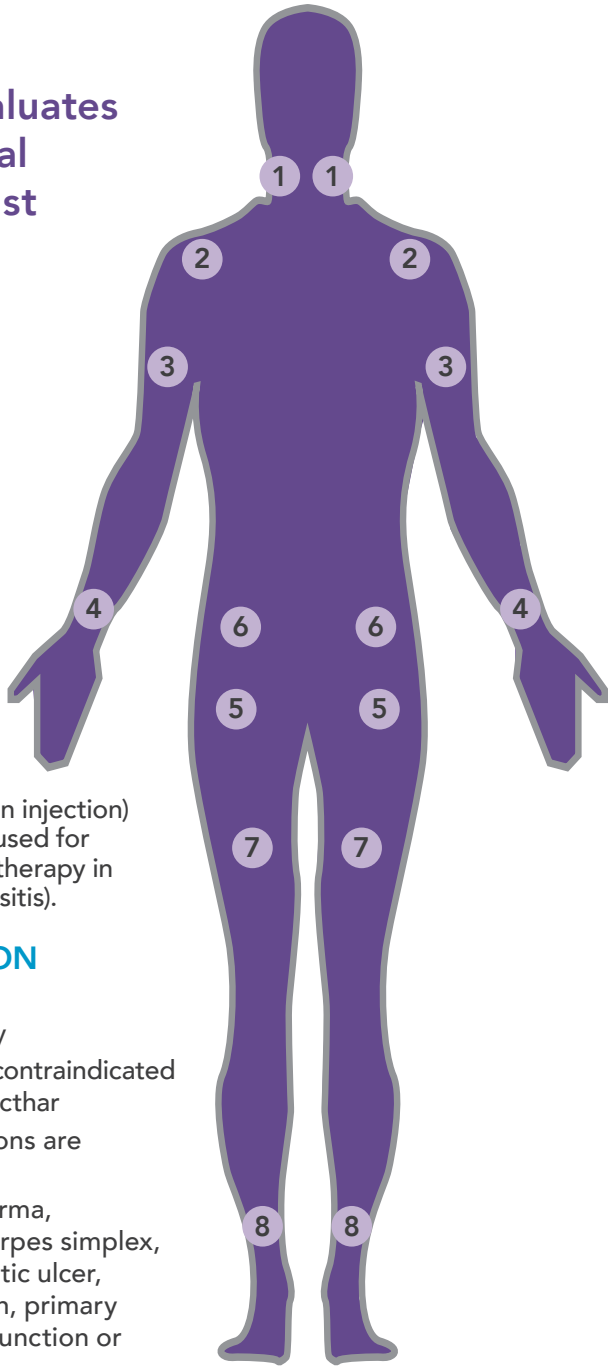
In dermatomyositis and polymyositis (DM/PM)

The Role of Manual Muscle Testing as an Assessment Tool

Manual muscle testing (MMT) evaluates function and strength of individual muscles and muscle groups against gravity or manual resistance[1,2]



Indication: H.P. Acthar® Gel (repository corticotropin injection) is an adrenocorticotropic hormone (ACTH) analogue used for treatment during an exacerbation or as maintenance therapy in selected cases of systemic dermatomyositis (polymyositis).

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 origins

Please see additional Important Safety Information inside and on back cover.
Please see accompanying full Prescribing Information.

H.P. Acthar® GEL
(repository corticotropin injection) 80 U/mL

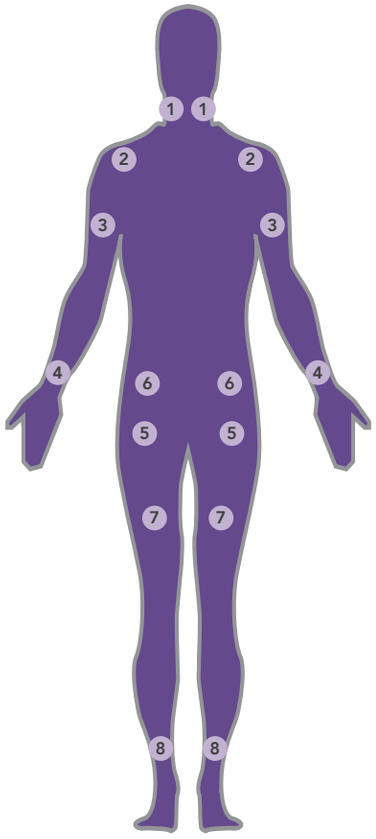
MMT was a measurement in a prospective, open-label study (N=11) that evaluated Acthar in the treatment of DM/PM[3]*

KEY TO MUSCLE GRADING[†]

	Function of the Muscle	Grade 0-10 Scale
No Movement	No contractions felt in the muscle	0
	Tendon becomes prominent or feeble contraction felt in the muscle, but no visible movement of the part	T
Test Movement	**Movement in the Horizontal Plane**	
	Moves through partial range of motion	1
	Moves through complete range of motion	2
	Antigravity Position	
	Moves through partial range of motion	3
Test Position	Gradual release from test position	4
	Holds test position (no added pressure)	5
	Holds test position against slight pressure	6
	Holds test position against slight to moderate pressure	7
	Holds test position against moderate pressure	8
	Holds test position against moderate to strong pressure	9
	Holds test position against strong pressure	10

CALCULATING COMPOSITE MMT SCORES[1,2]

Muscle Group	Muscle	Right	Left	Axial
Axial	Neck flexors			0-10
Proximal	Deltoid	0-10	0-10	
	Biceps	0-10	0-10	
	Gluteus maximus	0-10	0-10	
	Gluteus medius	0-10	0-10	
	Quadriceps	0-10	0-10	
Distal	Wrist extensors	0-10	0-10	
	Ankle dorsiflexors	0-10	0-10	
	Subtotal Score	0-70	0-70	0-10
	Total Score	0-150		



Typical muscles evaluated for DM/PM include[‡§]:

1. neck flexors
2. deltoids
3. biceps
4. wrist extensors
5. gluteus maximus
6. gluteus medius
7. quadriceps
8. ankle dorsiflexors

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-axis (HPA) 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 on page 4 and back cover.

Please see accompanying full Prescribing Information.

Patients demonstrated a 19.3% median (IQR=11.5 to 25.4) improvement in MMT scores after Acthar treatment[3‖¶]

6 patients with DM and 4 patients with PM:

- Exhibited refractory and active disease and either failed or exhibited intolerance to glucocorticoid and/or ≥1 immunosuppressive agent
- Were on concomitant doses of other therapies for DM or PM for at least 4 to 8 weeks and on a stable dose for 2 to 4 weeks, prior to the start of the trial

MMT8 scores for this study were based on a composite score out of 150 of all muscles and graded on a scale of 0 to 10

MMT SCORES FOR ALL PATIENTS COMPLETING THE STUDY (N=10)[3#]

	Start	End	Change
Patient 1: 37.9 years old, DM	138	150	+12
Patient 2: 47.9 years old, DM	149	150	+1
Patient 3: 27.5 years old, PM**	93	132	+39
Patient 4: 58.7 years old, PM**	116	139	+23
Patient 5: 75.0 years old, DM**	118	148	+30
Patient 6: 53.2 years old, DM	146	150	+4
Patient 7: 54.1 years old, DM**	119	142	+23
Patient 8: 51.0 years old, PM**	123	143	+20
Patient 9: 45.4 years old, PM**	106	113	+7
Patient 10: 64.0 years old, DM**	96	107	+11

Study Limitations

Results are based on 10 patients who completed the study. This study may not be fully representative of outcomes in the overall patient population. All patients were on multiple therapies; therefore, the clinical outcomes may not be solely attributable to Acthar. Acthar has not been formally studied in combination with other treatments.

IQR=interquartile range.

*Ten of the 11 enrolled patients completed the study. One patient dropped out due to heart block unrelated to the study drug and was not included in the analysis, as he did not complete the minimum 8 weeks of the study drug required for outcome assessment as per study protocol.

[†]Adapted with approval by Kendall F, McCreary E, Provance P. *Muscles, Testing and Function*. © 1993 Wolters Kluwer Health, Lippincott Williams & Wilkins. All rights reserved.

[‡]MMT8 is a set of 8 designated muscles tested unilaterally. Generally, for bilateral muscle testing, each muscle group is tested, first on the right and then on the left, prior to proceeding to the next muscle group.

[§]This list is only an example of MMT subset 58.

[‖]Percentage is derived from the 7 of 10 patients who showed severe muscle weakness (defined as ≤125/150 of MMT) at baseline.

[¶]The primary endpoint of this study was improvement based on the International Myositis Assessment & Clinical Studies Group (IMACS) definition of improvement (DOI); worsening measure could not include the MMT. This endpoint was also separately evaluated on a subset of patients with severe muscle weakness and moderate to severe cutaneous DM rashes.

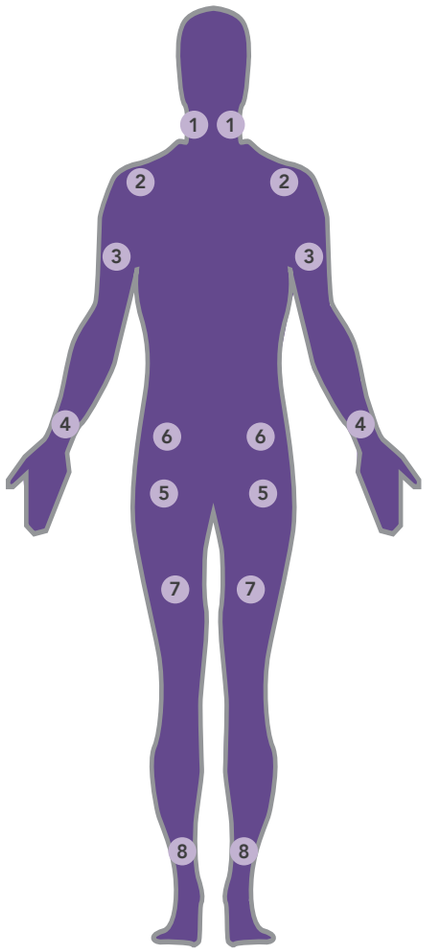
[#]Increase in MMT is an improvement.

**Denotes severe muscle weakness at study entry.

MMT was a measurement in a retrospective case review (N=5) that evaluated Acthar in the treatment of DM/PM[4]

Typical muscles evaluated for DM/PM include*†:

1. neck flexors
2. deltoids
3. biceps
4. wrist extensors
5. gluteus maximus
6. gluteus medius
7. quadriceps
8. ankle dorsiflexors



KEY TO MUSCLE GRADING[1‡]

	Function of the Muscle	Grade 0-5 Scale
No Movement	No contractions felt in the muscle	0
	Tendon becomes prominent or feeble contraction felt in the muscle, but no visible movement of the part	1
Test Movement	**Movement in the Horizontal Plane**	
	Moves through partial range of motion	2-
	Moves through complete range of motion	2
	Antigravity Position	
	Moves through partial range of motion	2+
Test Position	Gradual release from test position	3-
	Holds test position (no added pressure)	3
	Holds test position against slight pressure	3+
	Holds test position against slight to moderate pressure	4-
	Holds test position against moderate pressure	4
	Holds test position against moderate to strong pressure	4+
	Holds test position against strong pressure	5

SELECT IMPORTANT SAFETY INFORMATION

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

Please see additional Important Safety Information on page 2 and back cover.
Please see accompanying full Prescribing Information.

All patients treated with Acthar demonstrated improvement in MMT scores[4]

3 patients with DM and 2 patients with PM:

- Experienced a disease exacerbation and either failed or exhibited tolerability issues with previous treatments
- Received at least 3 previous treatments
- Were on stable doses of at least 1 other commonly used therapy for DM or PM 60 days prior to and during treatment with Acthar

MMT8 scores for this study were based on 2 specific muscles tested at baseline and at treatment assessment, and graded on a scale of 0 to 5

MMT SCORES

	Muscles tested	Baseline	At assessment
Patient 1: 45 years old, DM	Iliopsoas	3	4+
	Quadriceps	3	4+
Patient 2: 25 years old, DM	Iliopsoas	3	4
	Quadriceps	3–	4+
Patient 3: 43 years old, DM	Deltoids	2	4
	Triceps	3	4
Patient 4: 55 years old, PM	Deltoids	3	4+
	Triceps	3	4+
Patient 5: 68 years old, PM	Iliopsoas	4	4+
	Quadriceps	4	5

Study Limitations

These results are based on a retrospective 5-patient case series and may not be fully representative of outcomes in the overall patient population. All 5 patients were on multiple therapies. The clinical outcomes may not be solely attributable to Acthar.

For more information about the clinical experience of Acthar, visit actharrheumatology.com/dermatomyositis-and-polymyositis/efficacy

*MMT8 is a set of 8 designated muscles tested unilaterally. Generally, for bilateral muscle testing, each muscle group is tested, first on the right and then on the left, prior to proceeding to the next muscle group.

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IMPORTANT SAFETY INFORMATION (cont'd)

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-axis (HPA) 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
- 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, and 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 mask other seizures, which become visible once the clinical spasms from IS resolve

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

References: 1. National Institute of Environmental Health Sciences. Manual muscle testing procedures for MMT8 testing. https://www.niehs.nih.gov/research/resources/assets/docs/mmt8_grading_and_testing_procedures_for_the_abbreviated_8_muscle_groups_508.pdf. Accessed January 25, 2018. **2.** Rider LG, Koziol D, Giannini EH, et al. Validation of manual muscle testing and a subset of eight muscles for adult and juvenile idiopathic inflammatory myopathies. *Arthritis Care Res (Hoboken).* 2010;62:465-472. **3.** Aggarwal R, Marder G, Koontz DC, et al. Efficacy and safety of adrenocorticotropic hormone gel in refractory dermatomyositis and polymyositis. [published online December 13, 2017]. *Ann Rheum Dis.* Doi:10.1136/annrheumdis-2017-212047. Accessed December 14, 2017. **4.** Levine T. A retrospective case series of 5 patients with dermatomyositis or polymyositis. Treating refractory dermatomyositis or polymyositis with adrenocorticotropic hormone (ACTH) gel: a retrospective case series. *Drug Des Devel Ther.* 2012;61:133-139.

Please see additional Important Safety Information inside.
Please see accompanying full Prescribing Information.

Mallinckrodt Pharmaceuticals

H.P. Acthar® GEL
(repository corticotropin injection) 80 U/mL