Institute for Safe Medication Practices Canada
REPORT MEDICATION INCIDENTS
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A KEY PARTNER IN
CMIRPS Canadian Medication Incident Reporting and Prevention System
SCDPIM Système canadien de déclaration et de prévention des incidents médicamenteux

ISMP Canada Safety Bulletin

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Safety Checklist: A New Approach to Promote Safe Prescribing of and Counselling for DIANE-35 and Its Generics

Health Canada, in collaboration with the Institute for Safe Medication Practices Canada, the Canadian Pharmacists Association, and the Canadian Dermatology Association, has developed a practical checklist to assist healthcare professionals with the safe prescribing of DIANE-35 (cyproterone acetate and ethinyl estradiol) and its generics (known as CyEstra-35 and Novo-cyproterone/ethinyl estradiol). The checklist also promotes the communication of associated risk factors for and symptoms of thrombosis (formation of blood clots) to patients.

According to the product monographs, DIANE-35 and its generics are potent antiandrogen and estrogen combination products indicated in Canada "for the treatment of women with severe acne, unresponsive to oral antibiotic and other available treatments, with associated symptoms of androgenization, including seborrhea and mild hirsutism."[1-3] These products are considered second-line therapy, meant to be used on a short-term basis only after failure of other, less potent anti-acne therapy.[4] However, DIANE-35 also has contraceptive activity, and it is estimated that as much as 35% to 40% of DIANE-35 used in Canada may have been prescribed for long-term birth control, an off-label (unapproved) indication.[4]

A rare but well-documented risk of thrombosis has been observed with the use of DIANE-35 and combined oral contraceptive products.[4] This risk is increased by the presence of comorbidities and lifestyle factors such as hypertension, obesity, smoking, and prolonged immobilization.[1,4] Although the incidence of thrombosis associated with DIANE-35 and its generics was similar to that of some combined oral contraceptives,[4] this off-label use could expose Canadian patients who might otherwise have been offered lower-risk contraceptive choices to an unnecessary risk for thrombosis.

Health Canada released a drug safety review summary for DIANE-35 and its generics[4] as part of the newly launched Regulatory Transparency and Openness Framework, an initiative to help Canadian patients and prescribers to make informed decisions through improved access to timely drug information, risk data, and open and transparent decision-making processes.[5,6] In this review summary, Health Canada reported that when DIANE-35 and its generics are used in appropriate clinical situations for their approved indications, their benefits continue to outweigh their risks.[4]

The checklist was collaboratively developed and released with the framework's first drug safety summary review to help healthcare professionals in identifying the patient population for whom DIANE-35 and its generics can appropriately be prescribed. The checklist promotes awareness of key risk factors for thrombosis and offers focused counselling topics so that patients and care providers can identify critical symptoms warranting medical attention. The checklist also aims to prevent incidents where DIANE-35 or its generics are mistakenly used in addition to an oral contraceptive product.

The checklist and the drug safety review summary are intended to support all patients and healthcare professionals in making informed decisions that enhance safety and minimize risks associated with the use of DIANE-35 and its generics.

Figure 1. Checklist for prescribing of and counselling for DIANE-35 and its generics*

Suggested Prescriber/Counselling Checklist for DIANE-35 (cyproterone acetate/ethinyl estradiol) and its generics

DIANE-35 (cyproterone acetate and ethinyl estradiol) is indicated for the treatment of women with severe acne, unresponsive to oral antibiotic and other available treatments, with associated symptoms of androgenization, including seborrhea and mild hirsutism.

Note: **DIANE-35 is NOT indicated for the purposes of contraception.**

This suggested checklist can assist you when prescribing **DIANE-35** (cyproterone acetate/ethinyl estradiol) and its generics. Please see the Canadian Product Monograph (PM) for full prescribing information on indications, warnings and precautions, and adverse events (http://www.bayer.ca/files/DIANE-35-PM-ENG-11FEB2014-169560.pdf).

If any of the criteria below is checked YES, DO NOT prescribe DIANE-35

MEDICAL CONDITIONS/MEDICATIONS	YES	NO
Concomitant use with another hormonal contraceptive	☐	☐
History of or actual thrombophlebitis or thromboembolic disorders	☐	☐
History of or actual cerebrovascular disorders	☐	☐
History of or actual myocardial infarction or coronary arterial disease	☐	☐
History of cholestatic jaundice, previous or existing liver tumours or active liver disease	☐	☐
Smoker AND age > 35 years	☐	☐
Known or suspected carcinoma of the breast or estrogen-dependent neoplasia	☐	☐
Pregnancy is suspected or diagnosed	☐	☐
Any ocular lesion arising from ophthalmic vascular disease, such as partial or complete loss of vision or defect in visual fields	☐	☐
Severe diabetes with vascular changes	☐	☐
History of migraine with aura	☐	☐
Very high blood pressure e.g., systolic > 160 or diastolic > 100 mmHg	☐	☐
Very high blood lipids	☐	☐

THE FOLLOWING POTENTIAL ADDITIONAL RISK FACTORS HAVE BEEN DISCUSSED WITH THE PATIENT:			
☐	Smoking	☐	Age over 35 years
☐	Hypertension	☐	Diabetes
☐	Migraine	☐	Obesity BMI > 30 kg/m2
☐	Major surgery or a period of prolonged immobilization		

PATIENT HAS BEEN COUNSELLED TO SEEK MEDICAL ATTENTION IF THE FOLLOWING SYMPTOMS OCCUR:	
☐	Sudden unexplained breathlessness or rapid breathing; severe pain in the chest which may increase with deep breathing; sudden cough without an obvious cause (which may bring up blood) – indicating potential pulmonary embolism.
☐	Severe pain or swelling in either leg that may be accompanied by tenderness, warmth or changes in the skin colour such as turning pale, red or blue which may indicate a deep vein thrombosis.
☐	Chest pain, often acute, but may include just discomfort, pressure, heaviness, upper body discomfort, radiating to back, jaw, throat, or arm together with feelings of indigestion or choking, sweating, nausea, vomiting or dizziness. These symptoms could indicate a heart attack.
☐	Face, arm or leg weakness or numbness, especially on one side of the body; trouble speaking or understanding; sudden confusion; sudden loss of vision or blurred vision; severe headache/migraine that is worse than normal. This may indicate a stroke.

Health Canada Santé Canada

ISMP CANADA Institute for Safe Medication Practices Canada / L'Institut pour l'utilisation sécuritaire des médicaments du Canada

Canadian Dermatology Association / Association canadienne de dermatologie

Canadian Pharmacists Association / Association des pharmaciens du Canada

* Available from: http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/review-examen/checklist-verification-diane-35-eng.php.

Reported Confusion with Insulin Syringe Labelling

ISMP Canada recently received a near-miss incident report involving an incorrect insulin dose due to confusion related to labelling of insulin syringes.

Medication Incident

In this incident, a nurse interpreted a label reading "0.5 mL/cc" on the BD 0.5 mL insulin syringe (Figure 1) to mean "0.5 mL per cc" (cubic centimetre). This confusion led to preparation of an incorrect dose. As a result, a BD 1 mL insulin syringe labelled with "1 mL/cc" (Figure 2) was used instead, as this label was thought to be less confusing. The 1 mL/cc syringe seemed more intuitive to use, which allowed a correct dose to be drawn up, and subsequently avoided a medication error.

Both syringes also had "U-100 Insulin" printed on them, and it was later determined that none of the healthcare professionals at the site had a clear understanding of the intended meaning of "U-100." The reporter wanted to broadly share this information so that others could be alerted, in the hopes that similar incidents would be prevented.

Background

The "0.5 mL/cc" marking on the 0.5 mL syringe is meant to indicate that the syringe will hold a volume of 0.5 millilitres (mL) **or** 0.5 cubic centimeters (cc). These 2 volumes are effectively equivalent, but are expressed in different systems of units. On the BD syringes, the slash character ("/") does **not** indicate the word "per" but **rather** the word "or" (i.e., 0.5 mL or 0.5 cc).

The term "U-100 Insulin" refers to the concentration of insulin to be used with the syringe, i.e., 100 units of insulin per millilitre (100 units/mL). Canadian healthcare practitioners are most familiar with U-100 insulin; although U-500 (500 units/mL) is available and is occasionally prescribed.[1] U-500 insulin is 5 times more concentrated than U-100 insulin[1] and is generally reserved for patients who are insulin-resistant.[2] Other concentrations, such as U-40 (i.e., 40 units/mL), are also in current use around the world.[1]

A specific syringe is designed for use with each concentration of insulin; thus, for administration of U-100 insulin, a U-100 insulin syringe should be used. For ease of measuring doses, syringes are available in different sizes. For example, U-100 syringes come in sizes that can hold volumes of 0.3 mL, 0.5 mL, and 1 mL. When used for U-100 insulin (as intended), these syringes can hold up to 30 units, 50 units, and 100 units, respectively.

Recommendations

Facilities and Practitioners

- Share this alert widely with practitioners who administer insulin to enhance awareness regarding the labelling of insulin and insulin syringes.[1]
    - o An insulin syringe labelled as "U-100" or "U-500" is intended for use with any vial of insulin that has a concentration of 100 units/mL or 500 units/mL, respectively.
    - o As long as the correct insulin concentration and its corresponding syringe are used, any syringe size (e.g., 0.3 mL, 0.5 mL, or 1 mL) can be selected. The syringe size determines how many units of insulin the syringe can hold (i.e., 0.3 mL for doses of 30 units or less, 0.5 mL for doses of 50 units or less, and 1 mL for doses 100 units or less).

Manufacturers

- To prevent labelling confusion, avoid use of "/" (the slash character) to indicate "or". In healthcare settings, this symbol is primarily used to indicate "per".
- To express medication volumes, use only metric units of measure, such as "L" for litre or "mL" for millilitre. The term "cc" can be mistaken for "u" (units) according to the ISMP Canada's list of dangerous abbreviations, dose designations and symbols.[3]
- Consider employing usability testing to ensure that end users correctly interpret the meaning intended by wording used by product labels.[4]

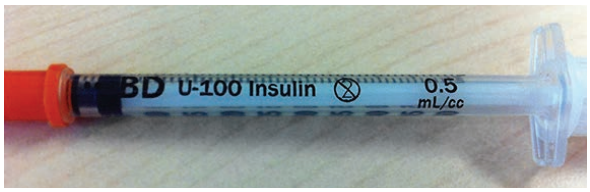

Figure 1. BD 0.5 mL U-100 insulin syringe for use with insulin 100 units/mL.

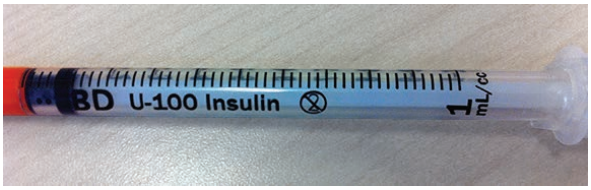

Figure 2. BD 1 mL U-100 insulin syringe for use with insulin 100 units/mL.

ISMP Canada contacted BD and their response has been positive to the reported concerns. BD is currently making plans to remove the 'cc' from their insulin syringe label.

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3. Do Not Use Dangerous Abbreviations, Symbols and Dose Designations. Toronto (ON): ISMP Canada; 2006 Jul [cited 2014 May 25]. Available from: http://www.ismp-canada.org/download/ISMPCanadaListOfDangerousAbbreviations.pdf
4. Usability testing in proactive risk assessments. ISMP Can Saf Bull. 2012 [cited 2013 Aug 7];12(11):1-4. Available from: http://www.ismp-canada.org/download/safetyBulletins/2012/ISMPCSB2012-11_Usability_Testing.pdf

This segment of the bulletin describes a recent SafeMedicationUse.ca publication from ISMP Canada's Consumer Program.

June 2014 - Newsletter:

Preventing Harm from Drug-Food Interactions

Although known drug-drug interactions are routinely screened by pharmacists, healthcare practitioners also need to be cognizant of the impact food can have on medications (i.e., a drug-food interaction). In an incident reported to SafeMedicationUse.ca, a consumer experienced adverse effects as a result of a drug-food interaction between indapamide and psyllium husk. Changes in the consumer's routine of drinking a smoothie containing psyllium husk after taking indapamide had interfered with the absorption of the medication, leading to fluctuations of the consumer's blood pressure.

The SafeMedicationUse.ca newsletter provides tips for consumers, including the importance of carefully reading product labels and being aware of the possibility of interactions between food products and medications. The newsletter advises practitioners to ask about patients' dietary habits when appropriate, in order to identify and avoid a drug-food interaction.

For additional recommendations for both consumers and practitioners, read the complete newsletter at:

www.safemedicationuse.ca/newsletter/newsletter_DrugFoodInteractions.html

References:

1. DIANE-35 [product monograph]. Toronto (ON): Bayer Inc.; [revised 2014 Feb 11; cited 2014 Apr 24]. Available from: http://www.bayer.ca/files/DIANE-35-PM-ENG-11FEB2014-169560.pdf
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CMIRPS SCDPIM
Canadian Medication Incident Reporting and Prevention System
Système canadien de déclaration et de prévention des incidents médicamenteux

The Canadian Medication Incident Reporting and Prevention System (CMIRPS) is a collaborative pan-Canadian program of Health Canada, the Canadian Institute for Health Information (CIHI), the Institute for Safe Medication Practices Canada (ISMP Canada) and the Canadian Patient Safety Institute (CPSI). The goal of CMIRPS is to reduce and prevent harmful medication incidents in Canada.

HIROC

The Healthcare Insurance Reciprocal of Canada (HIROC) provides support for the bulletin and is a member owned expert provider of professional and general liability coverage and risk management support.

ismp CANADA

The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada's mandate includes analyzing medication incidents, making recommendations for the prevention of harmful medication incidents, and facilitating quality improvement initiatives.

Report Medication Incidents

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ISMP Canada strives to ensure confidentiality and security of information received, and respects the wishes of the reporter as to the level of detail to be included in publications.

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