Immediate-Release Octreotide Acetate:

Quick Relief or "Rescue Medication" for Severe Diarrhea & Flushing Associated with Metastatic Neuroendocrine Tumors/Carcinoid Symptoms

Severe Diarrhea & Flushing Associated with Metastatic Neuroendocrine Tumors/Carcinoid Symptoms

What Can Be Done?

Carcinoid syndrome refers to a group of symptoms triggered by hormones that are released by functional neuroendocrine tumors – "functional" means that the hormones cause certain symptoms.[1] Severe diarrhea and flushing are two of the most common symptoms associated with carcinoid syndrome.[2]

Treatments called somatostatin analogues (SSAs) such as **octreotide acetate** are man-made proteins that act similarly to somatostatin, a naturally occurring hormone that regulates the production of other hormones.[3] SSAs have been successfully used to decrease hormone secretion and improve severe diarrhea and flushing associated with metastatic carcinoid tumors.[4]

Octreotide acetate is available in immediate-release and long-acting formulations.

Immediate-release formulations go into effect right away – hence the term "rescue medication" – and are administered two to four times a day.

Long-acting formulations are administered once every four weeks. They are given after initial treatment with immediate-release octreotide has been shown to be effective and well tolerated.

Octreotide should not be used by patients who are allergic to it. Octreotide may cause serious adverse effects, including gallstones, high or low blood sugar, thyroid effects, and slow heart rate.

"Immediate-release"

octreotide acetate provides quick relief ... and now there is a new way to administer it whenever and wherever you need.

Patients who are taking long-acting somatostatin analogues for metastatic neuroendocrine tumors may still experience breakthrough symptoms of severe diarrhea and flushing[4,5,6,7] and need something else for relief. Immediate-release octreotide acetate is designed to quickly address these breakthrough symptoms when they occur.

In a six-month clinical trial of long-acting octreotide, **50-70%** of patients had to use immediate-release octreotide to control breakthrough carcinoid symptoms (diarrhea and flushing) during the study.[8]

In a different four-month clinical trial, SSA-treated patients still needed rescue octreotide immediate-release therapy for breakthrough symptoms of severe diarrhea and flushing for almost 10 days per month.[9]

Different from how other immediate-release octreotide acetate is administered, BYNFEZIA PEN™ is the first-and-only immediate-release octreotide in a prefilled, multidose pen for self-administration. To optimize patient comfort, BYNFEZIA PEN™ utilizes low-volume doses and shorter, smaller diameter needles than prefilled octreotide acetate syringes. One BYNFEZIA PEN™ can last multiple days and does not require refrigeration for up to 28 days after first use. The most common side effects in carcinoid syndrome patients are headache, dizziness, muscle spasm; side effects were generally similar to those commonly seen with neuroendocrine tumors.

IMPORTANT SAFETY INFORMATION

INDICATIONS

BYNFEZIA PEN™ (octreotide acetate) injection is a prescription drug used:

- Treatment of severe diarrhea/flushing episodes associated with metastatic carcinoid tumors in adult patients
- Treatment of profuse watery diarrhea associated with vasoactive intestinal peptide tumors (VIPomas) in adult patients
- To reduce the amount of growth hormone and insulin like growth factor 1 in adult patients with acromegaly who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses

LIMITATIONS OF USE

- In patients with acromegaly, the effect of BYNFEZIA PEN™ to improve symptoms and reduce tumor size and
- In patients with carcinoid syndrome and VIPomas, the effect of BYNFEZIA PEN™ on size, rate of growth, and development of metastases has not been determined

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Do not use BYNFEZIA PEN™ if you are allergic to octreotide.

ADVERSE EFFECTS, WARNINGS AND PRECAUTIONS

BYNFEZIA PEN™ may cause serious adverse effects, including gallstones, high or low blood sugar, thyroid effects, and slow heart rate.

Tell your healthcare provider if you have any of the following:

- Signs or symptoms of gallstones (gallbladder/liver problems): May include unexplained pain in your upper right abdomen, sudden pain in your back/right shoulder or between your shoulder blades, yellowing of your skin and whites of your eyes, fever with chills, or severe nausea/vomiting
- Signs or symptoms of high or low blood sugar: May include increased thirst, urination, appetite, nausea, weakness, or tiredness
- Signs or symptoms of low blood sugar: May include nervousness, shakiness, sweating, fast heartbeat, irritability or mood changes, and hunger
- Signs or symptoms of slow heart rate: May include dizziness or lightheadedness, fainting or near fainting, chest pain, shortness of breath, confusion or memory problems, and weakness or extreme tiredness
- Signs or symptoms of low thyroid levels: May include unexplained weight gain, cold intolerance, slow heartbeat, severe constipation, unusual/extreme tiredness, growth/lump/swelling on the front of the neck, numbness, or tingling feeling that is not normal

It is not known if BYNFEZIA PEN™ will harm your unborn baby or pass into breast milk.

The most common side effects of BYNFEZIA PEN™ are:

- Acromegaly patients: Diarrhea, loose stools, nausea and stomach area (abdominal) pain
- Carcinoid syndrome patients: Headache, dizziness, muscle spasm; side effects were generally similar to those commonly seen with neuroendocrine tumors

Tell your healthcare provider right away if you have signs of an allergic reaction after receiving BYNFEZIA PEN™. Symptoms include swelling of your face, lips or tongue, breathing problems, fainting, dizziness or feeling lightheaded (low blood pressure), itching, skin flushing or redness, rash, or hives.

Before taking BYNFEZIA PEN™, tell your healthcare provider about other medical conditions, especially if you have diabetes, gallbladder, heart, thyroid, kidney or liver problems; or if you are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed.

Tell your healthcare provider about all the medicines you take. BYNFEZIA PEN™ may affect the way other medicines work, and other medicines may affect how BYNFEZIA PEN™ works. If you have diabetes, your healthcare provider may change your dose of diabetes medication when you first start receiving BYNFEZIA PEN™ or if your dose of BYNFEZIA PEN™ is changed.

Especially tell your healthcare provider if you take:

- Insulin or other diabetes medicines
- Cyclosporine
- Bromocriptine
- Medicines that lower your heart rate, such as beta-blockers

These are not all the possible side effects of BYNFEZIA PEN™. For more information, ask your healthcare provider.

You are encouraged to report any negative side effects of BYNFEZIA PEN™ to the FDA. Visit www.fda.gov/watch or call 1-800-FDA-1088. You are also encouraged to report side effects or adverse drug events to our Drug Safety Department at 1-800-406-7984 or drug.safetyUSA@sunpharma.com (preferred) with as much information as available.

Please see Full Prescribing Information.

References

1. Neuroendocrine Tumors: Introduction. Cancer.Net. Available at: https://www.cancer.net/cancer-types/neuroendocrine-tumors/introduction. Accessed September 8, 2020
2. Kulke MH. Somatostatin Analogues in Neuroendocrine Tumors. J Natl Compr Canc Netw. 2016 Mar;14(3):241-2
3. National Library of Medicine. Compound Summary - Octreotide. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Octreotide. Accessed August 3, 2020.
4. Kulke MH, Horsch D, Caplin ME, et al. Telotristat Ethyl, a Tryptophan Hydroxylase Inhibitor for the Treatment of Carcinoid Syndrome. J Clin Oncol. 2017;35(1):14-23.
5. Ferrari AC, Glasberg J, Riechelmann RP, Carcinoid syndrome: update on the pathophysiology and treatment. Clinics (Sao Paulo). 2018; 73(Suppl 1): e490s.
6. Sandostatin LAR Depot (octreotide acetate) injectable suspension [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation
7. Somalutine Depot (lanreotide) injection, for subcutaneous use [prescribing information]. Cambridge, MA: Ipsen Biopharmaceutcals
8. Sandostatin LAR Depot (octreotide acetate) injectable suspension [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation
9. Somalutine Depot (lanreotide) injection, for subcutaneous use [prescribing information]. Cambridge, MA: Ipsen Biopharmaceutcals

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