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Newer Classes of Medications for Diabetes Treatment: A Multi-Incident Analysis of Reports from the Community Pharmacy Setting

Diabetes management is complex, necessitating monitoring and frequent medication changes to achieve optimal glycemic targets. Medications for diabetes treatment are estimated to comprise the fifth most commonly prescribed therapeutic class.[1] The newer agents for diabetes also account for several top classes of medications in terms of spending.[2] Safety efforts related to diabetes treatment have focused on insulin and older antihyperglycemic agents; errors related to the newer classes of oral and subcutaneous injectable agents are now being reported.[3] This bulletin is focused on an analysis of community pharmacy incidents involving newer classes of medications for diabetes treatment, and offers strategies to prevent errors.

METHODOLOGY

Reports of incidents with newer classes of antihyperglycemic medications (also known as antidiabetic medications) (Table 1) occurring in the community pharmacy setting were extracted from

TABLE 1. Generic and Brand Names of the 3 Newer Classes of Antidiabetic Medications Included in the Analysis*

Class	Generic Names	Brand Names
Dipeptidyl peptidase IV (DPP-4) inhibitors (first marketed in Canada between 2008 and 2014)	alogliptin	Nesina, Kazano
	linagliptin	Trajenta, Jentadueto
	saxagliptin	Onglyza, Komboglyze
	sitagliptin	Januvia, Janumet
Sodium-glucose cotransporter-2 (SGLT2) inhibitors (first marketed in Canada between 2014 and 2016)	canagliflozin	Invokana, Invokamet
	dapagliflozin	Forxiga, Xigduo
	empagliflozin	Jardiance, Synjardy
Glucagon-like peptide 1 (GLP-1) receptor agonists (first marketed in Canada between 2015 and 2018)	dulaglutide	Trulicity
	liraglutide	Victoza, Xultophy
	semaglutide	Ozempic, Rybelsus
	lixisenatide	Adlyxine, Soliqua

* Drug names were obtained through online queries of the Health Canada Drug Product Database (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp) conducted in the period November 16–23, 2022.

3 ISMP Canada reporting databases (Individual Practitioner Reporting, National Incident Data Repository for Community Pharmacies, and Consumer Reporting) for the period from November 1, 2019, to October 31, 2022. Search criteria included all generic and brand names for the 3 classes of antidiabetic medications available in Canada to extract potentially relevant data.

Reports were excluded from analysis if the incident descriptions were unclear or nonspecific to these classes (e.g., involving errors inputting the incorrect number of refills). The expansion of indications beyond diabetes, for some of the newer medications, has increased the complexity of medication management; there is evidence that some of these medications are being used off-label for weight management. To focus the scope on diabetes treatment, incidents related to Saxenda (liraglutide), which is indicated only for weight loss, and Ozempic (semaglutide), when used off-label for weight loss, were excluded. The analysis was conducted according to the multi-incident analysis methodology outlined in the Canadian Incident Analysis Framework.[4]

QUANTITATIVE FINDINGS

A total of 770 reports were extracted and screened against the exclusion criteria, with 441 incidents included in the final analysis. Figure 1 highlights the antidiabetic products most commonly reported to be involved in these incidents. The majority of incidents were reported as near misses or as having resulted in no harm; only a small proportion (3.6%) were reported as having caused harm to the patient.

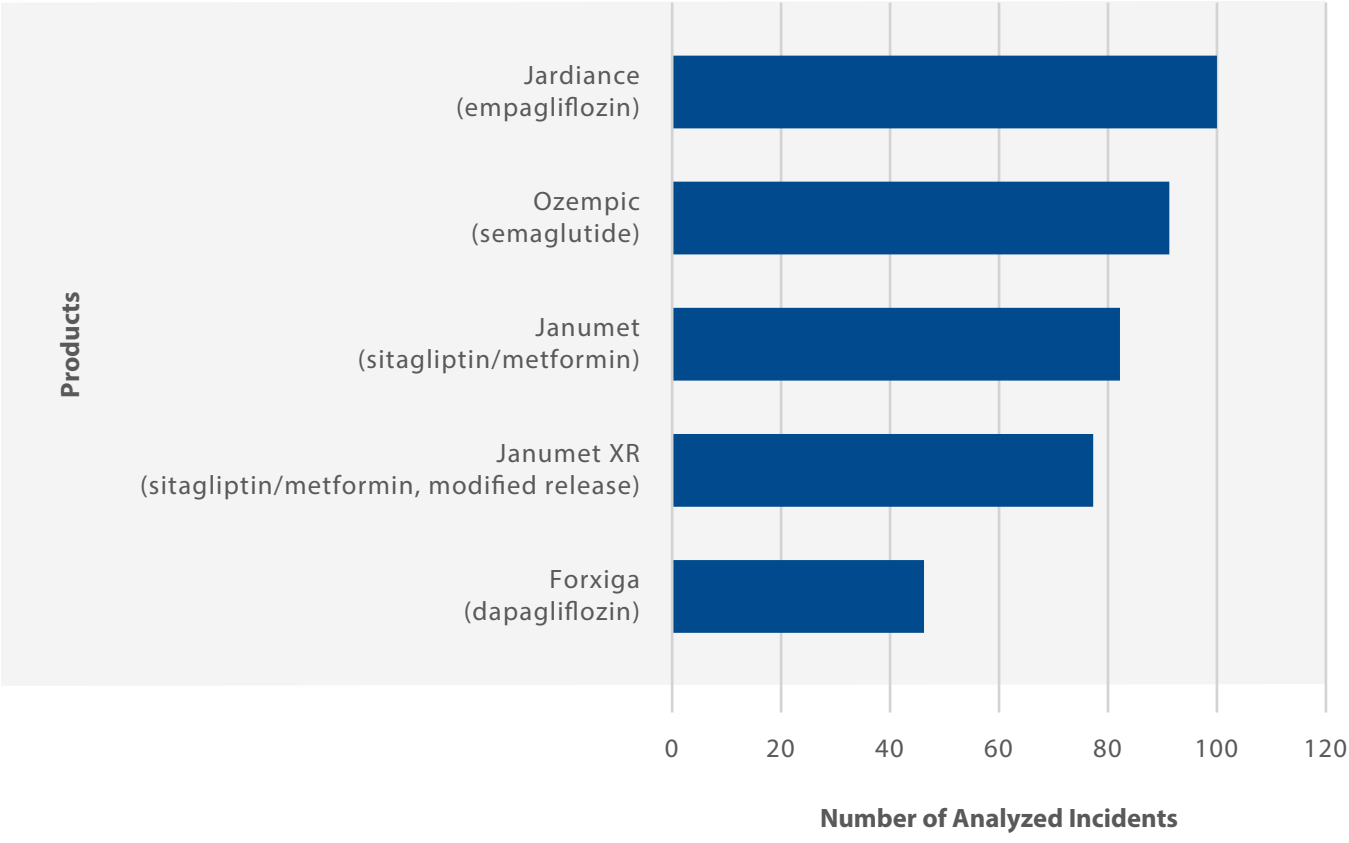

Figure 1. Newer antidiabetic products most commonly reported in analyzed incidents.

QUALITATIVE ANALYSIS

The multi-incident analysis identified 3 themes and several subthemes, as summarized in Figure 2 and discussed below.

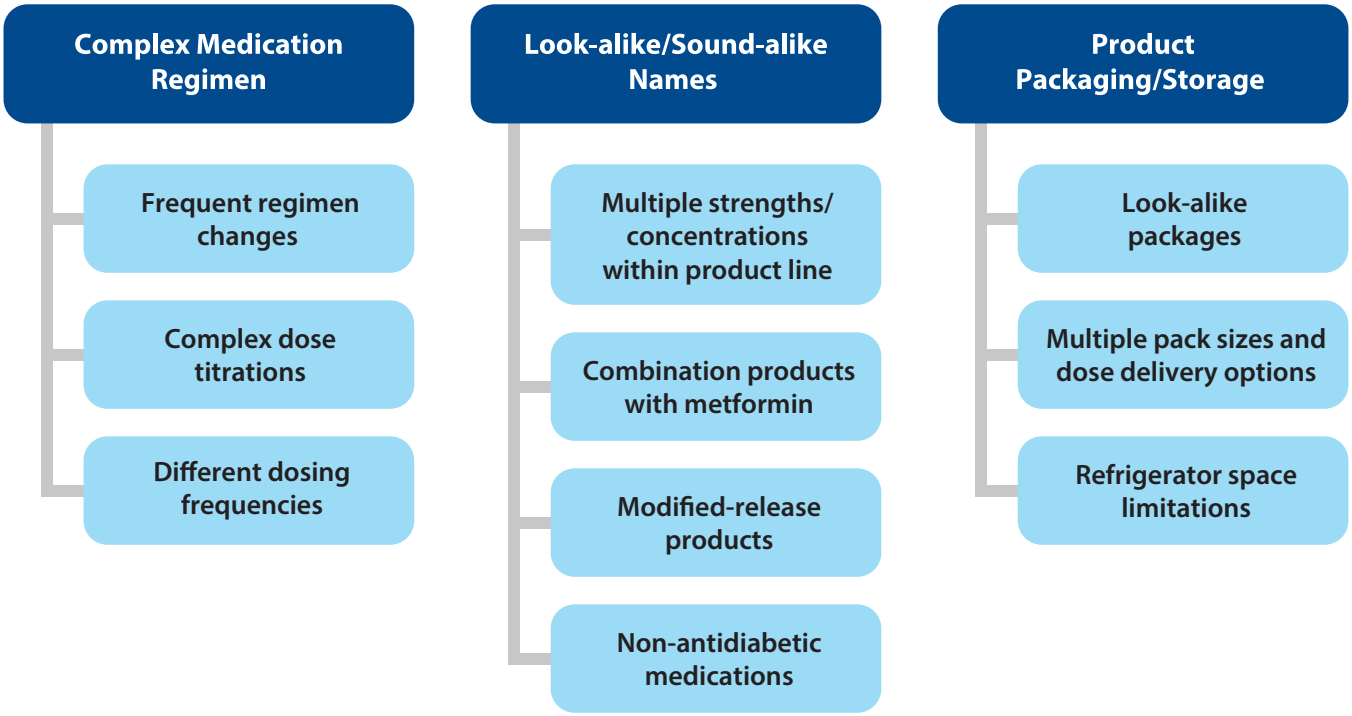

Figure 2. Themes and subthemes identified in the qualitative analysis.

THEME: Complex Medication Regimen

Frequent Regimen Changes

Diabetes management often requires adjustments in a patient's medication regimen. Changes may include dose modifications, addition of an agent from a different medication class, or a switch in medications. A common contributing factor in incidents involving changes to a medication regimen is the copy-over practice, whereby an existing prescription file from the pharmacy system is copied to create an entry for a new prescription.[5,6]

TIP: Ask the patient/caregiver, at every interaction, about glucose management and current antidiabetic medications and doses. Update the patient's profile by inactivating prescriptions for discontinued medications and previous doses.

TIP: Limit the "copy" function to prescriptions that are unchanged from the previous prescriptions in the patient's profile.[5]

TIP: Encourage prescribers to prominently indicate medication and dose changes on the prescription (e.g., STOP [previous medication]; INCREASE dose).

Complex Dose Titrations

Many medications require dose titration. As one example, for the glucagon-like peptide 1 (GLP-1) receptor agonist class (e.g., semaglutide), titration regimens may be required for a period of weeks and may involve different product strengths; as such, the team must be knowledgeable about the various products available and how to use them.

TIP: Design the label instructions with the end-user in mind. Suggestions shared include the following:

- Inputting each step in the titration as a separate prescription (instead of inputting the multi-step titration on one prescription and refilling this prescription); by design, this necessitates patient counselling with each step. If a refill approach is used, incorporate a flag in the system to ensure the pharmacist speaks with the patient at each dose change.
- Numbering each step in the titration (i.e., Step 1, Step 2) for clarity.

TIP: Provide a personalized calendar to support the patient's understanding of the dosing titration.[6] Scan a copy of the calendar into the prescription file.

Incident Example: *A patient brought in a new prescription for a titrating dose of semaglutide, to be filled at a later date (i.e., the prescription was to be placed on hold for the time being). Only the first part of the titration regimen was entered into the pharmacy system because pharmacy staff did not recognize that the titration would involve multiple steps and various products. Fortunately, this error was later identified and corrected.*

Recent reports of incidents described patients mistakenly administering a starting dose (e.g., semaglutide 0.25 mg weekly) instead of continuing semaglutide 0.5 mg weekly following the prescription refill because the refill label continued to include instructions for the initial starting dose.

Different Dosing Frequencies

Lack of knowledge about differences in dosing frequencies (twice daily vs. once daily) between immediate-release and modified-release formulations (e.g., Janumet and Janumet XR) was frequently described as a factor contributing to incidents. Additionally, lack of awareness of the range of dosing regimens among injectable medications in the GLP-1 receptor agonist class (e.g., once-weekly administration of semaglutide[7] and daily administration of liraglutide[8]) was also reported as contributing to the medication errors.

TIP: Develop educational materials (e.g., comparison tables) to inform staff about new medication formulations and dosing regimens, and to provide a quick reference in the pharmacy.

THEME: Look-alike/Sound-alike Names

Many incident reports identified look-alike/sound-alike names that affected the prescribing, order entry, and preparation stages. Confusion was reported in relation to the availability of multiple strengths and/or concentrations (e.g., empagliflozin [Jardiance] as 10 mg and 25 mg doses), combination products (sitagliptin alone [Januvia] vs. sitagliptin/metformin [Janumet]), and modified formulations (e.g., Janumet and Janumet XR), in addition to confusion with non-antidiabetic medications (e.g., Synjardy [empagliflozin/metformin] and Synthroid [levothyroxine]).

TIP: Emphasize key points of product distinction on the hard copy during verification (e.g., Janumet XR).

TIP: Work with information technology (IT) or software vendors to give prominence to key information in pharmacy software (e.g., Janumet XR [sitagliptin/metformin, **modified release**]).

TIP: Encourage prescribers to include both the brand and generic names in electronic and written prescriptions.

The following contributing factors, among others, were identified:

- The look-alike nature and use of brand names (e.g., **Jan**umet, **Jan**uvia, and **Jar**diance) in prescriptions without inclusion of generic names.
- The look-alike nature of generic names (e.g., cana**gliflozin**, dapa**gliflozin**, and empa**gliflozin**) without inclusion of brand names.
- Similarities in the display of medications with look-alike names in prescribing and pharmacy order entry systems.

THEME: Product Packaging/Storage

Look-alike Packages

One-third of the analyzed reports identified similar packaging as contributing to medication errors. Figure 3 shows images of product pairs that were involved in some of the incidents analyzed.

TIP: Incorporate barcode scanning into pharmacy processes, including inventory management and dispensing.

TIP: Separate look-alike medication packages using a shelf divider or individual bins.

Multiple Pack Sizes and Dose Delivery Options

Pharmacy teams may not be aware that certain products are available in different pack sizes, with capability of delivering different doses, which may lead to the dispensing of incorrect quantities. For example, liraglutide (Victoza) is available as a multidose pen capable of delivering 3 different doses (0.6 mg, 1.2 mg, or 1.8 mg), and the pens are packaged in 3 different pack sizes (1 pen, 2 pens, or 3 pens). A single pen can deliver 30 doses of 0.6 mg or 10 doses of 1.8 mg. As another example, semaglutide (Ozempic) is available as three different pens: a 2 mg pen that delivers 0.25 mg and 0.5 mg doses; a 4 mg pen that delivers 1 mg doses; and an 8 mg pen (approved, but currently not marketed in Canada) that delivers 2 mg doses.

TIP: Incorporate an independent double check into the dispensing process to confirm calculations for the dose and quantity to dispense.

TIP: Develop educational materials to inform staff about these product pack sizes and dose delivery options, and to provide a quick reference in the pharmacy.

Figure 3. Examples of look-alike packaging described in incident reports.

Incident Example: *A prescription for liraglutide (Victoza) 1.2 mg once daily for 90 days was filled with 1 box of 3 pens. Each pen delivers 15 doses of 1.2 mg; therefore, for the specified treatment duration, 6 pens (2 boxes) were required. The pharmacist corrected the quantity before dispensing it to the patient.*

Refrigerator Space Limitations

Newer antidiabetic medications for injection (e.g., semaglutide [Ozempic], liraglutide [Victoza], and dulaglutide [Trulicity]) are stored in the refrigerator before the package is opened and also after a prescription is filled (but before it is provided to the patient). Selecting the wrong patient's filled prescription from the refrigerator was a commonly reported error. These reports highlighted the need to assess and better organize refrigerator space for filled prescriptions to avoid selection errors.

TIP: Organize filled, refrigerated prescriptions alphabetically by patient surname.

TIP: Position filled products in the refrigerator in a way that makes the label with the patient's name visible.

CONCLUSION

This thematic analysis highlights errors related to DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 receptor agonists occurring in the community pharmacy setting and shares selected safety tips. Key considerations include modifying pharmacy software display for look-alike product names, implementing barcode scanning technology in pharmacy processes, organizing refrigerator space to ensure separation and visibility of products and individual prescriptions, and reviewing label instructions with patients at prescription pick-up to ensure the information matches what the patient expects to receive. Community-based teams, including prescribers, nurses, pharmacists, and pharmacy technicians, are encouraged to review their own incidents, in addition to the learning from this analysis, to guide improvements to their medication-use process.

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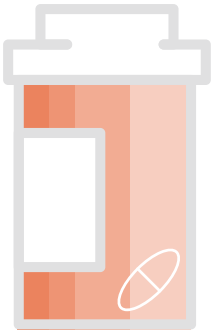
Pharmacy Automatic Refill Programs – Improvements Needed

Automatic refill programs are designed to provide patients with continuity of medication supply. This automated process, which is used by many community pharmacies, prompts the pharmacy team to refill long-term medications without requiring the patient to request a refill. Patient experiences shared with SafeMedicationUse.ca have pointed to medication safety concerns with these programs.

In one case, the person was informed through the pharmacy's auto-refill program that a medication had been refilled. However, the medication had previously been discontinued by the prescriber. Fortunately, the patient knew about the change and did not take the medication. The error occurred a second time when the automatic system refilled the medication again at a later date.

In the second case, the person was not aware of having been asked to sign up or having been added to the auto-refill program. Instead, the person found out when they were asked to pick up a medication refill that had not been requested and was not needed.

SafeMedicationUse.ca has the following tips for practitioners to help prevent errors related to automatic refill programs:



- Obtain permission from patients before enrolling them in an auto-refill program.
- Confirm the following information with the patient when they pick up their medication(s) to ensure mutual understanding of the following aspects of their therapy:
  - dose changes
  - discontinued medications
  - required medications and directions for use.
- Keep medication profiles accurate and up-to-date. Inactivate previous medications or doses of medications from the patient's profile when changes are made to the patient's regimen. Medication reviews can help to ensure that profiles are up to date.
- Review and strengthen the organizational/pharmacy return-to-stock process to prevent errors. An increased need to return filled medications to stock is a consequence of automatic refill programs.

The SafeMedicationUse.ca newsletter is available here:
https://safemedicationuse.ca/newsletter/downloads/202301NewsletterV14N01-Auto-refill.pdf

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