Mycapssa®
(octreotide) capsules 20mg

Starter Kit

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.

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

Chiesi TOTAL care℠

Consistent control for patients with acromegaly with daily oral MYCAPSSA®

What's inside

Getting a Patient Started on MYCAPSSA
- Rx form
- Patient consent form

MYCAPSSA Prior Authorization and Access Guide
- Medical necessity letter template
- Appeal letter template

MYCAPSSA Dosing and Administration Guide

Copay Support Information
Please refer to the full Terms and Conditions in the back pocket for additional eligibility requirements.

US Prescribing Information

Contact Information Card

Mycapssa®
(octreotide) capsules 20mg

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

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CONTRAINDICATIONS

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

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.

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.

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 taking an oral contraceptive to use an alternative non-hormonal method of contraception or a back-up method when taking MYCAPSSA.

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

PREGNANCY

Advise premenopausal females of the potential for an unintended pregnancy.

To report SUSPECTED ADVERSE REACTIONS, please contact Chiesi Farmaceutici S.p.A. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

For more information, visit mycapssa.com.
Chiesi Total Care℠ Program offered through AcariaHealth Specialty Pharmacy.

PP-MC-0001 V2.0 2024

Chiesi

Becky,
MYCAPSSA
patient

Mycapssa®
(octreotide) capsules 20mg

Getting Started Guide

To get a patient started on MYCAPSSA®
follow 2 steps outlined in this guide

Visit chiesitotalcare.com
or call 1-833-346-2277
We're ready to help!

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

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Chiesi TOTAL care℠

Step 1: Fill out the Prescription and Patient Consent Forms

Chiesi TOTAL care℠

Prescription Form

To Be Completed by Prescriber

Mycapssa® (octreotide) capsules 20mg

1. First prescription for the patient: Fax completed form to 1-833-746-2277
2. Subsequent prescription: May be e-script via AcariaHealth Specialty Pharmacy in your EMR/HMR system Call 1-833-346-2277 if you have questions regarding this form or contact Chiesi Total Care℠

1. PATIENT INFORMATION (all fields in this section are mandatory)

Patient Name (First, Middle, Last) _____ Email _____
Last 4 of Social Security # _____ Gender at birth ☐ Male ☐ Female Date of Birth_____ (mm/dd/yyyy)
Address _____ City _____ State _____ Zip _____
Mobile # _____ Alternative Phone # _____ Language: ☐ English ☐ Other _____

Caregiver Name _____ ☐ OK to leave message
Email _____ Caregiver Phone # _____
Allergies _____ Current Medications: _____
☐ No known drug allergies (NKDA)

2: INSURANCE INFORMATION (check the relevant box and complete as much as possible)

Please attach copies of both sides of the patient's insurance card.

☐ Medicare ☐ Medicaid ☐ Commercial/Private ☐ Other ☐ Uninsured
Primary Insurance Payer _____ Plan Name _____
Phone # _____ Policy ID # _____
Group # _____ BIN _____
PCN _____ Policy Holder's Name: _____
Policy Holder's Date of Birth _____ Policy Holder's Relationship to Patient _____

3: PRESCRIBER INFORMATION* (all fields in this section are mandatory)

The prescriber is to comply with his/her state specific prescription requirements such as e-prescribing, state specific prescription form fax language, etc. Non-compliance with state specific requirements could result in outreach to the prescriber.

Name (First, Middle, Last) _____ Prescriber NPI # _____
Prescriber Tax ID #: _____ Facility Name _____
Facility Address _____ City _____ State _____ Zip _____
Facility Phone # _____ Preferred Fax # _____

Primary Contact Name _____ Title/Role _____
Primary Contact Phone # _____ Primary Contact Email _____

4: TREATMENT AND PRESCRIBING INFORMATION (mandatory)

Rx Treatment: MYCAPSSA® (octreotide) delayed-release oral capsules NDC: 69880-120-28. Dispense as written.
Please check a box below for medication strength* (mandatory)

Patient, at any time, has been prescribed octreotide or lanreotide
☐ yes
☐ no

A

☐ **ICD-10/Diagnosis: E22.0 (acromegaly and pituitary gigantism)**
☐ ICD-10/Diagnosis: D35.2 (benign neoplasm of the pituitary gland)
☐ ICD-10/Diagnosis: F40.231(needle phobia)
☐ Other ICD-10/Diagnosis: _____

B

Recommended to check additional strengths for titration needs

☐ **MYCAPSSA 40 mg**
Starting Dose
Dispense:
MYCAPSSA 20 mg capsules Sig: Take 1 capsule PO BID
☐ **QTY:** 56
☐ **QTY:** 168
Number of Refills_____

☐ **MYCAPSSA 60 mg**
Dispense:
MYCAPSSA 20 mg capsules Sig: Take 2 capsule PO QAM and 1 capsule PO QPM
☐ **QTY:** 84
☐ **QTY:** 252
Number of Refills_____

☐ **MYCAPSSA 80 mg**
Dispense:
MYCAPSSA 20 mg capsules Sig: Take 2 capsule PO BID
☐ **QTY:** 112
☐ **QTY:** 336
Number of Refills_____

PRESCRIBER AUTHORIZATION* (mandatory)

By signing below, I certify that I am part of the Chiesi Total Care Program, that the therapy described above is medically necessary, and that the information provided is accurate to the best of my knowledge. I also attest that I have obtained the patient's authorization to release the above information and such other personal information as may be necessary to the Chiesi Total Care Program and/or their agents. If the patient is 18 years old or younger, I attest that I have obtained permission from the patient's legal guardian.

Licensed Prescriber Signature (required–no stamps) _____

Printed Name _____ Date _____

ATTENTION: E-prescribe or use the official state prescription form where required by state law.
No stamped signatures or signing on behalf of the prescriber.

Scan for digital RX form.

Product: MYCAPSSA®

Phone: 1-833-346-2277

…SA, Inc. ("Chiesi") product. Program support may include:
… and reviewing eligibility for financial assistance and copay
…, and (4) providing disease-, medication-, and adherence-

… (MM/DD/YY): _____

…RE

…iesi USA, Inc., and its affiliates, service providers, agents,
…viders, and their staff, my health plan, patient assistance
…out my diagnosis, treatment, and lab results), personal
…as prescriptions and plans) (together my "Information") in
…duct other business activities, and complete government
…tives (together, "Chiesi") including providers of alternate
…Program") for Healthcare Providers and patients for the
… mail, phone, email, and text message*), tailor Program-
…pense Chiesi products to me. Chiesi may also de-identify
…usiness purposes. I understand that once my Information
…ever, Chiesi will only process and disclose my Information
…w.chiesiusa.com/privacy-policy/.

…l Care Program, you understand that Chiesi USA, Inc. may
…s://www.chiesiusa.com/privacy-policy/. To opt-out of the use
…87. Only you, or someone legally authorized to act on your
… defined in the California Consumer Privacy Act ("CCPA").

…affect my treatment, insurance coverage, or eligibility for

… letter requesting cancellation to Chiesi Total Care, 8517
…d personal data rights, Chiesi will no longer process my
…d on this Authorization prior to receipt of the cancellation.
…quired by state or local law.

…n to Chiesi. I acknowledge that if I am eligible for infusion
…knowledge that if I am enrolled in a government-funded
…stand and agree that if my insurance information changes
…ossible, and any such change may affect my eligibility for

…tal Care support programs on page 2 of this document.

…esi about opportunities for you to provide feedback to us

…vide feedback.

…consent to receiving text messages is not a condition of
…ext messages by replying STOP to any text from Chiesi

…ges.

…ate (MM/DD/YY):_____

… to Patient:_____

…and I agree that Chiesi Total Care will not pay those fees.

_____

_____

Office Contact Person:_____ **Office Phone:**_____

IMPORTANT SAFETY INFORMATION

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.

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

Specify appropriate ICD-10 Diagnosis code(s) for secondary diagnosis

(Other uses are at prescriber's discretion)

A

ICD-10 Diagnosis Codes	
Diagnosis	**Current indication**
E22.0	Acromegaly and pituitary gigantism
D35.2	Benign neoplasm of the pituitary gland
F40.231	Needle phobia

Intended as a reference for coding and billing for product and associated services. Not intended to be a directive, nor does the use of the recommended codes guarantee reimbursement. Providers are responsible for ensuring the accuracy and validity of all billing and claims for appropriate reimbursement.

Specify formulation and dosing schedule

B

Start

Manage patients' expectations when starting MYCAPSSA

- Start 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

Titrate

- Titrate based on IGF-1 levels and patients signs and symptoms.
- Titrate in 20 mg increments from 40 mg up to a maximum daily dosage of 80 mg.
- Recommended to select additional strengths for titration needs.

Step 2: Once you have completed the form:

1. **Attach copies of patient insurance and prescription cards – front and back.**
2. **First prescription for the patient:**
   THE FIRST COPY OF THE FORM MUST BE FAXED FOR EACH PATIENT. Fax completed form to Chiesi Total Care℠ at **1-833-746-2277. PLEASE COMPLETE ONE FORM PER PATIENT.**
3. **Subsequent prescriptions:**
   If you wish to send additional forms via e-script please search for "AcariaHealth" in your EMR/HMR's e-prescribing software.

The fillable pdf can be downloaded and saved for future use.

Scan the QR code to download a copy.

Chiesi TOTAL care℠

Mycapssa®
(octreotide) capsules 20mg

If you have questions, visit chiesitotalcare.com or call 1-833-346-2277 – we're ready to help!

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.

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.

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.

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 taking an oral contraceptive to use an alternative non-hormonal method of contraception or a back-up method when taking MYCAPSSA.

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

PREGNANCY

Advise premenopausal females of the potential for an unintended pregnancy.

To report SUSPECTED ADVERSE REACTIONS, please contact Chiesi Farmaceutici S.p.A. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

References: 1. Mycapssa® (octreotide) Prescribing Information. Amryt, March 2022.

For more information, visit mycapssa.com.
Chiesi Total Care℠ Program offered through AcariaHealth Specialty Pharmacy.

PP-MC-0002 V1.0 2024

Chiesi

Bonnie,
MYCAPSSA
patient

Mycapssa®
(octreotide) capsules 20mg

Dosing and Administration Guide

**Visit chiesitotalcare.com
or call 1-833-346-2277
We're ready to help!**

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

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Chiesi TOTAL care℠

Getting Patients Started on Daily Oral MYCAPSSA is Straightforward

Example dosing schedule:

Take MYCAPSSA on an empty stomach* twice daily with a glass of water

Morning dose:

Just after waking

Evening dose:

Right before bed

Each wallet of MYCAPSSA comes with 28 capsules. Each MYCAPSSA capsule is 20 mg.

* One hour before or two hours after a meal

IMPORTANT SAFETY INFORMATION

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.

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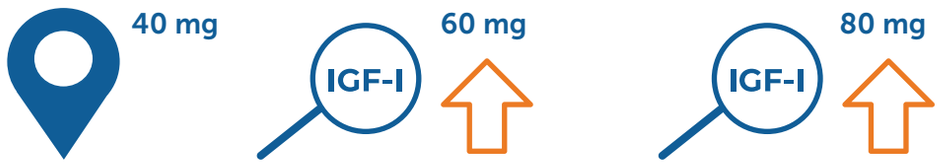
Starting and Optimizing MYCAPSSA

Example titration schedule:*



Week 1:	Week 2–3:	Week 4–5:
Start MYCAPSSA at 40 mg	Evaluate IGF-I, signs, and symptoms. Titrate MYCAPSSA to 60 mg as early as week 2-3	Evaluate IGF-I, signs, and symptoms. Titrate to 80 mg† as needed, as early as week 4-5

Once the maintenance dosage of MYCAPSSA is achieved, monitor IGF-I levels and acromegaly signs and symptoms monthly.

*The example titration schedule above reflects the total daily dose of MYCAPSSA. Refer to the full Prescribing Information for a detailed dosing schedule.

† The maximum daily dose of MYCAPSSA is 80 mg.

Mycapssa®
(octreotide) capsules 20mg

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WARNINGS AND PRECAUTIONS

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

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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 taking an oral contraceptive to use an alternative non-hormonal method of contraception or a back-up method when taking MYCAPSSA.

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

PREGNANCY

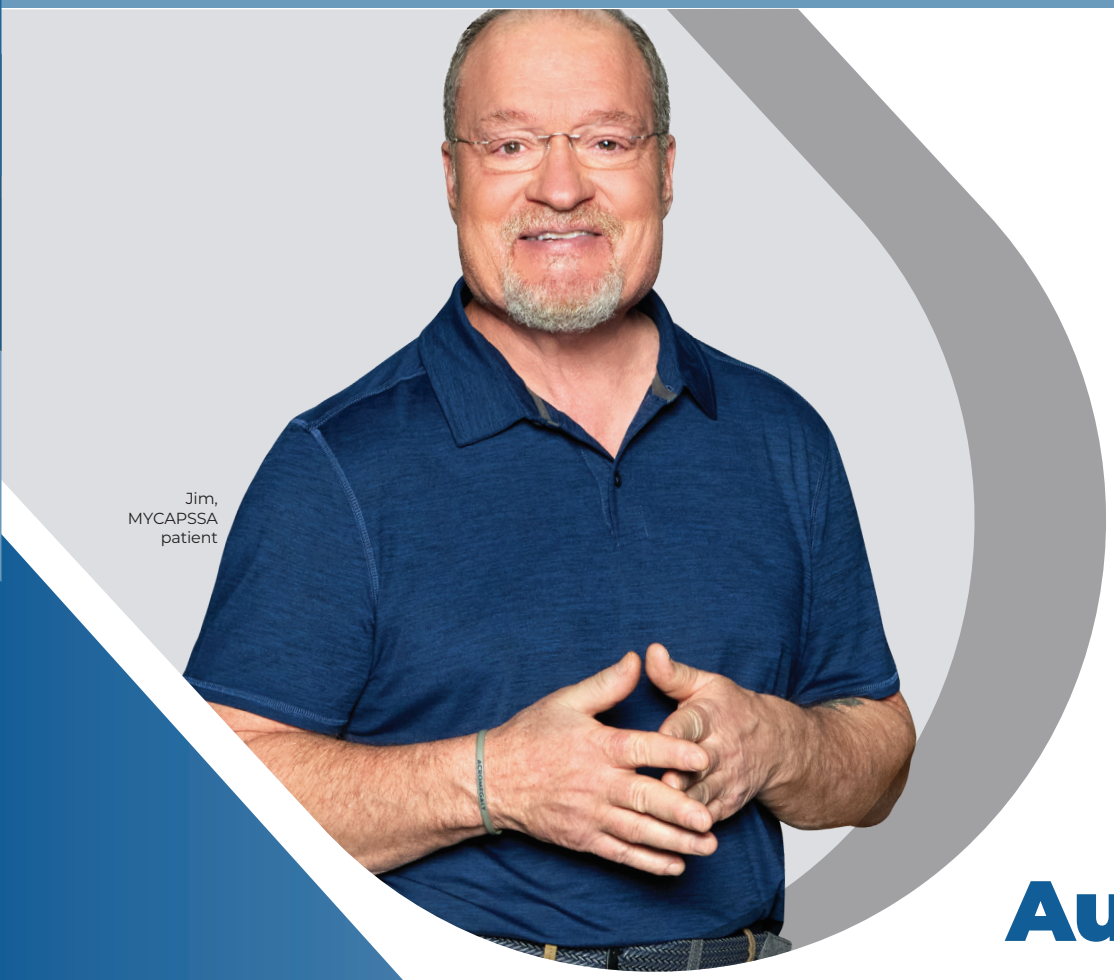
Advise premenopausal females of the potential for an unintended pregnancy.

To report SUSPECTED ADVERSE REACTIONS, please contact Chiesi Farmaceutici S.p.A. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

For more information, visit mycapssa.com.
Chiesi Total Care℠ Program offered through AcariaHealth Specialty Pharmacy.

PP-MC-0004 V1.0 2024

Chiesi



Jim,
MYCAPSSA
patient

Mycapssa®
(octreotide) capsules 20mg

Prior Authorization and Access Guide

Visit chiesitotalcare.com
or call 1-833-346-2277
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Chiesi TOTAL care℠

Chiesi Total Care℠ (CTC) will submit for insurance reimbursement and help you navigate prior authorization (PA).

Here's a step-by-step look at the process

1 Submission

Your Chiesi Total Care Team starts the process when a new Rx form has been submitted. The Chiesi Total Care team can help with the preparation of PA documents.†

† Chiesi offers additional detailed PA and Appeal process assistance through Field Reimbursement Directors (FRD). They can provide 1:1 assistance and work with you through the PA and appeal process.

2 Monitoring PA

Chiesi Total Care monitors and tracks PA submission until an outcome is determined by payor.

3

PA is approved

- Your office and/or patient is notified

PA is denied

- Send denial documentation to Chiesi Total Care
- Chiesi Total Care can help in denial situations with a high success rate

APPEAL

Based on the letter Chiesi Total Care can submit a patient level appeal with signed patient consent.

OR

CTC can help to pull documents together for a physician level appeal. Chiesi Total Care can assist and coach on best practices.*

*Chiesi Total Care assistance is neither medical guidance nor a suggestion that you submit an appeal. The resources and information provided in this guide is general in nature and is not intended to be conclusive or exhaustive. As the patient's healthcare provider, you are responsible for applying your clinical judgment regarding appropriate care and treatment of each patient.

4 PA or Appeal Approved

Pharmacy fills Rx and medication is dispensed to the patient

Contact your dedicated Chiesi Total Care program specialist with any questions you may have about your case.

Chiesi also offers patient education liaison (PEL) services for enrolled patients to further support your patients on MYCAPSSA.

PA denied? Chiesi Total Care is here to help.

It's not uncommon for the first PA submission to be denied. With a long track record of success in gaining PA and appeal approvals, Chiesi Total Care is here to provide assistance with the appeal process. Chiesi Total Care will assist in providing additional resources and/or publications depending on the reasons for denial. To request a copy of an additional resource or publication, please reach out directly to us.medical@chiesi.com.

Visit chiesitotalcare.com or call 1-833-346-2277

Chiesi TOTAL care℠

We provide updates on your patient's therapy and alert the office should there be any concerns. We also support patients by helping them cope with side effects and answering questions.

We can help by:

- Alerting when to refill or when refills are being missed
- Counseling patients on managing side effects
- Providing 24/7 pharmacist access
- Enrolling patients in the MYCAPSSA Copay Program – patients may pay as little as $0 if eligible‡

‡ Please refer to the full Terms and Conditions in the back pocket for additional eligibility requirements.

Lesa, Chiesi Total Care pharmacist

Here is a checklist of best practices for Prior Authorization submission:

- ☐ Include pertinent clinical notes, dates, and laboratory findings
- ☐ Include medical rationale for why the patient cannot use preferred formulary drugs
- ☐ Include prescribing practitioner NPI number and contact information
- ☐ Include therapeutic alternatives that were tried in the past

Important Safety Information

Drug interactions

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Mycapssa®
(octreotide) capsules 20mg

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For more information, visit mycapssa.com.
Chiesi Total Care℠ Program offered through AcariaHealth Specialty Pharmacy.

PP-MC-0003 V1.0 2024

Chiesi

Chiesi

TOTAL care℠

SCAN THE QR CODE
FOR THE DIGITAL RX FORM

BY PHONE
1-833-346-2277

BY FAX
1-833-746-2277

HOURS OF OPERATION
Monday to Friday 7:00am – 7:00pm
(Central Time)

For more information, visit chiesitotalcare.com

Chiesi Total Care Program offered through AcariaHealth Specialty Pharmacy.

PP-MC-0005 V2.0 2024

Sample Letter of Appeal

Using this template:

- ☐ Fill in the template using the instructions highlighted in blue.
- ☐ Once you have filled in the information, remove any remaining instructions in blue.
- ☐ Select all the text and change the font to black so the whole document appears as one letter.

Use the list above as a checklist to make sure you have completed these steps prior to sending. **It is important to follow these steps to ensure the letter is clear and concise.**

[Insurance Company]
[Address]
[City, State, Zip]

Re: **[Patient Name]**
[Policy #]
[DOB]
[Address]
[City, State, Zip]

To Whom It May Concern:

I am writing to appeal the denial of benefits for the use of **[Product name (generic name)]** for services requested for **[Patient Name, ID#, Group #]**. Included in this letter of appeal are information on the treatment rationale, medical records, medical necessity data and medical studies confirming currently prescribed product as an effective treatment for the diagnosis associated with **[ICD10 Code]**.

Treatment Rationale:
[Provide information on patient response and history to past treatments and anticipated prognosis and rationale for the currently prescribed product].

Outline of Medical Studies:
[Outline a brief overview of the studies evaluating the use of the currently prescribed product in this condition and/or patient population. Remember to include the FDA approved indications and usage].

Medical Record Information:
[Highlight key dates and entries of the medical record how the currently prescribed product is used].

Per the included medical information, it is my professional opinion that the currently prescribed product is medically necessary in treating the patient and the denials for the patient's use of the drug should be reversed. Please call my office at **[Office Phone Number]** if I can provide further information or speak with a review board to appeal the denial of coverage decision. I look forward to reaching resolution of overturning the denied status of the currently prescribed product for this patient.

Sincerely,
[Physician Name and Signature]
[Phone Number]
Enclosure: [Original denial notification copy]

Sample Letter of Medical Necessity

Using this template:

- ☐ Fill in the template using the instructions highlighted in blue.
- ☐ Once you have filled in the information, remove any remaining instructions in blue.
- ☐ Select all the text and change the font to black so the whole document appears as one letter.

Use the steps above as a checklist to make sure you have completed these steps prior to sending. **It is important to follow these steps to ensure the letter is clear and concise.**

[Insurance Company]
[Address]
[City, State, Zip]

Re: **[Patient Name]**
[Policy #]
[DOB]
[Address]
[City, State, Zip]

To Whom It May Concern:

I am writing this letter of medical necessity on behalf of **[Patient Name, ID#, Group #]** to request coverage for **[Product name (generic name)].** Included in this letter of medical necessity is information on the treatment rationale, medical records, medical necessity data and medical studies confirming currently prescribed product as an effective treatment for the diagnosis associated with **[ICD10 Code]**.

Treatment Rationale:
[Provide information on patient response and history to past treatments and anticipated prognosis and rationale for the currently prescribed product].

Outline of Medical Studies:
[Outline a brief overview of the studies evaluating the use of the currently prescribed product in this condition and/or patient population. Remember to include the FDA approved indications and usage].

Medical Record Information:
[Highlight key dates and entries of the medical record how the currently prescribed product is used].

Per the included medical information, it is my professional opinion that the currently prescribed product is medically necessary in treating the patient and the denials for the patient's use of the drug should be reversed. Please call my office at **[Office Phone Number]** if I can provide further information.

Sincerely,
[Physician Name and Signature]
[Phone Number]
Enclosure: [As required]

Prescription Form

To Be Completed by Prescriber

Chiesi TOTAL care℠

Mycapssa® (octreotide) capsules 20mg

1. First prescription for the patient: Fax completed form to 1-833-746-2277
2. Subsequent prescription: May be e-script via AcariaHealth Specialty Pharmacy in your EMR/HMR system Call 1-833-346-2277 if you have questions regarding this form or contact Chiesi Total Care℠

1. PATIENT INFORMATION (all fields in this section are mandatory)

Patient Name (First, Middle, Last) _____ Email _____

Last 4 of Social Security # _____ Gender at birth ☐ Male ☐ Female Date of Birth_____ (mm/dd/yyyy)

Address _____ City _____ State _____ Zip _____

Mobile # _____ Alternative Phone # _____ Language: ☐ English ☐ Other _____

Caregiver Name _____ ☐ OK to leave message

Email _____ Caregiver Phone # _____

Allergies _____ Current Medications: _____

☐ No known drug allergies (NKDA)

2: INSURANCE INFORMATION (check the relevant box and complete as much as possible)

Please attach copies of both sides of the patient's insurance card.

☐ Medicare ☐ Medicaid ☐ Commercial/Private ☐ Other ☐ Uninsured

Primary Insurance Payer _____ Plan Name _____

Phone # _____ Policy ID # _____

Group # _____ BIN _____

PCN _____ Policy Holder's Name: _____

Policy Holder's Date of Birth _____ Policy Holder's Relationship to Patient _____

3: PRESCRIBER INFORMATION* (all fields in this section are mandatory)

The prescriber is to comply with his/her state specific prescription requirements such as e-prescribing, state specific prescription form fax language, etc. Non-compliance with state specific requirements could result in outreach to the prescriber.

Name (First, Middle, Last) _____ Prescriber NPI # _____

Prescriber Tax ID #: _____ Facility Name _____

Facility Address _____ City _____ State _____ Zip _____

Facility Phone # _____ Preferred Fax # _____

Primary Contact Name _____ Title/Role _____

Primary Contact Phone # _____ Primary Contact Email _____

4: TREATMENT AND PRESCRIBING INFORMATION (mandatory)

Rx Treatment: MYCAPSSA® (octreotide) delayed-release oral capsules NDC: 69880-120-28. Dispense as written.
Please check a box below for medication strength* (mandatory)

Patient, at any time, has been prescribed octreotide or lanreotide

☐ yes
☐ no

☐ **ICD-10/Diagnosis: E22.0 (acromegaly and pituitary gigantism)**

☐ ICD-10/Diagnosis: D35.2 (benign neoplasm of the pituitary gland)

☐ ICD-10/Diagnosis: F40.231(needle phobia)

☐ Other ICD-10/Diagnosis: _____

Recommended to check additional strengths for titration needs

☐ **MYCAPSSA 40 mg**
Starting Dose
Dispense:
MYCAPSSA 20 mg capsules Sig: Take 1 capsule PO BID

☐ **QTY:** 56
☐ **QTY:** 168

Number of Refills_____

☐ **MYCAPSSA 60 mg**

Dispense:
MYCAPSSA 20 mg capsules Sig: Take 2 capsule PO QAM and 1 capsule PO QPM

☐ **QTY:** 84
☐ **QTY:** 252

Number of Refills_____

☐ **MYCAPSSA 80 mg**

Dispense:
MYCAPSSA 20 mg capsules Sig: Take 2 capsule PO BID

☐ **QTY:** 112
☐ **QTY:** 336

Number of Refills_____

PRESCRIBER AUTHORIZATION* (mandatory)

By signing below, I certify that I am part of the Chiesi Total Care Program, that the therapy described above is medically necessary, and that the information provided is accurate to the best of my knowledge. I also attest that I have obtained the patient's authorization to release the above information and such other personal information as may be necessary to the Chiesi Total Care Program and/or their agents. If the patient is 18 years old or younger, I attest that I have obtained permission from the patient's legal guardian.

Licensed Prescriber Signature (required–no stamps) _____

Printed Name _____ Date _____

ATTENTION: E-prescribe or use the official state prescription form where required by state law.
No stamped signatures or signing on behalf of the prescriber.

Scan for digital RX form.

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.

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.

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.

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 taking an oral contraceptive to use an alternative non-hormonal method of contraception or a back-up method when taking MYCAPSSA.

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

PREGNANCY
Advise premenopausal females of the potential for an unintended pregnancy.

To report SUSPECTED ADVERSE REACTIONS, please contact Chiesi Farmaceutici S.p.A. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Chiesi Total Care Program offered through AcariaHealth Specialty Pharmacy.

CHIESI TOTAL CARE

PHONE
1-833-346-2277

HOURS OF OPERATION
Monday to Friday
7:00am - 7:00pm (Central Time)

FAX
1-833-746-2277

WEBSITE
chiesitotalcare.com

For more information, visit mycapssa.com.

PP-MC-0028 V1.0

Mycapssa® (octreotide) capsules 20mg

Patient Consent Form

Product: MYCAPSSA®

Fax completed form to Chiesi Total Care℠ at 1-833-746-2277 | Phone: 1-833-346-2277

Chiesi Total Care (the "Program") provides product support to eligible patients who have been prescribed a Chiesi USA, Inc. ("Chiesi") product. Program support may include: (1) reimbursement and financial support (such as investigating insurance coverage, confirming out-of-pocket costs, and reviewing eligibility for financial assistance and copay programs); (2) working with patients and pharmacies to fill prescriptions; (3) home infusion support (if applicable); and (4) providing disease-, medication-, and adherence-related educational resources and communications, including access to a Chiesi Patient Education Liaison.

Patient Name:_____ Date of Birth (MM/DD/YY): _____

ENROLLMENT INTO CHIESI TOTAL CARE

By signing this authorization form ("Authorization"), I confirm I would like to enroll in the Program and authorize Chiesi USA, Inc., and its affiliates, service providers, agents, and successors (together, "Chiesi") to provide me with Program support. I authorize Chiesi, my healthcare providers, and their staff, my health plan, patient assistance programs, and my pharmacies to process and share my personal health information (such as information about my diagnosis, treatment, and lab results), personal identifying information (such as contact information and program preferences), and insurance information (such as prescriptions and plans) (together my "Information") in order to enroll me in the Program, provide Program support, administer the Program, meet legal obligations, conduct other business activities, and complete government reporting activities to Chiesi, its affiliated companies, vendors, agents, collaboration partners, and representatives (together, "Chiesi") including providers of alternate sources of funding for prescription drug costs, and other service providers supporting Chiesi Total Care (the "Program") for Healthcare Providers and patients for the purposes described below. For example, Chiesi may use my Information to communicate with me (such as by mail, phone, email, and text message*), tailor Program-related communications and services to my needs, and share my Information with my healthcare providers to dispense Chiesi products to me. Chiesi may also de-identify my Information, combine it with information about other patients, and use the results for Chiesi's and its affiliate's business purposes. I understand that once my Information is disclosed, my Information may no longer be protected by federal privacy laws and could be re-disclosed. However, Chiesi will only process and disclose my Information as described in this Authorization. Additional information on Chiesi's privacy practices can be found at https://www.chiesiusa.com/privacy-policy/.

For California Residents: By completing this form and submitting it for the purposes of enrollment in the Chiesi Total Care Program, you understand that Chiesi USA, Inc. may collect and use your Personal Information for the business purposes noted in the Chiesi Privacy Policy located at https://www.chiesiusa.com/privacy-policy/. To opt-out of the use of this Personal Information, you may email us at us.privacy@chiesi.com or by contact us via phone at 1-866-271-8587. Only you, or someone legally authorized to act on your behalf, may make an opt-out request. Please note that Chiesi USA, Inc does not sell or share Personal Information as defined in the California Consumer Privacy Act ("CCPA").

I understand that this Program is optional. I can refuse to sign this Authorization and refusing to sign will not affect my treatment, insurance coverage, or eligibility for benefits or Chiesi products. However, I understand that I need to sign this form to participate in the Program.

I understand that I may cancel this Authorization at any time or receive a copy of this Authorization by mailing a letter requesting cancellation to Chiesi Total Care, 8517 South Park Circle, Suite 200, Orlando, FL 32819. Upon cancellation, to the extent required by applicable law and personal data rights, Chiesi will no longer process my Information. I understand my cancellation will not apply to any of my Information already used or disclosed based on this Authorization prior to receipt of the cancellation. Unless canceled earlier, this Authorization expires ten (10) years from the date signed below, or as otherwise required by state or local law.

By signing below, I acknowledge that my pharmacy will receive payment from Chiesi for disclosing my Information to Chiesi. I acknowledge that if I am eligible for infusion co-pay assistance, the payment will be submitted to my healthcare facility where the infusion occurred. I acknowledge that if I am enrolled in a government-funded healthcare program, I am not eligible for and will not accept any co-pay assistance from Chiesi Total Care. I understand and agree that if my insurance information changes at any time while I am participating in the Chiesi Total Care Program, I will notify Chiesi Total Care as soon as possible, and any such change may affect my eligibility for such assistance programs.

By signing below, I also acknowledge that I have read and agree to the terms and conditions of the Chiesi Total Care support programs on page 2 of this document.

Feedback: We greatly appreciate your feedback. Please indicate whether you would like to be contacted by Chiesi about opportunities for you to provide feedback to us (such as Program feedback surveys or market research):

☐ YES, I would like to be contacted to provide feedback. ☐ NO, I would not like to be contacted to provide feedback.

TEXT: Please indicate whether you authorize Chiesi to send text messages to the number(s) you provide. Your consent to receiving text messages is not a condition of receiving medication or services from Chiesi. I may also revoke my authorization to receive automated calls or text messages by replying STOP to any text from Chiesi Total Care or by contacting Chiesi Total Care in writing at the address above.

☐ YES, I consent to receive text messages. ☐ NO, I do not consent to receive text messages.

Patient or Legal Guardian Signature:_____ **Signature Date** (MM/DD/YY):_____

Please specify any additional contacts with whom Chiesi Total Care is allowed to discuss your Information:

Additional Contact Name:_____ **Relationship to Patient:**_____

*Additional charges may apply. I understand that my telephone provider may charge me fees for calls or texts I receive, and I agree that Chiesi Total Care will not pay those fees.

Prescriber's Name (Print):_____

Name of Institution/Practice Name:_____

Office Contact Person:_____ **Office Phone:**_____

Patient Consent Form

Fax completed form to Chiesi Total Care℠ at 1-833-746-2277 | Phone: 1-833-346-2277

CHIESI TOTAL CARE TERMS AND CONDITIONS

Chiesi Total Care Patient Support Services Program Terms and Conditions

To enroll in Chiesi Total Care (the "Program") and to assess eligibility for patient support services of the Program, patient must complete the Program Enrollment and Authorization Form and have a valid prescription for an eligible product of the Program. Additional documentation may be required. The patient must be a resident of the United States or one of its territories. If the patient is incapable of acting on their own behalf or if the patient is under 18 years old, enrollment into the Program may be completed by another person acting on their behalf (such as a caregiver).

A patient who receives healthcare benefits under any plan or program funded in whole or in part by federal or state governments including Medicare, Medicaid, TRICARE, Veterans Affairs (VA), State Prescription Assistance Plans (SPAPs) (other than health insurance for federal government employees), or any state healthcare program such as Medicaid, Children's Health Insurance Program, programs funded under Maternal and Child Health Program, or programs funded under Social Services Block Grant (collectively, "Government-funded Plans") are not eligible for the financial patient support services of the Program. A patient covered under a commercial health plan purchased through a health insurance marketplace or exchange is not a government-funded Plan beneficiary even if the costs of such coverage are subsidized by the federal government. If a change in prescription drug coverage should occur, the patient must notify the Program; such change may affect eligibility for the support services provided in the Program. Patients who have prescribed a product for an indication that is not consistent with the US Food and Drug Administration-approved labeling will not be eligible for financial patient support services offered through the Program.

Patients residing in or receiving treatment in certain states may not be eligible for certain patient support services of the Program. Patients may not seek reimbursement for value received from the Program. The Program does not obligate the use of any specific medication or healthcare provider. Patients who receive treatment or reside in Massachusetts, Michigan, Minnesota, or Rhode Island are not eligible for co-pay assistance for infusion services or routine testing services.

Chiesi Total Care may recommend contacting an independent financial assistance foundation. Independent financial assistance foundations have their own rules for eligibility. Chiesi USA does not fund independent financial assistance foundations, nor does Chiesi Total Care have involvement or influence in independent foundation decision making or eligibility criteria and does not know if a foundation will be able to help you. Chiesi Total Care can only refer you to a foundation that supports your disease state. This information is provided as a resource for you. Chiesi Total Care does not endorse or show preference for any foundation. The foundations recommended to you may not be the only ones that might be able to help you.

Chiesi Patient Education Liaisons ("PELs") may be available to assist you with disease education, provide relative educational or informational resources, and to answer questions you may have about your disease. Chiesi Field Reimbursement Managers ("FRMs") may be available to assist you with your product prescription drug coverage, including prior authorization, appeals, and denials.

PELs and FRMs are employees of Chiesi USA, Inc. PELs and FRMs are not healthcare providers and are not part of your healthcare team. PELs or FRMs will not provide medical care or advice. All treatment decisions should be made by you and your treating healthcare professional. To assist you, PELs and FRMs may need your Information. If you choose to opt out of services by PELs and FRMs, you may do so at any time. Please see Chiesi's Privacy Policy at www.chiesiusa.com/privacy-policy/.

Program benefits may not be sold, purchased, traded, or offered for sale, purchase, or trade. The Chiesi Total Care patient support services are not valid where prohibited by law, taxed, or otherwise restricted. Offer subject to change or discontinuance without notice. Restrictions, including monthly maximums, may apply. This is not health insurance.

This is a voluntary program. Patients who choose not to enroll in the Program will be able to receive medication. Patients may participate in Chiesi Total Care without participating in a patient support services program of Chiesi Total Care. After enrolling in Chiesi Total Care, participants may opt out by contacting the Program, as outlined in the Chiesi Total Care Enrollment and Authorization Form. Patients must renew their eligibility by December 31 of each year to continue to receive support under the Program.

By participating in the Program, participants acknowledge that they understand and agree to comply with the Program Terms and Conditions.

PP-MC-0047 V1.0

PATIENT GUIDE

Mycapssa® (octreotide) capsules 20mg

MYCAPSSA® [my (as in sky)-cap-sah] (octreotide) delayed-release capsules, for oral use

What is MYCAPSSA?

- MYCAPSSA is an oral prescription medicine used in the long-term maintenance treatment of acromegaly in people for whom initial treatment with octreotide or lanreotide has been effective and tolerated.
- It is not known if MYCAPSSA is safe and effective in children.

Do not take MYCAPSSA if you:

- are allergic to octreotide acetate or any of the ingredients in MYCAPSSA. MYCAPSSA can cause a serious allergic reaction including anaphylactic shock. Stop taking MYCAPSSA right away and get emergency help if you have any of these symptoms:
  - swelling of your tongue, throat, lips, eyes or face
  - severe itching of the skin with rash or raised bumps
  - chest pain
  - trouble swallowing or breathing
  - feeling faint
  - rapid heart beat

See the end of this leaflet for a complete list of ingredients in MYCAPSSA.

Before you take MYCAPSSA, tell your healthcare provider about all of your medical conditions, including if you:

- have liver cirrhosis or liver problems
- have kidney problems
- are pregnant or plan to become pregnant. It is not known if MYCAPSSA will harm your unborn baby. MYCAPSSA may increase your chance of becoming pregnant.
- are breastfeeding or plan to breastfeed. It is not known if MYCAPSSA passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take MYCAPSSA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. MYCAPSSA may affect the way other medicines work, and other medicines may affect how MYCAPSSA works.

Especially tell your healthcare provider if you take oral contraceptives. Use an alternative non-hormonal method of contraception or a back-up method while taking MYCAPSSA.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take MYCAPSSA?

- **Read the detailed "Instructions for Use" at the end of this Patient Information about the right way to take MYCAPSSA.**
- Take MYCAPSSA exactly as your healthcare provider tells you to take it.
- Take MYCAPSSA with a glass of water on an empty stomach.
- Take MYCAPSSA at least 1 hour before a meal or at least 2 hours after a meal (for example, you could take your morning dose 1 hour before breakfast and your evening dose at bedtime).

Swallow the capsules whole. Do not crush or chew the capsules before swallowing.

What are the possible side effects of MYCAPSSA?

- **gallbladder problems.** MYCAPSSA may cause problems with the gallbladder. Tell your healthcare provider if you have sudden pain in your upper right stomach (abdomen), sudden pain in your right shoulder or between your shoulder blades, yellowing of your skin or the whites of your eyes, fever with chills, nausea.
- **blood sugar problems.** MYCAPSSA may cause you to have high blood sugar (hyperglycemia), low blood sugar (hypoglycemia), or diabetes. Tell your healthcare provider if you have problems with high or low blood sugar. Your healthcare provider will check your blood sugar when you start taking MYCAPSSA or when your dose is changed.
- **thyroid problems.** MYCAPSSA may keep your thyroid from releasing thyroid hormones leading to hypothyroidism. Your thyroid function will be checked regularly during your treatment with MYCAPSSA.
- **heart rhythm problems.** Tell your healthcare provider if you have an irregular heartbeat (your heart is not beating normally).
- **low vitamin B12 levels in your blood.** Your healthcare provider may check your vitamin B12 levels during treatment with MYCAPSSA.

The most common side effects of MYCAPSSA include:

- headache
- nausea
- diarrhea
- joint pain
- weakness
- sweating a lot

These are not all the possible side effects of MYCAPSSA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects.
You may report side effects to FDA at 1-800-FDA-1088.

How should I store MYCAPSSA?

- **Before first use**, store unopened wallets of MYCAPSSA in a refrigerator between 36°F to 46°F (2°C to 8°C).
- **Do not** freeze.
- **After first use**, store opened wallets at room temperature between 68°F to 77°F (20°C to 25°C) for up to 1 month.

Keep MYCAPSSA and all medicines out of the reach of children.

General information about the safe and effective use of MYCAPSSA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information. Do not use MYCAPSSA for a condition for which it was not prescribed. Do not give MYCAPSSA to other people, even if they have the same symptoms you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about MYCAPSSA that is written for health professionals.

What are the ingredients in MYCAPSSA?

Active ingredient: octreotide acetate

Inactive ingredients: polyvinylpyrrolidone (PVP-12), sodium caprylate, magnesium chloride, polysorbate 80, glyceryl monocaprylate, glyceryl tricaprylate, gelatin, gelatin capsules, and Acryl-EZE® (methacrylate).

AMRYT PHARMA

Amryt Pharmaceuticals DAC, Dublin, Ireland
For more information about MYCAPSSA call the product information department at 1-855-303-2347 or go to www.MYCAPSSA.com and select patient information.
This Patient Information has been approved by the U.S. Food and Drug Administration. Approved: 06/2020

INSTRUCTIONS FOR USE

Mycapssa® (octreotide) capsules 20mg

MYCAPSSA® [my (as in sky)-cap-sah] (octreotide) delayed-release capsules, for oral use

Read this Instructions for Use before you start taking MYCAPSSA and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. Talk to your healthcare provider or pharmacist if you have any questions about how to use MYCAPSSA.

Important information: Each MYCAPSSA wallet contains twenty-eight 20-mg capsules. The number of wallets required in a 28-day period depends on your prescribed dose.

How to Use the MYCAPSSA Wallet

- Each MYCAPSSA wallet has a locking mechanism that helps to keep the medicine away from children.
- Become familiar with using the MYCAPSSA wallet so you will know how to use it the right way.

To open the wallet:

Step 1. With your left thumb, gently press the tip of the release button on the left side of the wallet (see Figure A).

Step 2. While holding the release button, grasp the medicine card at the notch on the right side and pull it out (see Figure A).

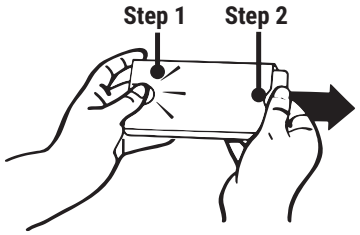
Step 3. Unfold the medicine card (see Figure A).

How to Remove a Capsule from the MYCAPSSA Wallet

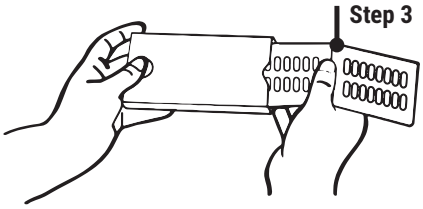
Capsules need to be removed carefully, because if they are cracked or broken they may not be as effective. Follow these instructions to easily remove capsules without damaging them.

- Place the tip of a thumb at the edge of a capsule's plastic cavity (see Figure B).
- Gently push the capsule until it is removed. Collect the removed capsule in your hand.
- **Do not** use two thumbs to push a capsule as this could damage it.
- **Do not** press the middle of a capsule. This could also damage it.
- If a capsule is cracked or broken, throw it away (discard it) and remove another capsule.

Figure A: How to Open the MYCAPSSA Wallet

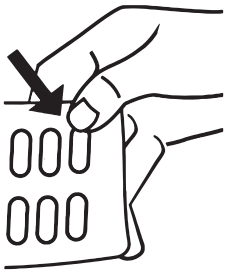


Push first... ...then pull



Unfold the pack

Figure B: How to Remove a Capsule from the Medicine Card Inside the MYCAPSSA Wallet



Gently push capsule with tip of thumb

DO NOT use two thumbs

DO NOT press the middle of a capsule

Amryt Pharmaceuticals DAC, Dublin, Ireland
For more information about MYCAPSSA call the product information department at 1-855-303-2347 or go to www.MYCAPSSA.com and select patient information.
This Instructions for Use has been approved by the U.S. Food and Drug Administration. Approved: 06/2020

AMRYT PHARMA

PRESCRIBING INFORMATION

Mycapssa® (octreotide) capsules 20mg

HIGHLIGHTS

These highlights do not include all the information needed to use MYCAPSSA® safely and effectively. See full prescribing information for MYCAPSSA.

MYCAPSSA (octreotide) delayed-release capsules, for oral use

Initial U.S. Approval: 1988

INDICATIONS AND USAGE

MYCAPSSA is a somatostatin analog indicated for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide (1).

DOSAGE AND ADMINISTRATION

- Take MYCAPSSA orally with a glass of water on an empty stomach, at least 1 hour before a meal or at least 2 hours after a meal (2.1).
- Initiate MYCAPSSA at a dosage of 40 mg daily, administered as 20 mg orally twice daily (2.2).
- Monitor insulin-like growth factor 1 (IGF-1) levels and patient's signs and symptoms every two weeks during the dose titration or as indicated (2.2).
- Titrate the MYCAPSSA dosage, based on IGF-1 levels and patient's signs and symptoms. Increase the dosage in increments of 20 mg (2.2).
- The maximum recommended dosage is 80 mg daily (2.2).
- Once the maintenance dosage of MYCAPSSA is achieved, monitor IGF-1 levels and patient's signs and symptoms monthly or as indicated (2.2).
- For patients with end-stage renal disease, initiate at a dosage of 20 mg orally once daily. Titrate and adjust the maintenance dosage based on IGF-1 levels, patient's signs and symptoms and tolerability (2.4).

DOSAGE FORMS AND STRENGTHS

Delayed-release capsules: 20 mg.

CONTRAINDICATIONS

Hypersensitivity to octreotide or any of the components of MYCAPSSA.

WARNINGS AND PRECAUTIONS

Cholelithiasis and Complications of Cholelithiasis: Monitor periodically. Discontinue if complications of cholelithiasis are suspected (5.1).

Hypoglycemia or Hyperglycemia: Monitor glucose and adjust antidiabetic treatment as needed (5.2).

Thyroid Function Abnormalities: Hypothyroidism may occur. Assess thyroid function periodically (5.3).

Cardiac Function: Bradycardia, arrhythmia, or conduction abnormalities may occur. Drugs that have bradycardia effects may need dosage adjustments (5.4, 7.2).

Decreased Vitamin B12 Levels and Abnormal Schilling's Tests: Decreased vitamin B12 levels and abnormal Schilling's tests have been observed in some patients receiving octreotide. Monitor vitamin B12 levels during treatment (5.5).

ADVERSE REACTIONS

Most common adverse reactions (incidence >10 %) are nausea, diarrhea, headache, arthralgia, asthenia, hyperhidrosis, peripheral swelling, blood glucose increased, vomiting, abdominal discomfort, dyspepsia, sinusitis, osteoarthritis (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact the medical information department at 1-855-303-2347 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

DRUG INTERACTIONS

- *Proton Pump Inhibitors, H2-receptor Antagonists, or Antacids:* may decrease bioavailability of MYCAPSSA and the MYCAPSSA dose may need to be increased (7).
- *Cyclosporine:* may have decreased bioavailability and require dose adjustment (7).
- *Insulin and Antidiabetic Drugs:* patients receiving insulin or antidiabetic drugs agents may require dose adjustment (7).
- *Digoxin:* exposure may be decreased and assessment of clinical response to digoxin should be performed (7).
- *Lisinopril:* bioavailability may be increased, monitor patient's blood pressure and adjust dose of lisinopril if needed (7).
- *Levonorgestrel:* counsel women to use an alternative non-hormonal method of contraception or a back-up method when MYCAPSSA is used with combined oral contraceptives (7).
- *Bromocriptine:* dose adjustment of bromocriptine may be necessary (7).
- *Beta Blocker and Calcium Channel Blockers:* dose adjustment of beta blockers or calcium channel blockers may be necessary (7).
- *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 (7).

USE IN SPECIFIC POPULATIONS

Females and Males of Reproductive Potential: Advise premenopausal females of the potential for an unintended pregnancy (8.3).

See 17 for PATIENT COUNSELING INFORMATION.

Revised 03/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

- Take MYCAPSSA orally with a glass of water on an empty stomach, at least 1 hour before a meal or at least 2 hours after a meal.
- Swallow MYCAPSSA capsules whole. Do not crush or chew the capsules.

2.2 Recommended Dosage, Titration, and Monitoring

- Initiate MYCAPSSA at a dosage of 40 mg daily, administered as 20 mg orally twice daily.
- Monitor insulin-like growth factor 1 (IGF-1) levels and patient's signs and symptoms every two weeks during the dose titration or as indicated.
- Titrate the MYCAPSSA dosage based on IGF-1 levels and patient's signs and symptoms. Increase the dosage in increments of 20 mg daily.
- 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.
- The maximum recommended dosage of MYCAPSSA is 80 mg daily.
- Once the maintenance dosage of MYCAPSSA is achieved, monitor IGF-1 levels and patient's signs and symptoms monthly or as indicated.

2.3 Dosage Interruptions and Modifications

- If IGF-1 levels remain above the upper normal limit after treatment with the maximum recommended dosage of 80 mg daily or the patient cannot tolerate treatment with MYCAPSSA, consider discontinuing MYCAPSSA and switching patient to another somatostatin analog.
- Withdraw MYCAPSSA therapy periodically to assess disease activity. If IGF-1 levels increase and signs and symptoms recur, resume MYCAPSSA therapy.

2.4 Recommended Dosage in Patients with End Stage Renal Disease

For patients with end-stage renal disease, initiate MYCAPSSA at a dosage of 20 mg orally once daily. Titrate and adjust the maintenance dosage of MYCAPSSA based on IGF-1 levels, patient's signs and symptoms and tolerability *[see Dosage and Administration (2.2, 2.3), Use in Specific Populations (8.6)]*.

2.5 Dosage Modifications with Concomitant Use of Proton Pump Inhibitors, H2-receptor Antagonists, or Antacids

Patients taking proton pump inhibitors, H2-receptor antagonists, or antacids concomitantly with MYCAPSSA may require increased dosages of MYCAPSSA *[see Drug Interactions (7.1)]*.

3 DOSAGE FORMS AND STRENGTHS

Delayed-release capsules: 20 mg. White hard gelatin capsules imprinted with "OT" on one half of the capsule and "20" on the other half. Each capsule contains 20 mg octreotide, provided as octreotide acetate.

4 CONTRAINDICATIONS

Hypersensitivity to octreotide or any of the components of MYCAPSSA. Anaphylactoid reactions, including anaphylactic shock, have been reported in patients receiving octreotide *[see Adverse Reactions (6.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Cholelithiasis and Complications of Cholelithiasis

MYCAPSSA may inhibit gallbladder contractility and decrease bile secretion, which may lead to gallbladder abnormalities or sludge. Gallbladder-related adverse reactions have been reported in clinical trials in patients receiving MYCAPSSA. There have been postmarketing reports of cholelithiasis (gallstones) in patients taking somatostatin analogs resulting in complications, including cholecystitis, cholangitis, pancreatitis and requiring cholecystectomy *[see Adverse Reactions (6)]*. Monitor patients periodically. If complications of cholelithiasis are suspected, discontinue MYCAPSSA and treat appropriately.

5.2 Hyperglycemia and Hypoglycemia

MYCAPSSA alters the balance between the counter-regulatory hormones, insulin, glucagon, and growth hormone, which may result in hypoglycemia, or hyperglycemia, or diabetes mellitus. In clinical trials with MYCAPSSA, the following adverse reactions were reported: increased blood glucose (7%), hypoglycemia (4%), and diabetes mellitus (1%) *[see Adverse Reactions (6.1)]*. Blood glucose levels should be monitored when MYCAPSSA treatment is initiated, or when the dose is altered. Adjust antidiabetic treatment accordingly.

5.3 Thyroid Function Abnormalities

MYCAPSSA suppresses the secretion of thyroid-stimulating hormone, which may result in hypothyroidism. In clinical trials with MYCAPSSA, the following adverse reactions were reported: hypothyroidism (1%), increased TSH (1%), or decreased free T4 (1%) *[see Adverse Reactions (6.1)]*. Assess thyroid function periodically during treatment with MYCAPSSA.

5.4 Cardiac Function Abnormalities

Cardiac conduction abnormalities and other ECG changes including QT prolongation, axis shifts, early repolarization, low voltage, R/S transition, and early R wave progression, have occurred during treatment with octreotide. In MYCAPSSA clinical trials the following adverse reactions were reported: bradycardia (2%), conduction abnormalities (1%), and arrhythmias/tachycardia (2%) *[see Adverse Reactions (6)]*. These ECG changes may occur in patients with acromegaly. Dosage adjustments of concomitantly used drugs that have bradycardia effects (i.e. beta-blockers) may be necessary *[see Drug Interactions (7.2)]*.

5.5 Decreased Vitamin B_{12} Levels and Abnormal Schilling's Tests

MYCAPSSA may alter absorption of dietary fats in some patients. Decreased vitamin B_{12} levels and abnormal Schilling's tests have been observed in some patients receiving octreotide. Monitor vitamin B_{12} levels during treatment with MYCAPSSA.

6 ADVERSE REACTIONS

The following important adverse reactions are described below and elsewhere in the labeling:

- Cholelithiasis and Complications of Cholelithiasis *[see Warnings and Precautions (5.1)]*
- Hyperglycemia and Hypoglycemia *[see Warnings and Precautions (5.2)]*
- Thyroid Function Abnormalities *[see Warnings and Precautions (5.3)]*
- Cardiac Function Abnormalities *[see Warnings and Precautions (5.4)]*
- Decreased Vitamin B_{12} Levels and Abnormal Schilling's Tests *[see Warnings and Precautions (5.5)]*

6.1 Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

MYCAPSSA has been evaluated in patients with acromegaly in a placebo-controlled study *[see Clinical Studies (14)]* and an open-label baseline-controlled study. The data reflect exposure of 183 patients to MYCAPSSA for a mean duration of 29 weeks. In the overall study population, 56% were female and the average age of patients was 54.3 years. Adverse reactions occurring ≥5% and greater than placebo for the placebo-controlled study are presented in Table 1 and adverse reactions occurring ≥5% in the open-label study are presented in Table 2.

Table 1: Adverse Reactions Occurring ≥5% and Greater than Placebo in a Placebo-Controlled Study with MYCAPSSA in Acromegaly Patients

	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

*Includes blood glucose increased, hyperglycemia and glycosylated hemoglobin increased.

Table 2: Adverse Reactions Occurring ≥5% in an Open-Label Study with MYCAPSSA in Acromegaly Patients

	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*	6
Vomiting	6
Flatulence	6
Back pain	6
Abdominal pain	5
Dizziness	5
Fatigue	5
Upper respiratory tract infection	5
Hypertension	5

*Includes blood glucose increased, hyperglycemia and impaired fasting glucose

Other Adverse Reactions

Gallbladder Abnormalities

In the placebo-controlled study, in patients treated with MYCAPSSA, acute cholecystitis occurred in 4% of patients.

In the open-label study, cholelithiasis occurred in 4.5% of patients and bile duct obstruction, bile duct stone, acute cholecystitis and jaundice occurred in 1% of patients each.

Hypoglycemia/Hyperglycemia

In the placebo-controlled study, 18% of patients treated with MYCAPSSA and 4% of patients treated with placebo developed at least one glucose value above the upper normal limit. All patients with abnormal glucose values were asymptomatic. Asymptomatic hypoglycemia was reported in 4% of patients.

In the open-label study 16% of patients developed a glucose value above the upper limit of normal. Asymptomatic hypoglycemia was reported in 4% and symptomatic hypoglycemia was reported in 1% of patients. Diabetes was reported in 1% of patients.

Hypothyroidism

In the open-label study, hypothyroidism, increased TSH, or decreased free T4 were reported in 1% of patients.

Cardiac

In the open-label study, bradycardia was reported in 2%, conduction abnormalities in 1%, and arrhythmias/tachycardia in 2% of patients.

Gastrointestinal

Gastrointestinal symptoms were the most commonly reported adverse reactions with MYCAPSSA.

In the placebo-controlled study, gastrointestinal adverse reactions were reported in 68% of patients treated with MYCAPSSA. These adverse reactions were diarrhea, nausea, vomiting, abdominal discomfort, dyspepsia, large intestinal polyp, abdominal pain, constipation, and flatulence. The adverse reactions were mild to moderate, occurred mostly during the initial 3 months of treatment, and resolved on treatment within a median duration of 8 days.

In the open-label study, gastrointestinal adverse reactions were reported in 57% of patients. Gastrointestinal adverse reactions occurring in ≥1% of patients were nausea, diarrhea, dyspepsia, abdominal pain, abdominal distention, vomiting, flatulence, constipation, gastroesophageal reflux disease, abdominal discomfort, frequent bowel movement, gastritis, hemorrhoids, dry mouth, and gastrointestinal motility disorder. Large intestinal polyp was reported in 1 patient. The adverse reactions were mostly mild to moderate, occurred during the initial 2 months of treatment, and resolved on treatment within a median of 13 days. Ten patients discontinued treatment due to gastrointestinal adverse reactions.

6.2 Immunogenicity

As with all therapeutic peptides, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other octreotide acetate products may be misleading.

No antibodies to the octreotide peptide from MYCAPSSA were detected in 149 patients assessed in the open-label study throughout 13 months of treatment.

6.3 Postmarketing Experience

The following adverse reactions have been identified during the post-approval use of octreotide acetate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- *Blood and lymphatic:* pancytopenia, thrombocytopenia
- *Cardiac:* myocardial infarction, cardiac arrest, atrial fibrillation
- *Ear and labyrinth:* deafness
- *Endocrine:* diabetes insipidus, adrenal insufficiency in patients 18 months of age and under, pituitary apoplexy
- *Eye:* glaucoma, visual field defect, scotoma, retinal vein thrombosis
- *Gastrointestinal:* intestinal obstruction, peptic/gastric ulcer, abdomen enlarged
- *General and administration site:* generalized edema, facial edema
- *Hepatobiliary:* gallbladder polyp, fatty liver, hepatitis
- *Immune:* anaphylactoid reactions including anaphylactic shock
- *Infections and infestations:* appendicitis
- *Laboratory abnormalities:* increased liver enzymes, CK increased, creatinine increased
- *Metabolism and nutrition:* diabetes mellitus
- *Musculoskeletal:* arthritis, joint effusion, Raynaud's syndrome
- *Nervous System:* convulsions, aneurysm, intracranial hemorrhage, hemiparesis, paresis, suicide attempt, paranoia, migraines, Bell's palsy, aphasia
- *Renal and urinary:* renal failure, renal insufficiency
- *Reproductive and breast:* gynecomastia, galactorrhea, libido decrease, breast carcinoma
- *Respiratory:* status asthmaticus, pulmonary hypertension, pulmonary nodule, pneumothorax aggravated
- *Skin and subcutaneous tissue:* urticaria, cellulitis, petechiae
- *Vascular:* orthostatic hypotension, hematuria, gastrointestinal hemorrhage, arterial thrombosis of the arm

7 DRUG INTERACTIONS

7.1 Effects of Other Drugs on MYCAPSSA

Proton Pump Inhibitors, H2-receptor Antagonists, or Antacids	
Clinical Impact:	Concomitant administration of MYCAPSSA with esomeprazole resulted in a decrease in the bioavailability for MYCAPSSA *[See Clinical Pharmacology (12.3)].* Drugs that alter the pH of the upper GI tract (e.g., other proton pump inhibitors (PPIs), H2-receptor antagonists, and antacids) may alter the absorption of MYCAPSSA and lead to a reduction in bioavailability.
Intervention:	Co-administration of MYCAPSSA with PPIs, H2-blockers, or antacids may require increased doses of MYCAPSSA.

7.2 Effects of MYCAPSSA on Other Drugs

Cyclosporine	
Clinical Impact:	Concomitant administration of MYCAPSSA with cyclosporine resulted in a decrease in cyclosporine bioavailability *[see Clinical Pharmacology (12.3)]*.
Intervention:	Adjustment of cyclosporine dose to maintain therapeutic levels may be necessitated.
Insulin and Antidiabetic Drugs	
Clinical Impact:	MYCAPSSA inhibits the secretion of insulin and glucagon.
Intervention:	Monitor blood glucose levels in diabetic patients upon MYCAPSSA initiation and subsequent dose adjustment. Patients receiving insulin or antidiabetic drugs agents may require dose adjustment of these therapeutic agents.
Digoxin	
Clinical Impact:	Concomitant administration of MYCAPSSA with digoxin resulted in a decrease in digoxin peak exposure *[see Clinical Pharmacology (12.3)]*.
Intervention:	Digoxin has a narrow therapeutic ratio and careful assessment of clinical response should be performed when digoxin is concomitantly administered with MYCAPSSA.
Lisinopril	
Clinical Impact:	Concomitant administration of MYCAPSSA increases lisinopril bioavailability *[see Clinical Pharmacology (12.3)]*.
Intervention:	Monitor patient's blood pressure and adjust the dosage of lisinopril if needed.
Levonorgestrel	
Clinical Impact:	Concomitant administration of MYCAPSSA with levonorgestrel decreases levonorgestrel bioavailability *[see Clinical Pharmacology (12.3)]*.
Intervention:	Decreased bioavailability may potentially diminish the effectiveness of combined oral contraceptives (COCs) or increase breakthrough bleeding. Counsel women to use an alternative non-hormonal method of contraception or a back-up method when MYCAPSSA is used with COCs.
Bromocriptine	
Clinical Impact:	Concomitant administration of MYCAPSSA with bromocriptine may increase the systemic exposure of bromocriptine *[see Clinical Pharmacology (12.3)]*.
Intervention:	Dose adjustment of bromocriptine may be necessary.
Beta Blocker and Calcium Channel Blockers	
Clinical Impact:	MYCAPSSA may cause bradycardia in acromegaly patients.
Intervention:	Patients receiving beta blockers or calcium channel blockers may require dose adjustments of these therapeutic agents.
Drugs Metabolized by CYP 450 Enzymes	
Clinical Impact:	Limited published data indicate that somatostatin analogs including MYCAPSSA may decrease the metabolic clearance of compounds known to be metabolized by cytochrome P450 enzymes, which may be due to the suppression of GH.
Intervention:	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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from case reports with octreotide acetate use in pregnant women are insufficient to identify a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with MYCAPSSA. No adverse developmental effects were observed with intravenous administration of octreotide to pregnant rats and rabbits during organogenesis at doses 7 and 13 times, respectively, the clinical dose based on octreotide injection body surface area. Transient growth retardation, with no impact on postnatal development, was observed in rat offspring from a pre- and post-natal study of octreotide at intravenous doses below the clinical dose based on octreotide injection body surface area *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2%-4% and 15%-20%, respectively.

Data

Animal Data

In embryo-fetal development studies in rats and rabbits, pregnant animals received intravenous doses of octreotide up to 1 mg/kg/day during the period of organogenesis. A slight reduction in body weight gain was noted in pregnant rats at 0.1 and 1 mg/kg/day. There were no maternal effects in rabbits or embryo-fetal effects in either species up to the maximum dose tested. At 1 mg/kg/day in rats and rabbits, the dose multiple was approximately 7 and 13 times, respectively, the clinical dose based on octreotide injection body surface area.

In a pre- and post-natal development rat study at intravenous doses of 0.02-1 mg/kg/day, a transient growth retardation of the offspring was observed at all doses which was possibly a consequence of growth hormone inhibition by octreotide. The doses attributed to the delayed growth are below the clinical dose based on octreotide injection body surface area.

8.2 Lactation

Risk Summary

There is no information available on the presence of octreotide in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Studies show that octreotide administered subcutaneously passes into the milk of lactating rats (see Data). When a drug is present in animal milk, it is likely that the drug will be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for MYCAPSSA and any potential adverse effects on the breastfed child from MYCAPSSA or from the underlying maternal condition.

Data

Following a subcutaneous dose (1 mg/kg) of octreotide to lactating rats, transfer of octreotide into milk was observed at a low concentration compared to plasma (milk/plasma ratio of 0.009).

8.3 Females and Males of Reproductive Potential

Discuss the potential for unintended pregnancy with premenopausal women as the therapeutic benefits of a reduction in GH levels and normalization of IGF-1 concentration in acromegalic females treated with octreotide may lead to improved fertility.

8.4 Pediatric Use

Safety and efficacy of MYCAPSSA in pediatric patients have not been established.

In post-marketing reports, serious adverse reactions, including hypoxia, necrotizing enterocolitis, and death, have been reported with octreotide injection use in pediatric patients, most notably in children under 2 years of age.

8.5 Geriatric Use

Clinical studies of octreotide did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In MYCAPSSA clinical studies, 39 patients (21%) were age 65 years or over and 1 patient was age 75 years or over. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

In patients with mild, moderate, or severe renal impairment there is no dose adjustment recommended for MYCAPSSA. There is a significant increase in octreotide exposure in patients with end stage renal disease (ESRD). Start patients with ESRD on MYCAPSSA 20 mg orally daily. Adjust the maintenance dose thereafter based on IGF-1 levels, patient's signs and symptoms, and tolerability *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

Patients with liver cirrhosis and patients with fatty liver disease showed prolonged elimination of octreotide following subcutaneous administration of drug *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

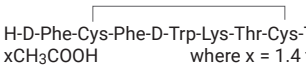
A limited number of accidental overdoses of injectable octreotide acetate in adults has been reported. The doses ranged from 2.4 mg/day to 6 mg/day administered by continuous infusion or subcutaneously 1.5 mg three times a day. Adverse reactions in some patients included arrhythmia, hypotension, cardiac arrest, brain hypoxia, pancreatitis, hepatic steatosis, hepatomegaly, lactic acidosis, flushing, diarrhea, lethargy, weakness, and weight loss.

If overdose occurs, contact Poison Control (1-800-222-1222) for latest recommendations.

11 DESCRIPTION

MYCAPSSA delayed release capsules contain octreotide acetate, a somatostatin analog. Octreotide is known chemically as L-cysteinamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[2-hydroxy-1-(hydroxy-methyl) propyl]-, cyclic (2→7)-disulfide; [R-(R*,R*)].

The molecular weight of octreotide is 1019.3 (free peptide, $C_{49}H_{66}N_{10}O_{10}S_2$) and its amino acid sequence is:



MYCAPSSA (octreotide) delayed-release capsules are enteric-coated capsules for oral use. Each capsule contains 20 mg of octreotide (provided as octreotide acetate). Octreotide is present as a salt with 1.4 to 2.5 molar equivalents of acetate. The capsules contain the following inactive ingredients: polyvinylpyrrolidone (PVP-12), sodium caprylate, magnesium chloride, polysorbate 80, glyceryl monocaprylate, glyceryl tricaprylate, gelatin capsules, and Acryl-EZE® (methacrylate). The capsule is printed with "OT 20" in Opacode® black ink.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Octreotide exerts pharmacologic actions similar to the natural hormone somatostatin, but is a more potent inhibitor of GH, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses luteinizing hormone (LH) response to gonadotropin-releasing hormone (GnRH), decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide.

12.2 Pharmacodynamics

In a single-dose PK study conducted in healthy volunteers, inhibition of GH (as measured by C_{avg}) was observed in all subjects receiving MYCAPSSA, as compared to their GH levels prior to MYCAPSSA.

In a study designed to assess the duration of MYCAPSSA-induced increased intestinal permeability, an increase in paracellular permeability was observed 2 hours after MYCAPSSA administration and returned to baseline by 5.5 hours after MYCAPSSA administration. MYCAPSSA-induced permeability is completely reversible within this timeframe.

MYCAPSSA maintained GH and IGF-1 levels in patients with acromegaly.

Single doses of octreotide acetate given subcutaneously have been shown to inhibit gallbladder contractility and to decrease bile secretion in normal volunteers. In clinical trials the incidence of gallstone or biliary sludge formation was markedly increased *[see Warnings and Precautions (5.1)]*.

Octreotide acetate may cause clinically significant suppression of TSH *[see Warnings and Precautions (5.3)]*.

12.3 Pharmacokinetics

Absorption

In healthy subjects, similar systemic exposure (AUC) was observed between a single dose oral administration of MYCAPSSA (20 mg octreotide acetate), and a single dose of subcutaneous Sandostatin IR (0.1 mg octreotide acetate). Peak octreotide levels (C_{max}) were 33% lower following oral administration compared to the subcutaneous route. Absorption time was longer following oral administration compared to the subcutaneous route; peak concentrations were reached at a median of 1.67–2.5 hours after 20 mg MYCAPSSA administration compared to 0.5 hours for the subcutaneous administration.

In healthy subjects, after single-dose oral administration of MYCAPSSA, the systemic exposure of octreotide (C_{max}, AUC_{0-24}, and AUC_{0-inf}) increased dose-proportionally at doses ranging from 3–40 mg.

In patients with acromegaly, there was a dose-related increase in the mean plasma octreotide concentrations after chronic administration of MYCAPSSA 40 mg (20 mg bid), 60 mg (40 mg AM / 20 mg PM), and 80 mg (40 mg AM / 40 mg PM) bid. Mean peak concentrations (C_{max}) following chronic dosing were lower in patients with acromegaly (mean [CV%] = 2.51 ng/mL [80%] and 5.30 ng/mL [76%] at 20 and 40 mg bid, respectively) compared to single-dose peak concentrations observed in healthy subjects at the same dose (mean [CV%] = 3.62 [53%] and 8.21 ng/mL [88%] at 20 and 40 mg, respectively).

Effect of Food on Oral Absorption

In healthy subjects, data from a single-dose, crossover PK study of food effect demonstrated that administration of MYCAPSSA 20 mg capsules with food led to an approximate 90% decrease in the rate (C_{max}) and extent of absorption (AUC_{0-t}).

Distribution

In healthy volunteers, the distribution half-life ($t_{\alpha½}$) of octreotide acetate from plasma after subcutaneous administration was 0.2 h, the volume of distribution (Vdss) was estimated to be 13.6 L, and the total body clearance ranged from 7–10 L/hr. In blood, the distribution into the erythrocytes was found to be negligible and about 65% was bound in the plasma in a concentration-independent manner. Binding was mainly to lipoprotein and, to a lesser extent, to albumin.

In patients with acromegaly, the Vdss following subcutaneous administration was increased compared to healthy volunteers, estimated to be 21.6 L; mean peak concentrations were lower in acromegaly patients compared to healthy volunteers (2.8 ng/mL vs 5.2 ng/mL, respectively after 0.1 ng/mL dose).

Elimination

According to data obtained with the immediate-release octreotide subcutaneous injection, approximately 32% of the dose is excreted unchanged in the urine.

In healthy subjects, there was no effect of route of administration on octreotide elimination, and comparable mean elimination half-lives ($t_{½}$) of 2.3 hours and 2.7 hours were demonstrated between subcutaneous injection and oral octreotide treatments, respectively.

In patients with acromegaly, elimination after chronic dosing was slightly slower than that seen in healthy volunteers, with mean apparent half-life values at steady state ranging from 3.2–4.5 hours across doses (20 mg, 40 mg, 60 mg, and 80 mg). Elimination is complete approximately 48 hours after the last dose in patients who have achieved steady-state plasma levels. Minimal accumulation (approximately 10%) was observed in patients after repeat administration of MYCAPSSA.

Specific Populations

Geriatric Patients

In patients 65 years of age and older, after subcutaneous administration of octreotide acetate, the half-life of octreotide increased significantly (46%) and clearance of octreotide decreased significantly (26%).

Patients with Renal Impairment

Exposure in patients with severe renal impairment was not substantially different from that of the matched controls. Following oral administration of a single dose of 20 mg MYCAPSSA to patients with severe renal impairment (eGFR 15–29 mL/min/1.73m^2) and patients with end-stage renal disease (ESRD) requiring dialysis, patients with ESRD on dialysis had a 46% decrease in clearance with a corresponding 87% increase in AUC and 85% increase in $t_{½}$ compared to matched healthy subjects. ESRD patients had higher mean plasma concentrations than did those with severe renal impairment with higher mean values for C_{max} (9.30 ng/mL compared to 6.13 ng/mL in the matched controls), AUC_{0-t} (68.0 h•ng/mL compared to 32.2 h•ng/mL in the matched controls), AUC_{inf} (69.5 h•ng/mL compared to 32.4 h•ng/mL in the matched controls), and $t_{½}$ (7.09 hr compared to 3.84 hr in the matched controls), consistent with the known effect of renal impairment on octreotide exposure *[see Use in Specific Populations (8.6)]*.

Patients with Hepatic Impairment

In patients with liver cirrhosis, after subcutaneous administration of octreotide acetate, prolonged elimination of drug was observed, with octreotide acetate $t_{½}$ increasing from 1.9–3.7 hr and total body clearance decreasing from 7–10 L/hr to 5.9 L/hr, whereas patients with fatty liver disease showed $t_{½}$ increased to 3.4 hr and total body clearance of 8.2 L/hr.

Drug Interactions

Limited published data indicate that somatostatin analogs including MYCAPSSA may decrease the metabolic clearance of compounds known to be metabolized by cytochrome P450 enzymes, which may be due to the suppression of GH *[see Drug Interactions (7.2)]*.

Octreotide has been associated with alterations in nutrient absorption, so it may have an effect on absorption of orally administered drugs.

Table 3 Effect of Co-administered Drugs on MYCAPSSA Systemic Exposure

Co-administered drug and dosing regimen	MYCAPSSA		
	Dose (mg)	Mean Ratio (ratio with/without co-administered drug) No Effect=1.0	
		Change in AUC	Change in C_{max}
Esomeprazole 40 mg QD on days 2-7	20 mg on Day 1 and 20 mg on Day 7	0.59[1] (0.40 – 0.88)[2]	0.55[1] (0.40 – 0.75)[2]
Metoclopramide 20 mg	40 mg	0.91 (0.61 – 1.35)	0.95 (0.62 – 1.44)
Loperamide 4 mg	40 mg	0.97 (0.65 – 1.44)[2]	0.91 (0.59 – 1.39)[2]

[1]Clinically significant *[see Dosage and Administration (2) and Drug Interactions (7.1, 7.2)]*

[2]Mean ratio with 90% CI (with/without co-administered drug, e.g., 1= no change, 0.6 = 40% decrease,1.3=1.3-fold increase in exposure)

Table 4 Effect of MYCAPSSA on Systemic Exposure of Co-administered Drugs

Co-administered drug and dosing regimen	MYCAPSSA		
	Dose (mg)[1]	Mean Ratio (ratio with/without co-administered drug) No Effect=1.0	
		Change in AUC	Change in C_{max}
Cyclosporine 300 mg	20 mg	0.38[2] (0.31 – 0.46)[3]	0.29[2] (0.22 – 0.37)[3]
Digoxin 0.5 mg	40 mg	1.0 (0.94 – 1.13)[3]	0.63[2] (0.55 – 0.72)[3]
Lisinopril 20 mg	40 mg	1.40[2] (1.21 – 1.61)[3]	1.50[2] (1.32 – 1.71)[3]
Ethinyl Estradiol 0.06 mg	40 mg	0.94 (0.86 – 1.03)[3]	0.92 (0.83 – 1.01)[3]
Levonorgestrel 0.3 mg	40 mg	0.76[2] (0.67 – 0.86)[3]	0.62[2] (0.54 – 0.71)[3]

[1]Single dose

[2]Clinically significant *[see Dosage and Administration (2) and Drug Interactions (7.1, 7.2)]*

[3]Mean ratio with 90% CI (with/without co-administered drug, e.g., 1= no change, 0.6 = 40% decrease, 1.5=1.5-fold increase in exposure)

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies in laboratory animals have demonstrated no mutagenic potential of octreotide acetate.

No carcinogenicity studies have been conducted with MYCAPSSA. No carcinogenic potential was demonstrated in mice treated subcutaneously with octreotide acetate for 85–99 weeks at doses up to 2000 mcg/kg/day (8 times the clinical dose based on octreotide injection body surface area). In a 116-week subcutaneous study in rats administered octreotide acetate, a 27% and 12% incidence of injection-site sarcomas or squamous cell carcinomas was observed in males and females, respectively, at the highest dose level of 1250 mcg/kg/day (10 times the clinical dose based on octreotide injection body surface area) compared to an incidence of 8% to 10% in the vehicle-control groups. The increased incidence of injection-site tumors was most probably caused by irritation and the high sensitivity of the rat to repeated subcutaneous injections at the same site. There was also a 15% incidence of uterine adenocarcinomas in the 1250 mcg/kg/day females compared to 7% in the saline-control females and 0% in the vehicle-control females. The presence of endometritis coupled with the absence of corpora lutea, the reduction in mammary fibroadenomas, and the presence of uterine dilatation suggest that the uterine tumors were associated with estrogen dominance in the aged female rats, which does not occur in humans.

No fertility studies in animals have been conducted with MYCAPSSA. Injectable octreotide acetate did not impair fertility in rats at doses up to 1000 mcg/kg/day, which represents 7 times the clinical dose based on octreotide injection body surface area.

14 CLINICAL STUDIES

The efficacy of MYCAPSSA was established in a 9 month, randomized, double-blind, placebo-controlled study (NCT03252353) that enrolled 56 patients with acromegaly.

In the overall study population, 54% were female and the average age of patients was 55 years. 91% of patients were Caucasian, 5% Asian, 2% Black, and 2% Other. The percentage of patients with previous pituitary surgery was 88%. The baseline IGF-1 levels (the average of 2 assessments measured within 2 weeks of randomization) was 0.80 times ULN (range: 0.5–1.1 times ULN) in the patients treated with MYCAPSSA and 0.84 times ULN (range: 0.3–1.1 times ULN) in patients treated with the placebo.

In this study, 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 daily (40 mg in the morning and 40 mg in the evening) until patients were deemed adequately controlled based on biochemical results and/or clinical judgement. Patients then maintained their target dose until end of treatment.

The primary efficacy endpoint was somatostatin dose-adjusted proportion of patients who maintain their biochemical response, defined as an IGF-1 levels less than or equal to the ULN at the end of 9 months of treatment. 58% of patients treated with MYCAPSSA vs. 19% of patients treated with placebo maintained their biochemical response.

25% of patients treated with MYCAPSSA required discontinuation of MYCAPSSA and treatment with other somatostatin analogs at some point during the 9-month study. Criteria for somatostatin analog rescue were IGF-1 levels ≥1.3 times ULN and exacerbation of acromegaly signs and symptoms on two consecutive assessments while treated for at least 2 weeks with 80 mg/day or other reasons such as adverse reactions or patient's decision.

16 HOW SUPPLIED/STORAGE AND HANDLING

MYCAPSSA delayed-release 20 mg capsules are white hard gelatin capsules imprinted with "OT" on one half of the capsule and "20" on the other half.

The capsules are supplied as:

NDC Number	Package Size
69880-120-28	Wallet of 28 capsules

Storage

Until first use, store unopened wallets of MYCAPSSA refrigerated at 2° to 8°C (36° to 46°F). Do not freeze.

After first use, opened wallets may be stored at 20° to 25°C (68° to 77°F) for up to 1 month.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Cholelithiasis and Complications of Cholelithiasis

Advise patients to contact their healthcare provider if they experience signs or symptoms of gallstones (cholelithiasis) or complications of cholelithiasis (e.g., cholecystitis, cholangitis and pancreatitis) *[see Warnings and Precautions (5.1)]*.

Hypoglycemia and Hyperglycemia

Advise patients to contact their healthcare provider if they have problems with blood sugar levels, either hyperglycemia or hypoglycemia *[see Warnings and Precautions (5.2)]*.

Thyroid Function Abnormalities

Inform patients that their thyroid function will be assessed periodically during treatment *[see Warnings and Precautions (5.3)]*.

Cardiac Function Abnormalities

Inform patients to contact the health care provider in case they notice irregular heartbeat *[see Warnings and Precautions (5.4)]*.

Decreased Vitamin B12 Levels and Abnormal Schilling's Tests

Inform patients that Vitamin B12 levels may be monitored during the treatment *[see Warnings and Precautions (5.5)]*.

Females and Males of Reproductive Potential

Inform female patients that treatment with MYCAPSSA may result in unintended pregnancy *[see Use in Specific Populations (8.3)]*.

Rx ONLY

Manufactured by MW Encap Ltd., Scotland, UK.

AMRYT PHARMA

Amryt Pharmaceuticals DAC, Dublin, Ireland
NDA # 208232