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NOHARMe Newsletter

"Avoid errors… Optimize care"

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Octreotide Reports on NOHARMe Database: Analysis and Recommendations

The General Administration of Drug Utilization & Pharmacy Practice is pleased to publish a new issue of the NO HARMe newsletter.

The Central Administration of Pharmaceutical Care in the Egyptian Drug Authority has a fundamental interest in raising the level of all pharmaceutical services provided to the patient and is constantly keen on the rational use of drugs in the Egyptian market and in all governmental and non-governmental health facilities, which guarantees patient safety.

The NO HARMe unit is tasked with the responsibility of reviewing and analyzing the received reports of drug therapy problems and medication errors in order to promote the rational use of drugs according to the General Administration of Drug Utilization and Pharmacy Practice's goal of promoting meaningful changes in pharmacy practice.

By preventing future occurrences of these errors, we are able to fix the system errors as well as the individual errors that have been identified.

One main effective tool for correcting errors and encouraging safe practice is issuing alerts and newsletters targeting healthcare providers.

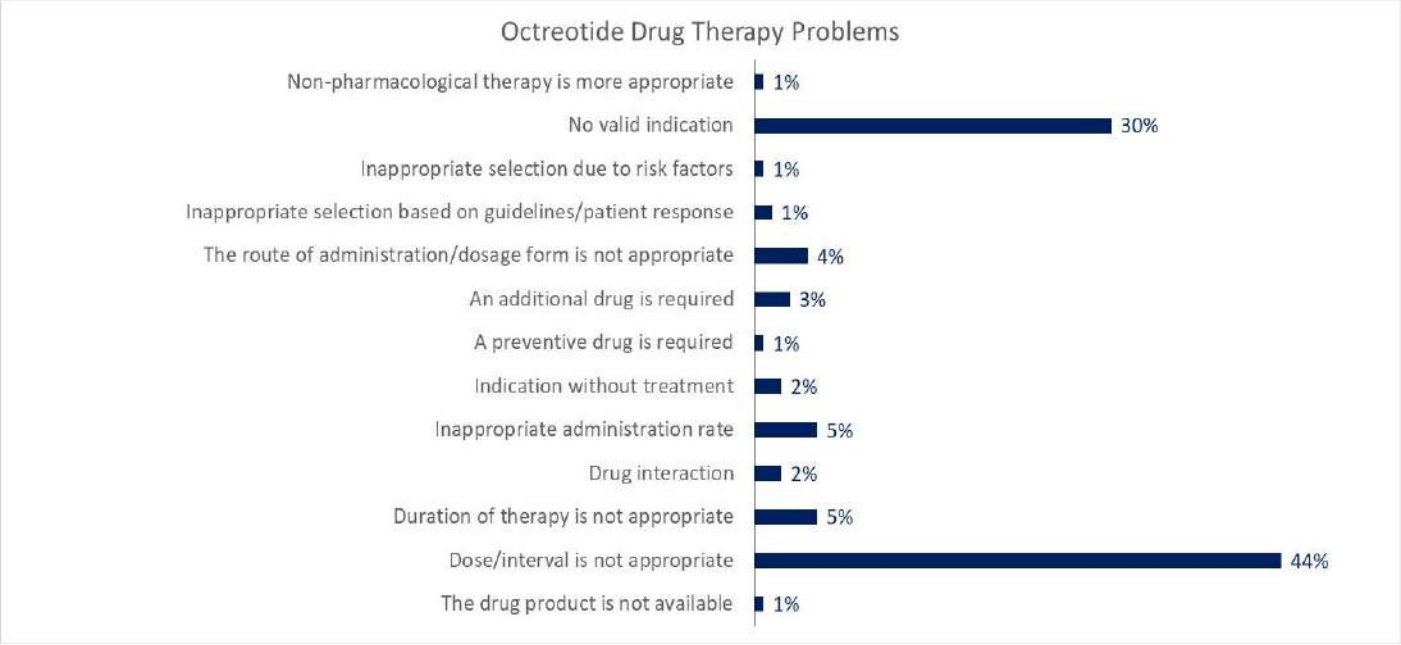
Hence, the "**NO HARMe Newsletter**" addresses the most serious and most frequent errors in Egyptian hospitals and demonstrates clearly the standard practice as per updated accredited drug information resources and evidence-based guidelines.

The "**NO HARMe**" has an account with the international platforms for collecting and analyzing reports on drug safety and scientific research.

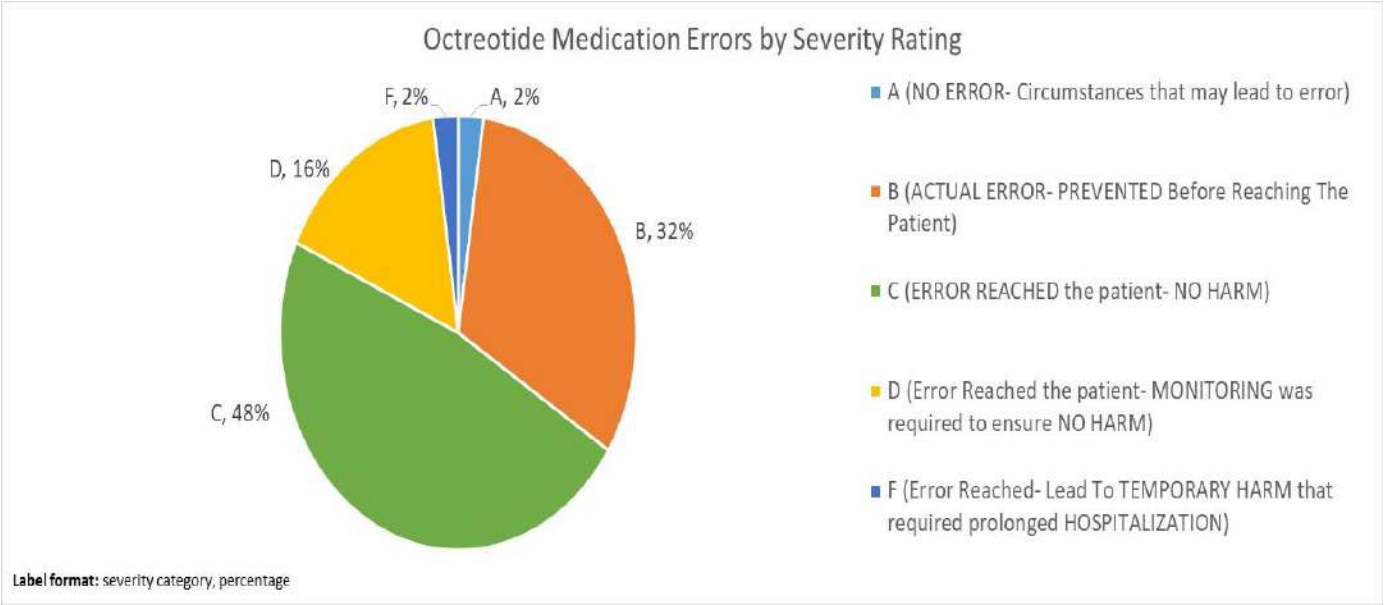
These international platforms main concern is the safe and effective use of medications. Hereby, we can compare the trends and patterns in Egyptian practice to the international experience.

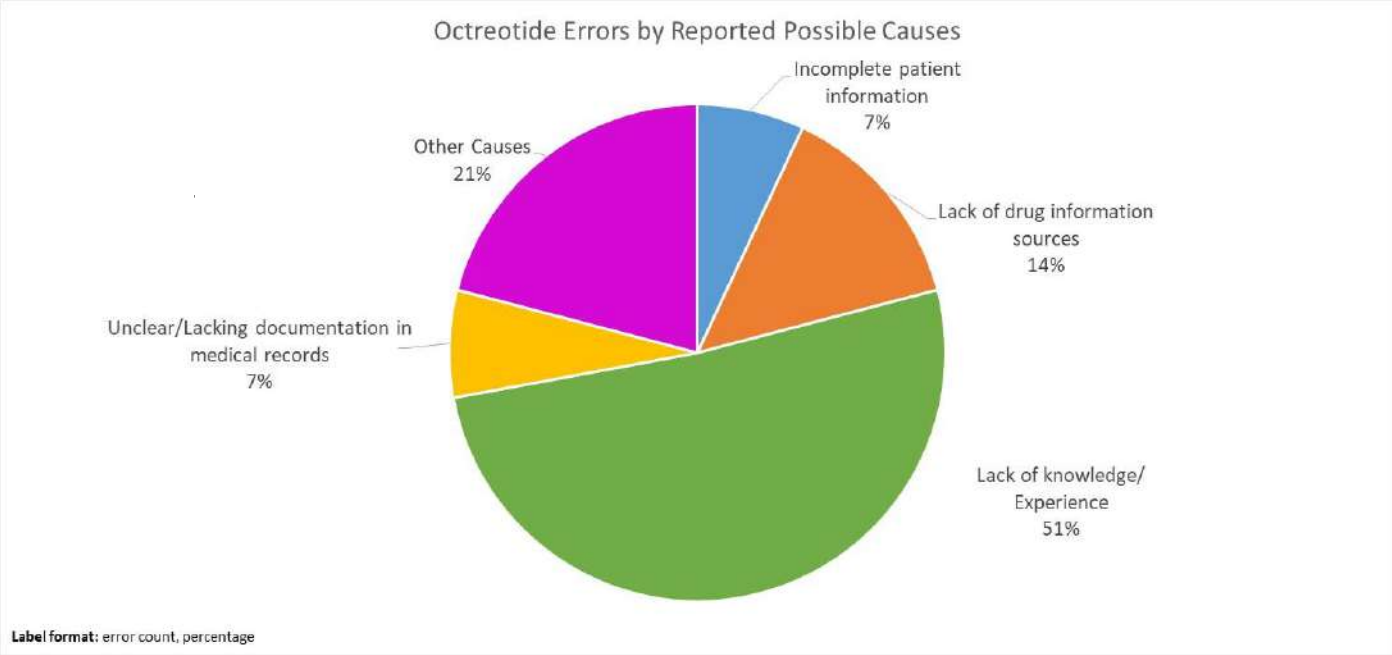
A Quick Overview of the NOHARMe Data (Octreotide)

- **Octreotide is the main focus of this issue as it is one of the most reported drugs in VigiFlow during the first quarter of 2023. It accounts for 16.0% of all reports.**
- **Of all the Drug Therapy Problems (DTPs) related to Octreotide use, the inappropriate dose regimen or no valid indication were the most reported. Since both DTPs make up around 74% of the reports, with 49% with an inappropriate dose regimen and 30% for use with no clear indication, this NO HARMe Newsletter issue will address the main indications and appropriate dose regimen of Octreotide.**



Medication Errors Associated with Octreotide





Octreotide

Octreotide is a somatostatin analog that mimics natural somatostatin by inhibiting serotonin release and the secretion of gastrin, vasoactive intestinal peptide (VIP), insulin, glucagon, secretin, motilin, and pancreatic polypeptide. It decreases growth hormone (GH) and insulin-like growth factor-1 (IGF-1) in acromegaly. Octreotide provides more potent inhibition of GH, glucagon, and insulin as compared to endogenous somatostatin. Also suppresses luteinizing hormone (LH) response to Gonadotropin hormone-releasing hormone (GnRH), secretion of thyroid-stimulating hormone (TSH), and decreases splanchnic blood flow.

Octreotide Adult Indications/Dosing

In conditions where the long-acting depot is indicated, the North American Neuroendocrine Tumor Society (NANETS) guidelines suggest that the long-acting depot may be appropriate as initial therapy. For patients experiencing breakthrough (uncontrolled) symptoms while taking the long-acting depot, supplementary doses of subcutaneous (SubQ) octreotide may be necessary.

Acromegaly	**IM intragluteally (depot):** **Initial:** 20 mg every 4 weeks for 3 months; after the initial 3 months, adjust the dose based on clinical response. **Dosage titration example provided from the manufacturer's labeling:** • **Growth hormone (GH) ≤1 ng/mL, insulin-like growth factor 1 (IGF-1) normal, and symptoms controlled:** Reduce octreotide depot to 10 mg every 4 weeks. • **GH >1 to ≤2.5 ng/mL, IGF-1 normal, and symptoms controlled:** Maintain octreotide depot at 20 mg every 4 weeks. • **GH >2.5 ng/mL, IGF-1 elevated, and/or symptoms uncontrolled:** Increase octreotide depot to 30 mg every 4 weeks. • **If GH, IGF-1, or symptoms remain uncontrolled,** may increase the dose to 40 mg every 4 weeks. Dosages >40 mg are not recommended by the manufacturer; however, in some cases, individualized doses up to 60 mg every 4 weeks have been used successfully in partial responders.

	SubQ: Initial: 50 mcg 3 times daily; titrate to achieve target GH and IGF-1 levels. Usual effective dose: 100 mcg 3 times daily; range: 300 to 1,500 mcg/day. **Doses above 300 mcg/day rarely result in additional benefit; if an increased dose fails to provide additional benefit, the dose should be reduced.**
Prevention of post-pancreatic surgery complications	**SubQ:** 100 mcg 3 times daily for 7 consecutive days, starting on the day of surgery at least 1 hour before laparotomy. Complications include pancreatic fistula, abscess and subsequent sepsis, and postoperative acute pancreatitis**.**
Carcinoid syndrome	**IM intragluteally (depot):** **Initial:** 20 mg every 4 weeks or 20 to 30 mg every 4 weeks. **Titration:** The dose may be modified based on the response as follows: may decrease to 10 mg every 4 weeks after 2 months if initially responsive to 20 mg dose. Increase to 30 mg every 4 weeks if symptoms are inadequately controlled after 2 months. ***Note:*** The US labeling states that higher doses are **NOT** recommended; however, if frequent supplementary SubQ doses are needed (eg, ≥3 to 4 times/week), may consider further increasing the dose by 10 mg every 4 weeks, or maintaining the same dose and reducing the dosing interval to every 3 weeks, up to a maximum off-label dose of 60 mg every 4 weeks.
	SubQ, IV: Initial: 100 to 600 mcg/day in 2 to 4 divided doses. If additional symptom control is needed, may increase by doubling the dose every 3 to 4 days until symptoms are controlled; usual range: 50 to 750 mcg/day. Experience with doses above 750 mcg/day is limited; however, may consider **a continuous SubQ infusion** of 1,000 to 2,000 mcg/day off-label in patients who remain symptomatic on intermittent doses.
Gastroentero-pancreatic neuroendocrine tumors, functional, gastrin-secreting (gastrinoma, Zollinger-Ellison syndrome), refractory (alternative agent) (off-label use)	**IM intragluteally (depot):** **Initial:** 20 mg every 4 weeks or 20 to 30 mg every 4 weeks. **Titration:** The dose may be modified based on the response as follows: May decrease to 10 mg every 4 weeks after 2 months if initially responsive to 20 mg dose. Increase to 30 mg every 4 weeks if symptoms are inadequately controlled after 2 months. ***Note:*** The US labeling states that higher doses are **NOT** recommended; however, if frequent supplementary. **SubQ doses** are needed (eg, ≥3 to 4 times/week), may consider further increasing the dose by 10 mg every 4 weeks, or maintaining the same dose and reducing the dosing interval to every 3 weeks, up to a maximum off-label dose of 60 mg every 4 weeks.
	SubQ: Initial: 100 mcg every 12 hours; may increase to 200 mcg every 12 hours or 100 to 500 mcg in 2 to 4 divided doses (usual dose: 150 mcg 3 times daily). If additional symptom control is needed, may increase by doubling the dose every 3 to 4 days until symptoms are controlled; may also consider a continuous SubQ infusion of 1,000 to 2,000 mcg/day.

Acute Gastroesophageal variceal hemorrhage (off-label use)	**IV:** **Initial:** 50 mcg bolus, followed by continuous infusion of 50 mcg/hour for 2 to 5 days; may repeat bolus in the first hour if the hemorrhage is not controlled.
Malignant bowel obstruction to decrease intestinal secretions and vomiting (off-label use)	***Note:*** For use in patients who are not candidates for surgery or who have inoperable obstruction. **SubQ:** 200 to 900 mcg/day in 2 to 3 divided doses or 300 mcg/day by continuous SubQ infusion. ***Note:*** Patients who respond to SubQ injections may be converted to IM depot injections (eg, 30 mg IM every 4 weeks) for maintenance therapy.
Gastroenteropancreatic neuroendocrine tumors, metastatic, tumor control (off-label use)	***Note:*** May be used to control tumor growth in patients with unresectable, metastatic, well-differentiated NETs with a high tumor burden (including thymus and lung NETs). **IM intragluteally (depot):** 30 mg every 4 weeks until tumor progression. ***or*** **IM intragluteally (depot):** **Initial:** 20 to 30 mg every 4 weeks. **Titration:** If frequent supplementary SubQ doses are needed (eg, ≥3 to 4 times/week), may increase the dose by 10 mg every 4 weeks, or maintain the same dose and reduce the dosing interval to every 3 weeks. Dosage range: 20 to 60 mg every 4 weeks.
	SubQ: **Initial:** 100 to 500 mcg in 2 to 4 divided doses (usual dose: 150 mcg 3 times daily). If additional symptom control is needed, may increase by doubling the dose every 3 to 4 days until symptoms are controlled; may also consider a continuous SubQ infusion of 1,000 to 2,000 mcg/day. ***With lutetium Lu 177 dotatate treatment:*** **IM intragluteally (depot):** 30 mg once following each lutetium Lu 177 dotatate dose (administer between 4 to 24 hours after the lutetium Lu 177 dotatate dose) for 4 doses and then continue 30 mg once a month after lutetium Lu 177 dotatate is completed. Rescue doses (dose not specified) of short-acting octreotide may be used in between for symptomatic management (for diarrhea or flushing), but discontinue at least 24 hours before each lutetium Lu 177 dotatate dose.

N.B. Off-label use means using an approved drug for an unapproved use to treat a disease or medical condition. One reason for the off-label use is that there might **NOT** be an approved drug to treat the disease or medical condition. Another is that the patient may have tried all approved treatments without seeing any benefits.

Octreotide Pediatric Indications/Dosing

Esophageal varices; gastrointestinal bleed: Limited data available:

Infants, Children, and Adolescents:
IV: Initial: 1 to 2 mcg/kg bolus followed by 1 to 2 mcg/kg/hour continuous IV infusion; titrate infusion rate to response up to 50 mcg/hour; taper dose by 50% every 12 hours when no active bleeding occurs for 24 hours; may discontinue when the dose is 25% of the initial dose.

Persistent hyperinsulinemic hypoglycemia unresponsive to diazoxide and glucose:
Dosing should be individualized to achieve and maintain a target BG >70 mg/dL.

Neonates:
SubQ: Initial: 2-5 mcg/kg/6-8 hours, adjusted according to response up to 7 mcg/kg/4 hour.

Infants, Children, and Adolescents:
SubQ: Intermittent SubQ: Initial: 5 mcg/kg/day in divided doses every 6 to 8 hours; titrate to response, 5 mcg/kg/day increments have been used; the usual reported effective range: 5 to 25 mcg/kg/day in divided doses; maximum daily dose: 35 mcg/kg/day.

Continuous SubQ infusion: Initial: 5 mcg/kg/day delivered over 24 hours; titrate to response, 5 mcg/kg/day increments have been used; usual reported effective range: 5 to 25 mcg/kg/day; max. daily dose: 35 mcg/kg/day.

Octreotide Dosage Forms Available in Egypt

- **Solution for injection:** 50, 100, 200 mcg/ml
- **Powder + solvent for suspension "LAR depot suspension":** 30mg/2ml

Special Instructions for Octreotide Administration

- **IM (for LAR depot suspension):** avoid deltoid admin. (***do not*** *administer LAR depot IV or SubQ)*
- **IV (for injection solution only): IV push** (undiluted over 3 minutes)**, intermittent IV infusion** (over 15 to 30 minutes), **or continuous IV infusion** over 24 hours.
- **SubQ (for injection solution):** Use the concentration with the smallest volume to deliver the dose to reduce injection-site pain. Rotate injection site; may bring to room temperature before injection.

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