (27%; final proteinuria <500 mg) | 6/11 (55%; ≥50% reduction and final proteinuria 500-3500 mg) | Hyperglycemia (n=2), weight gain (n=1), bone demineralization (n=1) |
| **Bomback 2012**[8] | Prospective, open label | 5 | 2.23 g/g to 12.46 g/g | 3 | 5/5 (100%) | 40 U 2× per week for 2 weeks + 80 U 2× per week for 22 weeks; 24 weeks total | 2/5 (40%) | 0/5 (0%; final proteinuria <500 mg) | 2/5 (40%; ≥50% reduction and final proteinuria 500-3500 mg) | 3 AEs led to discontinuation, including 2 cases of hyperglycemia. In all patients (N=15), insomnia (n=4), skin pigmentation (n=2) |
| **Hladunewich 2014**[15] | Phase 1b/2, dose finding | 20 | Mean (SD): 9068 g/d (3384) | Not reported | 7/20 (35%) | 40 U or 80 U/every 2 weeks for a month, then 2× a week for a total of 12 to 24 weeks | 12/20 (60%) | 2/20 (10%; final proteinuria <300 mg) | 10/20 (50%; ≥50% reduction and final proteinuria 300-3500 mg) | Increased blood glucose (n=13), fatigue/weakness (n=9), GI symptoms (n=7), mood fluctuations (n=6), insomnia (n=6), weight gain (n=5), muscle aches/pain (n=5), headaches (n=5), dizziness (n=5), injection site bruising (n=5), tremulousness (n=3), edema (n=3), acne (n=2), flushing (n=3), bronzing (n=2), blurred vision (n=2), hoarseness (n=2) |
| **Madan 2016**[11] | Retrospective case series | 11 | 1930 mg/d to 13,600 mg/d | 2 | 10/11 (91%) | 80 U 2× a week for ≥6 months[a] | 6/11 (54%) | 2/11 (18%; final proteinuria <500 mg) | 4/11 (36%; ≥50% reduction and final proteinuria 500-3500 mg | Treatment-related AEs occurred in 36.4% of patients, including one AE (fatigue) that led to early termination. Fatigue (n=1), dizziness (n=1), weight gain (n=2), hypokalemia (n=1) |
| **Tumlin 2017**[12] | Prospective | 9 | Median: 7.73 g/g ± 1.6 (95% CI) | ≥2 | 9/9 (100%) | 40 U to 80 U 2 to 3× a week[b] for a median of 9.6 (2.1) months; those with no response or PR received ACTH + TAC for another 6 months | ACTH monotherapy: 4/9 (44%)<br><br>ACTH + TAC: 8/8 (100%) | ACTH monotherapy: 0/9 (0%; final proteinuria <500 mg)<br><br>ACTH + TAC: 2/8 (75%; final proteinuria <500 mg) | ACTH monotherapy: 4/9 (44%; ≥50% reduction and final proteinuria 500-3500 mg)<br><br>ACTH + TAC: 6/8 (75%; ≥50% reduction and final proteinuria 500-3500 mg) | Out of all patients (N=22; 13 FSGS and 9 MN): hyperglycemia (n=5, 22%), edema (n=3, 14%), insomnia (n=2, 9%), dysgeusia (n=1, 4.5%) |
| **Synthetic ACTH** | | | | | | | | | | |
| **Berg 1999**[17] | Pilot, dose finding | 14 | Median (range): 4830 (3660-15,877) | 1 | 11/14 (79%) | 1 mg every other week, increased to 3× a week by week 8; then 2× week for 12 months | 14/14 (100%[22]) | 1/14 (7%[22]; final proteinuria <300 mg) | 13/14 (93%[22]; ≥50% reduction and final proteinuria 300-3500 mg) | Reversible fluid retention, alertness, sleep disturbances |
| **Berg 2004**[18] | Retrospective case series | 10 | 3500 mg/d to 25,560 mg/d | 0.5 | 5/10 (50%) | Median dose of 25 mcg/kg/week; 0.5 or 1 mg /week, 0.75 mg or 1 mg 2× week for 2 to 11 months | 10/10 (100%[22]) | 5/10 (50%[22]; final proteinuria <300 mg) | 5/10 (50%[22]; ≥50% reduction and final proteinuria 300-3500 mg) | Not reported |
| **Ponticelli 2006**[19] | Randomized pilot vs prednisone + cytotoxic agent | 16 | Mean (SD): 6.7 g/d ± 2.8 | Patients with prior IST use excluded from study | | 1 mg every other week to 2 injections per week for 1 year vs MP + CTX or chlorambucil cycling monthly for 6 months[c] | ACTH: 14/16 (87.5%)<br><br>MP + cytotoxic agent: 15/16 (94%) | ACTH: 10/16 (62.5%; final proteinuria <300 mg)<br><br>MP + cytotoxic agent: 5/16 (31%) | ACTH: 4/16 (25%; ≥50% reduction and final proteinuria 500-3500 mg)<br><br>MP + cytotoxic agent: 10/16 (63%) | 2 AEs led to withdrawal (dizziness and persistent NS); 6 cases of skin discoloration; 2 cases of glucose intolerance; 1 case of diarrhea, onychodystrophy, folliculitis |
| **Lorusso 2015**[20] | Pilot study | 9 | 3 g/d to 10 g/d | ≥1 | 9/9 (100%) | 1 mg/week for 12 months | 8/9 (88.9%) | 3/9 (33%; final proteinuria <300 mg) | 5/9 (56% ≥50% reduction and final proteinuria 300-3500 mg) | 1 withdrawal (fluid retention) |
| **van de Logt, 2015**[21] | Prospective open label cohort vs historical controls treated with CTX | 20 | Median (IQR): 8.7 g/10 mmol Cr (4.3-11) | Not reported | 4/20 (20%) | ACTH: 1 mg/weekly, increasing to twice weekly at week 8 for 18 further weeks, then tapered for a further 3 months. Total: 9 months<br><br>CTX: 1.5 mg/kg/day for 12 months | ACTH: 11/20 (55%)<br><br>CTX: 19/20 (95%) | ACTH: 4/20 (20%; final proteinuria <200 mg)<br><br>CTX: 13/20 (65%; final proteinuria <200 mg) | ACTH: 7/20 (35%; ≥50% reduction and final proteinuria 200-3000 mg)<br><br>CTX: 6/20 (30%; ≥50% reduction and final proteinuria 200-3000 mg) | SAEs occurred in 25% of patients<br>Top AEs: edema (60%), sleep disturbance (50%), mood alteration (40%), fever/infection (40%), hyperpigmentation skin (40%) |

AE, adverse event; CR, complete response; CTX, cyclophosphamide; GI, gastrointestinal; IST, immunosuppressive therapy; IV, intravenous; MP, methylprednisolone; NS, nephrotic syndrome; PR, partial response; SAE, serious adverse event; SD, standard deviation; TAC, tacrolimus. [a]One patient received 40 U twice weekly. [b]Patients with diabetes received 16 U of Acthar Gel daily. [c]For the MP plus cytotoxic agent arm, patients were treated with 1 g IVMP on 3 consecutive days, followed by 0.4 mg/kg oral MP daily for 27 days (Month 1). On Month 2, patients were treated with either 0.2 mg/kg daily oral chlorambucil or 2.5 mg/kg daily oral CTX. Treatment duration was 3 cycles for 6 months.



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## Citations


1. *Purified Cortrophin™ Gel (Repository Corticotropin Injection USP)*. ANI Pharmaceuticals, Inc.; 11/21. https://cortrophin.com/pdfs/purified-cortrophin-gel-prescribing-information.pdf

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