INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

MYCAPSSA (octreotide) delayed-release capsules, for oral use, is a somatostatin analog indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide.

CONTRAINDICATIONS

Hypersensitivity to octreotide or any of the components of MYCAPSSA. Anaphylactoid reactions, including anaphylactic shock, have been reported in patients receiving octreotide.

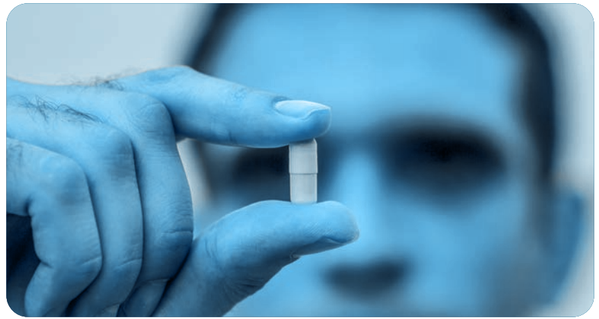
Please see additional Important Safety Information throughout and access full Prescribing Information here.

Introducing

Mycapssa®

(octreotide) capsules 20mg

MYCAPSSA is the first and only FDA-approved oral somatostatin analog (SSA) for appropriate patients with acromegaly, providing effective and consistent biochemical control while freeing patients from the burden of SSA injections.[1-3]



MYCAPSSA **maintained normal IGF-I levels** in most patients who switched from injectable SSAs[2,3]

BID oral dosing leads to **consistent biochemical control**[3]

MYCAPSSA (octreotide) was **generally well-tolerated in clinical trials**[2]

The majority of patients receiving MYCAPSSA in the CHIASMA OPTIMAL trial **chose to stay on MYCAPSSA**[3]

MYCAPSSA is powered by Transient Permeability Enhancer (TPE®) Technology[3]

Peptides and large molecule drugs are generally administered via injection because these agents can be degraded by digestive enzymes and/or blocked from crossing the intestinal epithelium via transcellular or paracellular routes, resulting in low bioavailability and sub-therapeutic levels in the blood.[4]

MYCAPSSA capsules are protected from degradation by the enteric coating[5]

The TPE formulation allows octreotide to be absorbed, intact, at therapeutic levels[5]

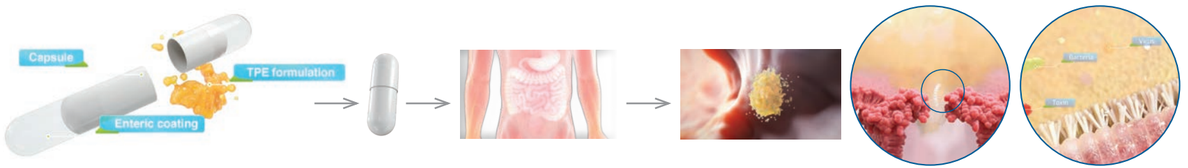


Figure adapted from Melmed S. *Nat Rev Endocrinol*. 2016;12(2):90-98.

1 MYCAPSSA capsules containing TPE have an **enteric coating, protecting them from enzymatic degradation** in the stomach and allowing them to reach the small intestine[5,6]

2 **Once in the small intestine**, the coated capsule dissolves, **releasing the TPE formulation**[5,6]

3 **Medium chain fatty acids then induce the expansion of tight junctions between intestinal epithelial cells** by leveraging a naturally occurring process, which the body normally uses to absorb nutrients through paracellular transport[5,6]

4 **This allows octreotide to enter the bloodstream at therapeutic levels** while excluding larger structures (≥70kDa) such as toxins, bacteria, and viruses[6]

INDICATION AND IMPORTANT SAFETY INFORMATION (Continued)

WARNINGS AND PRECAUTIONS

MYCAPSSA can cause problems with the gallbladder. Monitor patients periodically. Discontinue if complications of cholelithiasis are suspected.

Blood sugar, thyroid levels, and vitamin B_{12} levels should be monitored and treated accordingly.

Bradycardia, arrhythmia, or conduction abnormalities may occur. Treatment with drugs that have bradycardia effects may need to be adjusted.

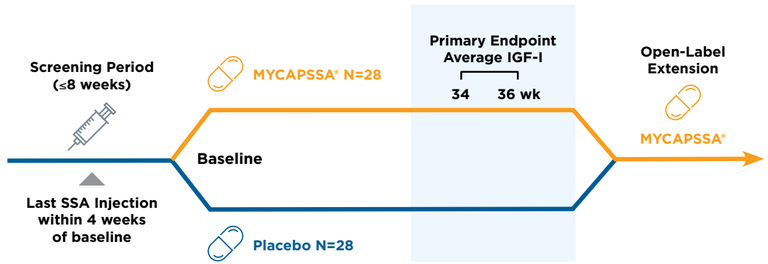
The safety and efficacy of MYCAPSSA were evaluated in the

CHIASMA OPTIMAL PIVOTAL TRIAL

CHIASMA OPTIMAL was a 9-month, randomized, double-blind, placebo-controlled study in 56 patients with acromegaly and IGF-I ≤1.0 x upper limit of normal (ULN) at screening[3]

The CHIASMA OPTIMAL trial utilized a rigorous study design[3]

Double-Blind, Placebo-Controlled Period (36 Weeks) Dose titration based on IGF-I and/or symptom control



- **Starting dose:** 40 mg (20 mg morning + 20 mg evening)[2]
- Dose titration was performed during the first 6 months of the study to a dose of 60 mg (40 mg morning + 20 mg evening) and up to a maximum dose of 80 mg daily (40 mg morning + 40 mg evening) based on **biochemical results or symptoms**[2]
- Patients then **maintained a fixed dose until end of treatment**[2]

Primary Endpoint[3]

- Proportion of patients who maintain biochemical response
  - Response was defined as an average of IGF-I ≤1.0 x ULN at weeks 34 and 36

Secondary Endpoints[3]

- Proportion of patients who maintained GH response at week 36 (average GH <2.5 ng/mL)
- Time to loss of IGF-I response, defined as either IGF-I >1.0 x or ≥1.3 x ULN for 2 consecutive visits
- Proportion of patients who reverted to prior injectable SSA up to and including week 36

The study population was comprised of a group of clinically diverse patients[3]

Baseline Characteristics[3]

Characteristics, n (%)	Placebo (N=28)	MYCAPSSA (N=28)
Duration of acromegaly, y		
<10	20 (71.4)	15 (53.6)
10-20	5 (17.9)	8 (28.6)
>20	3 (10.7)	5 (17.9)
Symptom burden		
≥1 symptom reported	24 (85.7)	23 (82.1)
≥2 symptoms reported	19 (67.9)	18 (64.3)
≥3 symptoms reported	14 (50.0)	10 (35.7)
Prior injectable treatment dose[a]		
Low	5 (17.9)	6 (21.4)
Middle or high	23 (82.1)	22 (78.6)
Sex		
Male	14 (50.0)	12 (42.9)
Female	14 (50.0)	16 (57.1)
Age at screening, y		
Mean (SD)	54.2 (10.96)	55.3 (11.97)
Median	54.5	57.0

>75%
of patients
were controlled on a middle or high dosage of SSA injection therapy at baseline[3]

>80%
of patients
reported ≥1 symptom at baseline[3]

[a]Low dose: octreotide 10 mg every 4 weeks; lanreotide 60 mg every 4 weeks or 120 mg every 8 weeks. Medium dose: octreotide 20 mg every 4 weeks; lanreotide 90 mg every 4 weeks or 120 mg every 6 weeks. High dose: octreotide 30 mg every 4 weeks; lanreotide 120 mg every 4 weeks. Patients were stratified based on the grouping of mid-high and low prior SRL doses.

INDICATION AND IMPORTANT SAFETY INFORMATION (Continued)

ADVERSE REACTIONS

The most common adverse reactions (incidence >10%) are nausea, diarrhea, headache, arthralgia, asthenia, hyperhidrosis, peripheral swelling, blood glucose increased, vomiting, abdominal discomfort, dyspepsia, sinusitis, and osteoarthritis.

Mycapssa® (octreotide) capsules 20mg

The Chiasma Optimal Phase 3 Clinical Trial

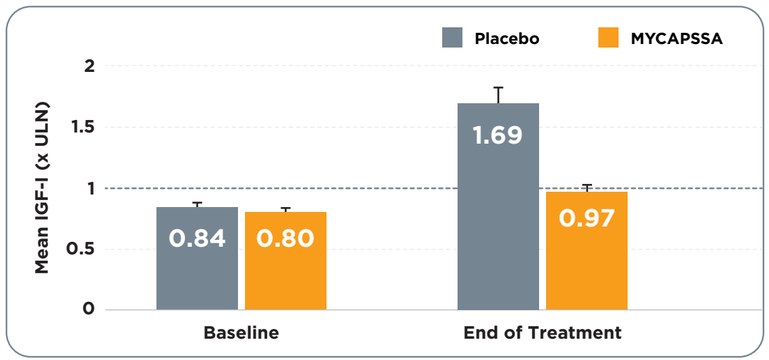
MET KEY ENDPOINTS INCLUDING PRIMARY AND SECONDARY[3]

Primary Endpoint

58% of patients receiving MYCAPSSA vs 19% of patients receiving placebo met the criteria for maintaining IGF-I response, defined as an average of week 34 and 36 IGF-I ≤1.0 x ULN (*p*=0.0079)[2]

Descriptive Endpoint

The mean IGF-I level was maintained within normal range in the group receiving MYCAPSSA at the end of oral treatment[3]



During the study period, **over 98% of the MYCAPSSA group were compliant with the drug dosing regimen.**[3]

Secondary Endpoints

Median time to loss of response was not met in the MYCAPSSA group[3]

Loss of response criteria was not met in the group receiving MYCAPSSA during the 36-week treatment period. The group receiving placebo met median time to loss of response with both IGF-I >1.0 x ULN and ≥1.3 x ULN at week 16

78% of patients on MYCAPSSA maintained GH response[3]

Of the patients with a mean GH <2.5 ng/mL at screening, at week 36, **78% of patients** receiving MYCAPSSA maintained GH <2.5 ng/mL vs 30% for patients receiving placebo (*p*=0.001)

75% of patients completed treatment on MYCAPSSA[2,3]

75% of patients treated with MYCAPSSA **did not require reversion to SSA injections** anytime throughout the 9 months for any reason vs 32% of patients treated with placebo (*p*<0.003)

INDICATION AND IMPORTANT SAFETY INFORMATION (Continued)

DRUG INTERACTIONS

The following drugs require monitoring and possible dose adjustment when used with MYCAPSSA: cyclosporine, insulin, antidiabetic drugs, calcium channel blockers, beta blockers, lisinopril, digoxin, bromocriptine, and drugs mainly metabolized by CYP3A4. Counsel women to use an alternative non-hormonal method of contraception or a back-up method when MYCAPSSA is used with combined oral contraceptives.

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The majority of patients receiving MYCAPSSA in the CHIASMA OPTIMAL trial

CHOSE TO STAY ON MYCAPSSA[3]

Following the double-blind period of the Pivotal Phase 3 clinical trial, eligible patients were provided the option to enter the Open-Label extension and receive MYCAPSSA[3]

90% of patients

receiving MYCAPSSA at the end of the double-blind period of the CHIASMA OPTIMAL trial **opted to remain on treatment for the Open-Label extension**[3]

More than 100 patients from CHIASMA OPTIMAL and the Open-Label Phase 3 Study* have received MYCAPSSA for ≥1 year[7†]

*__Open-Label Phase 3 Study Design:__ a single-arm, multicenter study evaluating 151 patients with acromegaly over a 7-month period.[8]
†Data as of January 2020

Across two Phase 3 studies and 183 patients, MYCAPSSA was generally well-tolerated[2]

GI symptoms were the most commonly reported adverse reactions with MYCAPSSA. They were mostly mild to moderate and resolved with continued treatment.[2]

- In the CHIASMA OPTIMAL placebo-controlled study, GI AEs occurred mostly during the initial 3 months of treatment, and resolved within a median duration of 8 days[2]
- In the Open-Label study, GI AEs occurred during the initial 2 months of treatment, and resolved on treatment within a median of 13 days[2]

Summary of Most Common (≥5% and >placebo) AEs in CHIASMA OPTIMAL by Preferred Term

	PLACEBO, % (N=28)	MYCAPSSA, % (N=28)
Diarrhea	21	29
Nausea	11	21
Blood glucose increased[a]	7	14
Vomiting	0	14
Abdominal discomfort	11	14
Dyspepsia	4	11
Sinusitis	0	11
Osteoarthritis	0	11
Urinary tract infection	4	7
Pain	0	7
Large intestine polyp	0	7
Cholelithiasis	4	7

Summary of Most Common (≥5%) AEs in the Open-Label Study with MYCAPSSA

	MYCAPSSA, % (N=155)
Headache	33
Nausea	30
Arthralgia	26
Asthenia	22
Hyperhidrosis	21
Diarrhea	18
Peripheral swelling	16
Dyspepsia	8
Abdominal pain upper	8
Abdominal distension	7
Nasopharyngitis	7
Influenza	7
Blood glucose increased[a]	6
Vomiting	6
Flatulence	6
Back pain	6
Abdominal pain	5
Dizziness	5
Fatigue	5
Upper respiratory tract infection	5
Hypertension	5

[a]Includes blood glucose increased, hyperglycemia and glycosylated hemoglobin increased.
AE, adverse event; **GI**, gastrointestinal

INDICATION AND IMPORTANT SAFETY INFORMATION (Continued)

DRUG INTERACTIONS (Continued)

Patients taking proton pump inhibitors, H2-receptor antagonists, or antacids concomitantly with MYCAPSSA may require increased dosages of MYCAPSSA.

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Successfully Transitioning Patients

TO MYCAPSSA

Start your patients on MYCAPSSA and titrate for optimal therapeutic benefit:

Work with your patient to identify the day to transition their treatment[2]

- Consider the originally planned timing of their next injection to help ease the patient into a new treatment routine and provide a smooth transition onto MYCAPSSA

Educate your patients on how to take MYCAPSSA properly and encourage adherence[2]

- Start your patients on the 20 mg BID oral dose
- Ensure they take MYCAPSSA with a glass of water
- Coach them on finding a routine for taking MYCAPSSA on an empty stomach, either 1 hour before or 2 hours after eating

Emphasize the importance of treatment compliance to the MYCAPSSA BID dosing regimen

- BID oral dosing leads to consistent biochemical control[3]
- In the randomized and open-label studies, compliance was 98% and 94%, respectively.[3,8]

Monitor their response to MYCAPSSA[2]

Initiate MYCAPSSA at a dosage of 40 mg daily (20 mg orally, twice daily)

40 mg — AM DOSE | PM DOSE

If needed, titrate the MYCAPSSA dosage by 20 mg daily, based on IGF-I levels and patient's signs and symptoms or as indicated

60 mg — AM DOSE | PM DOSE

If needed, titrate the MYCAPSSA dosage by 20 mg daily, based on IGF-I levels and patient's signs and symptoms or as indicated

80 mg — AM DOSE | PM DOSE

- **Monitor IGF-I levels and patient's signs and symptoms every 2 weeks during the dose titration or as indicated[2]**
- **Common symptoms of acromegaly, such as fatigue, headache, and perspiration can be early indicators that a patient may require dose titration[9,10]**

INDICATION AND IMPORTANT SAFETY INFORMATION (Continued)

PREGNANCY

Advise premenopausal females of the potential for an unintended pregnancy.

To report SUSPECTED ADVERSE REACTIONS, contact the product information department at 1-844-312-2462 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

Mycapssa® (octreotide) capsules 20mg

Chiasma Offers a

DEDICATED PATIENT SERVICES PROGRAM

Chiasma Access & Patient Support (CAPS) program offers a personalized and comprehensive patient support program to help patients with acromegaly get started on MYCAPSSA, and guide them throughout treatment

JOHN
Patient Care Specialist

Dedicated Patient Services

CAPS will provide your office with one-on-one support to ensure seamless:

- Reimbursement access
- Benefits investigation
- Specialty pharmacy interactions

Visit hcp.MYCAPSSA.com to fill out the enrollment form for all of your acromegaly patients that you would recommend transitioning to MYCAPSSA

We're looking forward to facilitating the process and supporting your practice and patients in their journey to start and manage their acromegaly with twice-daily MYCAPSSA

CAPS Services

A simple enrollment form helps start the process so dedicated CAPS Team members, working with your office, can alleviate access hurdles and ensure patient access to MYCAPSSA

The CAPS Team Will Facilitate

Benefits investigation to better understand insurance coverage for each patient and assist with authorization forms and paperwork

Specialty pharmacy interaction to coordinate set-up and delivery of MYCAPSSA for the patient

Financial assistance for out-of-pocket expenses or for individuals without insurance or for those who meet other eligibility requirements

Ongoing support services are available once patients have started on MYCAPSSA to guide them through their new treatment routine and ensure they have the support they need

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MYCAPSSA
(octreotide) capsules

MYCAPSSA is the **first and only FDA-approved oral somatostatin analog (SSA)** for appropriate patients with acromegaly, providing effective and consistent biochemical control while freeing patients from the burden of SSA injections.[1-3]

- MYCAPSSA **maintained normal IGF-I levels** in most patients who switched from injectable SSAs[2,3]
- BID oral dosing leads to **consistent biochemical control**[3]
- MYCAPSSA (octreotide) was **generally well-tolerated in clinical trials**[2]
- The majority of patients receiving MYCAPSSA in the CHIASMA OPTIMAL trial **chose to stay on MYCAPSSA**[3]
- **Personalized and comprehensive patient services program** offering benefits investigation, specialty pharmacy interaction, financial assistance, and ongoing education to support adherence to MYCAPSSA

For more resources on MYCAPSSA and to initiate enrollment, visit hcp.MYCAPSSA.com or call CAPS at 1-833-346-2277

REFERENCES

1. Colao A, et al. *Nat Rev Dis Primers*. 2019;5(1):20. **2.** MYCAPSSA [package insert]. Chiasma, Inc.; 2020. **3.** Samson SL, et al. *J Clin Endocrinol Metab*. 2020;105(10):dgaa526. **4.** Karsdal MA, et al. *Br J Clin Pharmacol*. 2015;79(5):720-732. **5.** Melmed S, et al. *Nat Rev Endocrinol*. 2016;12(2):90-8. **6.** Tuvia S, et al. *Pharm Res*. 2014;31(8):2010-2021. **7.** Data on File. Chiasma, Inc. **8.** Melmed S, et al. *J Clin Endocrinol Metab*. 2015;100(4):1699-1708. **9.** Katznelson L, et al. *J Clin Endocrinol Metab*. 2014;99(11):3933-3951. **10.** Mathioudakis N, et al. *Neurosurg Clin N Am*. 2012;23(4):621-638.

Mycapssa® (octreotide) capsules 20mg

CHIASMA®