Drug Monograph

Drug Name: **Mycapssa® (octreotide) delayed-release capsule**
Drug Class: **Somatostatin Analog**
Prepared For: MO HealthNet
Prepared By: Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms:	Mycapssa is available as a 20 mg delayed-release capsule of octreotide.
Manufacturer:	Manufactured by: MW Encap Ltd., Scotland, UK.
Summary of Findings:	The efficacy of Mycapssa was demonstrated in a single randomized, double-blind, placebo-controlled clinical trial of 56 patients. There was a statistically significant improvement in the maintaining of an (insulin-like growth factor-1 (IGF-1) response when compared with placebo (58% of patients receiving Mycapssa vs. 19% receiving placebo (p = 0.008)).

Status Recommendation:	☐ Clinical Edit ☒ Open Access	☐ PA Required ☐ PDL
Type of PA Criteria:	☐ Appropriate Indications ☒ No PA Required	☐ Non-Preferred ☐ Preferred

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [1-3]

Acromegaly is the clinical syndrome that results from excessive secretion of growth hormone (GH). It is most commonly caused by a somatroph (GH-secreting) adenoma of the anterior pituitary. Clinical features of acromegaly are attributable to high serum concentrations of both GH and IGF-1, which is GH dependent. Excess GH and IGF-1 have both somatic and metabolic effects. The somatic effects include stimulation of growth of many tissues, such as skin, connective tissue, cartilage, bone, viscera, and many epithelial tissues. The metabolic effects include nitrogen retention, insulin antagonism, and lipolysis. Current estimates of the prevalence of acromegaly range anywhere from 480 per million people to 1000 per million people with the mean age at diagnosis being 40 to 45 years old.

Dosage Form [4,5]

Mycapssa is available as a 20 mg delayed-release capsule of octreotide.

Manufacturer [4]

Manufactured by: MW Encap Ltd., Scotland, UK.

Indication(s) [4,5]

Mycapssa is indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

Clinical Efficacy [4,5] (mechanism of action/pharmacology, comparative efficacy)

Mycapssa, a somatostatin analog, inhibits serotonin release, and the secretion of gastrin, VIP, insulin, glucagon, secretin, motilin, and pancreatic polypeptide. In acromegaly, it decreases GH and IGF-1. It provides more potent inhibition of GH than endogenous somatostatin.

Pharmacokinetics:

Absorption	Time to peak: 1.67 – 2.5 hours
Metabolism	Hepatic
Excretion	Urine: 32% as octreotide
Half-life	In adults with acromegaly: 3.2 – 4.5 hours

Clinical Trials Experience[6]

STUDY 1 DESIGN	Randomized, double-blind, placebo-controlled study (n = 56)
INCLUSION CRITERIA	• ≥18 years of age • Had evidence of active disease (IGF-1 ≥ 1.3 x upper limit of normal (ULN) ≥ 3 months after last pituitary surgery) Had an average IGF-1 ≤ 1.0 x ULN on a stable dose of octreotide or lanreotide injections
EXCLUSION CRITERIA	• Patients taking injection of long-acting somatostatin receptor ligands (SRLs) not as indicated in the label • Pituitary surgery within six months • Conventional or stereotactic pituitary radiotherapy any time in the past • Patients who previously participated in CH-ACM-01 or OOC-ACM-302 • Any clinically significant uncontrolled concomitant disease • Symptomatic cholelithiasis • Pegvisomant within 24 weeks • Dopamine agonists within 12 weeks • Pasireotide within 24 weeks
TREATMENT REGIMEN	Patients initiated Mycapssa treatment twice daily 1 month after their last injection of somatostatin analogs. The starting dose was 40 mg (20 mg in the morning and 20 mg in the evening). Dose increase was allowed during dose titration to 60 mg (40 mg in the morning and 20 mg in the evening) and to a maximal dose of 80 mg (40 mg twice daily) until patients were deemed adequately controlled based on biochemical results and/or clinical judgement. Patients then maintained their target dose until the end of treatment (9 months).
RESULTS	The primary efficacy endpoint was somatostatin dose-adjusted proportion of patients who maintain their biochemical response, defined as an IGF-1 level less than or equal to the ULN at the end of 9 months treatment. The primary endpoint was met, as 58% of patients receiving Mycapssa maintained IGF-1 response vs. 19% receiving placebo (p = 0.008).
SAFETY	Discussed in the Adverse Effects section below.

Contraindications [4,5]

- Hypersensitivity to octreotide or any of the components of Mycapssa.

Warnings and Precautions [4,5]

- Cholelithiasis and complications of cholelithiasis: Monitor patients periodically. If complications of cholelithiasis are suspected, discontinue Mycapssa and treat appropriately.
- Hyperglycemia and hypoglycemia: Blood glucose levels should be monitored when Mycapssa treatment is initiated or when the dose is altered. Adjust antidiabetic treatment accordingly.
- Thyroid function abnormalities: Assess thyroid function periodically during treatment with Mycapssa.

- Cardiac function abnormalities: ECG changes such as bradycardia, conduction abnormalities, and arrhythmias/tachycardia may occur in patients with acromegaly. Dosage adjustments of concomitantly used drugs that have bradycardia effects (i.e. beta-blockers) may be necessary.
- Decreased vitamin B_{12} levels and abnormal Schilling's tests: Due to the possible altering of absorption of dietary fats in some patients, monitor vitamin B_{12} levels during treatment with Mycapssa.

Adverse Effects [4,5]

Most common, ≥ 1%	Mycapssa (n = 28) %	Placebo (n = 28) %
Diarrhea	29	21
Nausea	21	11
Blood glucose increased	14	7
Vomiting	14	0
Abdominal discomfort	14	11
Dyspepsia	11	4
Sinusitis	11	0
Osteoarthritis	11	0
Urinary tract infection	7	4
Pain	7	0
Large intestine polyp	7	0
Cholelithiasis	7	4

Drug Interactions [4,5]

- Proton pump inhibitors (PPIs), H_2-receptor antagonists, or antacids: Coadministration with PPIs, H_2-blockers, or antacids may require increased doses of Mycapssa. Drugs that alter the pH of the upper GI tract may alter the absorption of Mycapssa and lead to a reduction in bioavailability. Coadministration with esomeprazole resulted in a decrease in bioavailability for Mycapssa.
- Cyclosporine: Coadministration resulted in a decrease in cyclosporine bioavailability. Adjustment of cyclosporine dose to maintain therapeutic levels may be necessary.
- Insulin and antidiabetic drugs: Monitor blood glucose levels in diabetic patients upon Mycapssa initiation and make subsequent dose adjustments to these therapeutic agents.
- Digoxin: Concomitant administration resulted in digoxin peak exposure.
- Lisinopril: Concomitant administration increases lisinopril bioavailability. Monitor patient's blood pressure and adjust the dose of lisinopril if needed.
- Levonorgestrel: Concomitant administration decreases levonorgestrel bioavailability and may potentially diminish the effectiveness of combined oral contraceptives or increase breakthrough bleeding. Counsel women to use an alternative non-hormonal method of contraception or a back-up method.
- Bromocriptine: Concomitant administration may increase the systemic exposure of bromocriptine. Dose adjustment of bromocriptine may be necessary.
- Beta-blocker and calcium channel blockers: Patients may require dose adjustments if they are on these agents due to Mycapssa possibly causing bradycardia in acromegaly patients.
- Drugs metabolized by CYP 450 enzymes: Concomitant use with other drugs mainly

metabolized by CYP3A4 that have a narrow therapeutic index (e.g., quinidine) should be used with caution and increased monitoring may be required.

Dosage and Administration [4,5]

- Initiate Mycapssa at a dosage of 40 mg daily, administered as 20 mg twice daily.
- Titrate dosage based on IGF-1 levels and patient's signs and symptoms and increase the dosage in increments of 20 mg daily every 2 weeks or as indicated.
- For Mycapssa dosages of 60 mg daily, administer as 40 mg in the morning and 20 mg in the evening.
- For Mycapssa dosages of 80 mg daily, administer as 40 mg twice daily.
- Maximum recommended dosage is 80 mg daily.
- Monitor IGF-a and patient's signs and symptoms monthly or as indicated once maintenance dosage is achieved.
- End stage renal disease: Initiate Mycapssa at 20 mg once daily. Titrate and adjust maintenance dosage as described above.

Cost

Generic Name	Brand Name	Manufacturer	Dose	Cost**/ Month
Octreotide	Mycapssa	MW Encap Ltd.	20 mg twice daily (starting dose)	$92/capsule or $2,576/28 days

** Wholesale Acquisition Cost

Conclusion

Mycapssa is indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide. The efficacy of Mycapssa was demonstrated in a randomized, double-blind, placebo-controlled clinical trial of 56 patients. There was a statistically significant improvement in the maintaining of an IGF-1 response when compared with placebo (58% of patients receiving Mycapssa vs. 19% receiving placebo (p = 0.008)). The most common adverse reactions in patients taking Mycapssa (>10%) were diarrhea, nausea, increased blood glucose, vomiting, abdominal discomfort, dyspepsia, sinusitis, and osteoarthritis.

Recommendation

MO HealthNet Division recommends Open Access status for this product.

References

1) Melmed S, Katznelson L. Causes and clinical manifestations of acromegaly. *UpToDate*. Waltham,. MA: UpToDate, Inc.. https://www.uptodate.com/contents/causes-and-clinical-manifestations-of-acromegaly?search=mycapssa%20acromegaly&topicRef=6625&source=see_link. Accessed Oct 17, 2020.
2) Schneider HJ, Sievers C, Saller B, Wittchen HU, Stalla GK. High prevalence of biochemical acromegaly in primary care patients with elevated IGF-1 levels. *Clin Endocrinol (Oxf)*. 2008;69(3):432-435. doi:10.1111/j.1365-2265.2008.03221.x. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2265.2008.03221.x. Accessed Oct

17, 2020.
3) Rosario PW. Frequency of acromegaly in adults with diabetes or glucose intolerance and estimated prevalence in the general population. *Pituitary*. 2011;14(3):217-221. doi:10.1007/s11102-010-0281-0. https://link.springer.com/article/10.1007/s11102-010-0281-0. Accessed Oct 17, 2020.
4) Product Information: Mycapssa® (octreotide). MW Encap Ltd., Scotland, UK.
5) Octreotide: Drug Information. Lexi-Drugs. Wolters Kluwer Clinical Drug Information Inc.
6) Samson SL, Nachtigall LB, Fleseriu M, et al. OR23-07 Results From the Phase 3, Randomized, Double-Blind, Placebo-Controlled CHIASMA OPTIMAL Study of Oral Octreotide Capsules in Adult Patients with Acromegaly. *J Endocr Soc*. 2020;4(Suppl 1):OR23-07. Published May 8, 2020. doi:10.1210/jendso/bvaa046.211.

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