

**RETROSPECTIVE REVIEW:** Treatment with repository corticotropin injection in patients with rheumatoid arthritis, systemic lupus erythematosus, and dermatomyositis/polymyositis

Ho-Mahler N, Turner B, Eaddy M, Hanke ML, Nelson WW—Open Access Rheumatology: Research and Reviews, 2020

**Disclosure statement:** Funding to support the preparation of this content was provided by Mallinckrodt Pharmaceuticals.**Study endpoints<sup>1</sup>**

Study collected data on patient profiles, Acthar Gel treatment patterns, and physician's impression of change, as well as AEs and SAEs resulting in dose reduction or treatment discontinuation. *Index visit* was defined as date of first Acthar Gel prescription. Follow-up period started day after index visit, continuing up to 12 months, including Acthar Gel treatment cessation, loss to follow-up, death, or end of study period. Patients had  $\geq 3$  in-office visits at the same site and healthcare provider, including at least 1 visit before initiation of Acthar Gel, 1 visit at first Acthar Gel prescription, and 1 visit following the first Acthar Gel prescription (within at least 12 months and including  $\geq 1$  visit during Acthar Gel treatment).

**Patient overview<sup>1</sup>**

Patients in the retrospective study had a mean age of  $>49$  years (mean age range: 49.3 years to 54.8 years) and were mostly female (78% [RA], 97% [SLE], and 100% [DM/PM]).

Key inclusion criteria	Key exclusion criteria
Aged $\geq 18$ years	Not started Acthar Gel or were unable to take Acthar Gel due to allergy or contraindications
Physician-reported diagnosis of RA, SLE, or DM/PM, according to ACR criteria	Previous or current participation in an interventional trial for RA, SLE, or DM/PM
Treated with Acthar Gel between 1/1/2011 and 2/15/2016	Pregnancy
For patients with RA or DM/PM, Acthar Gel must have been used as adjunctive therapy; for patients with SLE, Acthar Gel must have been used during an exacerbation or as maintenance therapy	Diagnosis of Stage V or VI membranous or sclerosing lupus nephritis or central nervous system lupus

**Most commonly reported comorbidities in patients with RA, SLE, and DM/PM (N=92)**

	RA (N=54)	SLE (N=30)	DM/PM (N=8)
Arthralgia	96%	100%	100%
Osteoarthritis	39%	—	38%
Hypertension	33%	40%	—
Depression	30%	33%	50%
Anxiety	28%	27%	50%
Sjogren's syndrome	—	33%	—

ACR=American College of Rheumatology; AEs=adverse events; DM=dermatomyositis; PM=polymyositis; RA=rheumatoid arthritis; SAEs=serious adverse events; SLE=systemic lupus erythematosus.

**Indications**

Acthar® Gel (repository corticotropin injection) is indicated for:

- Treatment during an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus
- Treatment during an exacerbation or as maintenance therapy in selected cases of dermatomyositis (polymyositis)
- Adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), ankylosing spondylitis
- Adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in psoriatic arthritis
- The treatment of symptomatic sarcoidosis

**SELECT IMPORTANT SAFETY INFORMATION****Contraindications**

- Acthar should never be administered intravenously
- Administration of live or live attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of Acthar
- Acthar is contraindicated where congenital infections are suspected in infants
- Acthar 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, uncontrolled hypertension, primary adrenocortical insufficiency, adrenocortical hyperfunction, or sensitivity to proteins of porcine origin

Please see additional Important Safety Information throughout and full Prescribing Information.

**Acthar® GEL**  
(repository corticotropin injection) 80 U/mL

Clinical data in 92 patients with RA, SLE, and DM/PM<sup>1</sup>  
Most patients had been treated with multiple prior therapies, suggesting refractory disease<sup>1</sup>

Prior therapies included glucocorticoids, immunosuppressants, and biologic and nonbiologic DMARDs<sup>1</sup>

	RA (N=54) n (%)	SLE (N=30) n (%)	DM/PM (N=8) n (%)
Antimalarial drugs	–	–	1 (12)
Biologic DMARDs	47 (87)	–	–
Glucocorticoids	47 (87)	24 (80)	6 (75)
Immunoglobulins	–	–	1 (12)
Immunosuppressive drugs	–	17 (57)	7 (88)
Monoclonal antibodies	–	14 (47)	–
Nonbiologic DMARDs	51 (94)	22 (73)	–

Mean duration of Acthar Gel treatment was 4.8 months to 6.8 months<sup>1</sup>

- RA=4.8 months (3.4 months SD)
- SLE=6.5 months (3.3 months SD)
- DM/PM=6.8 months (2.2 months SD)

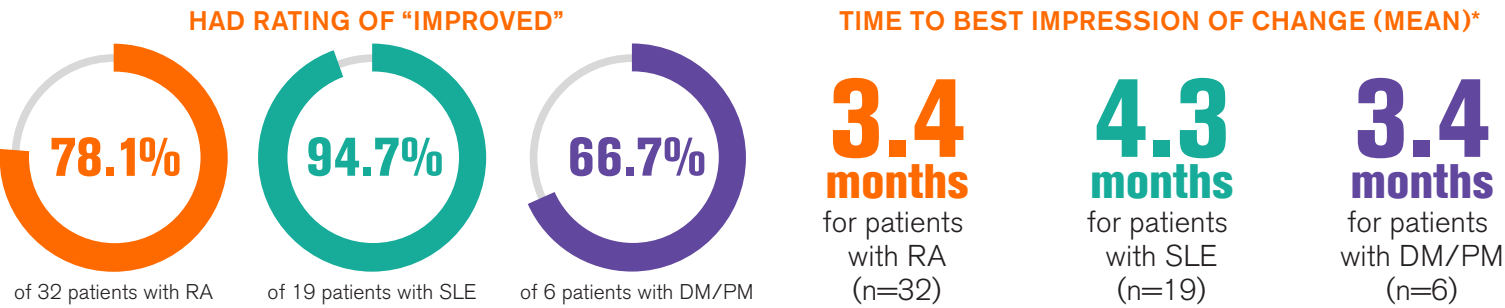
Most common starting dose and frequency of Acthar Gel

- 80 U twice weekly (for 84% of patients with RA [n=43]; 75% of patients with SLE [n=28]; and 86% of patients with DM/PM [n=7])<sup>1</sup>
- Changes in Acthar Gel dose occurred in 33% of patients with RA (N=54), 43% of patients with SLE (N=30), and 25% of patients with DM/PM (N=8)<sup>1</sup>
- The usual dose of Acthar Gel is 40–80 units given intramuscularly or subcutaneously every 24–72 hours<sup>2</sup>

Most common reasons for initiating treatment with Acthar Gel for patients with data<sup>1</sup>

- Inadequate response to prior therapies
- Need for an alternative therapy
- Acute exacerbation/flare

Among the 57 patients with data on physician’s impression of change with Acthar Gel<sup>1</sup>



DMARDs=disease-modifying antirheumatic drugs; SD=standard deviation.

\*Mean time plus SD was 3.4±2.5 months for RA, 4.3±2.7 months for SLE, and 3.4±1.6 months for DM/PM.

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- The adverse effects of Acthar are related primarily to its steroidogenic effects
- Acthar may increase susceptibility to new infection or reactivation of latent infections
- Suppression of the hypothalamic-pituitary-adrenal (HPA) axis may occur following prolonged therapy with the potential for adrenal insufficiency after withdrawal of the medication. Adrenal insufficiency may be minimized by tapering of the dose when discontinuing treatment. During recovery of the adrenal gland patients should be protected from the stress (e.g. trauma or surgery) by the use of corticosteroids. Monitor patients for effects of HPA suppression after stopping treatment

Please see additional Important Safety Information throughout and full [Prescribing Information](#).

Safety findings (N=92)<sup>1</sup>

- SAEs were reported in:
  - 1 (2%) patient with RA
    - A patient experienced both pancreatitis and urinary tract infection
  - 4 (13%) patients with SLE
    - Reported SAEs included altered musculoskeletal pain, dehydration, adrenal insufficiency, pneumonia, renal failure, and transient ischemic attack
  - 1 (12%) patient with DM/PM
    - A patient experienced shortness of breath
- AEs were reported in:
  - 14 (26%) patients with RA
    - Reported AEs included abdominal angina, bruising, diaphoresis, fatigue, gastroenteritis, heartburn, herpes flare, hypoglycemia, hypotension, injection-site reaction, irritability or mood changes, myalgia, upper respiratory infection, vomiting, and weight gain
  - 5 (17%) patients with SLE
    - Reported AEs included diarrhea, gastrointestinal upset, edema, neuralgia, pneumonia, and weight gain
  - 2 (25%) patients with DM/PM
    - Reported AEs included bruising and red or bloodshot eyes

Patients (N=92) who discontinued Acthar Gel<sup>1</sup>

RA (N=54) n (%)	SLE (N=30) n (%)	DM/PM (N=8) n (%)
24 (44)	6 (20)	5 (62)

Most common reasons for discontinuation of Acthar Gel among the 35 patients with data

	RA (n=24) n (%)	SLE (n=6) n (%)	DM/PM (n=5) n (%)
AE related to Acthar Gel	9 (38)	3 (50)	2 (40)
Disease resolution/remission/ treatment no longer necessary	4 (17)	0	0
Inadequate response	3 (12)	0	2 (40)
Patient choice	1 (4)	0	0
Physician choice	4 (17)	0	0
Missing data	3 (12)	3 (50)	1 (20)

Study limitations<sup>1</sup>

- This study was limited by retrospective design and small sample size
- Further limitations included utilization of patient medical records, which had missing data, and may include errors and omissions (such as care received at other clinics)
- Reliance on medical records increased difficulty of assessing disease activity, which is not routinely recorded in the medical records or recorded with the appropriate timing to allow evaluation of clinical response to therapy
- Additional limitations included utilization of physician’s impression of change as a descriptive endpoint, a subjective measure relying on an individual clinician’s own standards of improvement
- Physician’s impression of change was not available for 38% of the records evaluated
- The retrospective noncomparative study design did not allow us to determine responses to other therapies
- Results are exploratory and should be interpreted with these limitations in mind
- Results not solely attributable to Acthar Gel

## IMPORTANT SAFETY INFORMATION (CONT'D)

### Warnings and Precautions (Cont'd)

- Cushing's syndrome may occur during therapy but generally resolves after therapy is stopped. Monitor patients for signs and symptoms
- Acthar can cause elevation of blood pressure, salt and water retention, and hypokalemia. Blood pressure, sodium, and potassium levels may need to be monitored
- Acthar often acts by masking symptoms of other diseases/disorders. Monitor patients carefully during and for a period following discontinuation of therapy
- Acthar can cause GI bleeding and gastric ulcer. There is also an increased risk for perforation in patients with certain gastrointestinal disorders. Monitor for signs of bleeding
- Acthar may be associated with central nervous system effects ranging from euphoria, insomnia, irritability, mood swings, personality changes, and severe depression to psychosis. Existing conditions may be aggravated
- Patients with comorbid disease may have that disease worsened. Caution should be used when prescribing Acthar in patients with diabetes and myasthenia gravis
- Prolonged use of Acthar may produce cataracts, glaucoma, and secondary ocular infections. Monitor for signs and symptoms
- Acthar is immunogenic and prolonged administration of Acthar may increase the risk of hypersensitivity reactions. Neutralizing antibodies with chronic administration may lead to loss of endogenous ACTH activity
- There is an enhanced effect in patients with hypothyroidism and in those with cirrhosis of the liver
- Long-term use may have negative effects on growth and physical development in children. Monitor pediatric patients
- Decrease in bone density may occur. Bone density should be monitored for patients on long-term therapy
- Pregnancy Class C: Acthar has been shown to have an embryocidal effect and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

### Adverse Reactions

- Common adverse reactions for Acthar are similar to those of corticosteroids and include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite, and weight gain
- Specific adverse reactions reported in IS clinical trials in infants and children under 2 years of age included: infection, hypertension, irritability, Cushingoid symptoms, constipation, diarrhea, vomiting, pyrexia, weight gain, increased appetite, decreased appetite, nasal congestion, acne, rash, and cardiac hypertrophy. Convulsions were also reported, but these may actually be occurring because some IS patients progress to other forms of seizures and IS sometimes masks other seizures, which become visible once the clinical spasms from IS resolve

**Other adverse events reported are included in the full Prescribing Information.**

**Please see additional Important Safety Information throughout and full Prescribing Information.**

**References:** 1. 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*. In press 2020. 2. Acthar Gel (repository corticotropin injection) [prescribing information]. Bedminster, NJ: Mallinckrodt ARD LLC.