Federal Legislation

November 2011

Please make all necessary changes on your copies of the National Drug Schedules and applicable Federal Legislation. Updated copies of these documents are available on the NAPRA website at www.napra.ca

NAPRA National Drug Schedules Notice Board

NDSAC Final Recommendations for NSAIDs available on the Canadian market (excluding ASA and acetaminophen)
November 16, 2011

UPDATED November 18, 2011

The Initial Recommendations made by the National Drug Scheduling Advisory Committee (NDSAC) on September 11-12, 2011 for the scheduling of

- Ibuprofen and its salts containing 400 mg or less per oral dosage unit (when sold in package sizes of up to 18,000 mg) Unscheduled (no change)

- Ibuprofen and its salts containing 400 mg or less per oral dosage unit (when sold in package sizes exceeding 18,000 mg) Schedule III (from Unscheduled)

- Naproxen sodium 220 mg per oral dosage unit (when sold in products labeled with a recommended maximum daily dose of 440 mg, and in package sizes of up to 6,600 mg) Unscheduled (no change)

- Naproxen sodium 220mg per oral dosage unit (when sold in products labelled with a recommended maximum daily dose of 440 mg, and in package sizes exceeding 6,600 mg) Schedule III (no change)

- Diclofenac diethylamine in preparations for topical use on the skin in concentrations of not more than the equivalent of 1% diclofenac Unscheduled (no change)

were finalized effective November 16, 2011. Final approval of the Initial Recommendations were made by NAPRA’s Executive Committee, in consideration of comments received during the 30-day review period.

Further to the above notice, please note that the National Drug Schedules will be amended effective February 17, 2012.

NDSAC Meeting of December 4-5, 2011
October 06, 2011

The proposed meeting of the National Drug Scheduling Advisory Committee (NDSAC) for December 4-5, 2011 is cancelled.

November 2011
For a complete listing of the most recent changes to the National Drug Schedules, visit the Drug Schedules Notice Board at www.napra.ca
The next meeting for the Committee is scheduled for March 4-5, 2012. The deadline to receive submissions for a drug scheduling application for this meeting is by end of day Wednesday, January 4, 2012.
ANNOUNCEMENT
District Five Individual Study Grant

Criteria: District Five of NABP/AACP will make available grant money, not to exceed $3,000.00, to award a stipend within the District to study a topic which benefits students, pharmacy education or pharmacy practice. Topics of interest to the Boards and Colleges in District Five are suggested, but researchers will not be limited to these topics. The Grant Recipient or designee is expected to present their report or findings at the District V Annual Meeting in the year following the award. It is expected that the College or Board sponsoring the recipient will pay for the cost of attendance at the meeting. It is the policy of District V NABP/AACP that no indirect costs will be funded out of grant awards. Any funds not expended for the awarded purpose, must be returned to District V.

Eligibility: Individual students with faculty or Board of Pharmacy advisor, Student organizations with faculty or Board of Pharmacy advisor, Faculty members, and Board of Pharmacy members.

Application: Applications should not exceed five pages in length and should include the following information:
1. Rationale (background and reason for doing the study)
2. Specific goals of study (what are you trying to achieve)
3. Names of personnel involved.
4. Methods by which goals will be attained.
5. Date of completion. (Prior to the August 2012 District Five NABP/AACP meeting so that the results can be presented there.)
6. Justification of use for funds received. (Budget)

Selection of Recipient:
The District Secretary/Treasurer will call for applications to Deans, department heads, and ASP advisors at member colleges and to Boards. Applications will be due to the Secretary/Treasurer (Howard Anderson) by March 31, 2011 and distributed to the District Five Study Grant Committee. Selection of the recipient will be made by May 1, 2011 and the recipient notified.

Potential Topics:
- **Continuity of Care:** Examination of the impact of transfer of information (Hospital pharmacy to patient’s community pharmacy upon discharge) on patient outcomes and on patient perceptions of pharmacists.
- **Reimbursement for Pharmaceutical Care and Medication Therapy Management Services:** Establishing effective strategies for approaching/charging patients for these services.
- **Pharmacist Prescriptive Authority:** Establish effective strategies and collaborative partnerships with physicians authorizing pharmacists to prescribe drugs and monitor therapy.
- **Innovations in Continuing Pharmaceutical Education:** Establish innovative and creative programs for practicing pharmacists including nontraditional educational formats, distance learning, use of technology, telemedicine, certificate programs, and various active learning techniques and measure the impact/outcome of these innovative strategies on pharmacist practices and student learning.
- **Develop Interdisciplinary or Innovative Models of Practice and Education.**
- **Medication Errors and Patient Safety**

Applications are to be submitted to:
Howard Anderson * Secretary/Treasurer * District Five NABP/AACP * P O Box 1354 * Bismarck ND 58502-1354
Or E-mail to: ndboph@btinet.net
HEALTH CANADA ADVISORIES

All Health Canada Advisories, Warnings and Recalls for health professionals and the public may be accessed directly through MedEffect Canada at:

http://www.hc-sc.gc.ca/dhp-mps/medeff/index_e.html

At this site, pharmacists should subscribe directly to MedEffect e-Notice to receive the latest advisories, warning and recalls and the Canadian Adverse Reaction Newsletter (CARN) as they are issued by Health Canada. These alerts are an important source of information regarding the post-market safety and effectiveness of health and drug products and pharmacists are reminded of their responsibility to be aware of this vital information.

Pharmacy Managers are reminded to continue to maintain a system within the pharmacy for the communication of all important notices to employees from the MPhA and MedEffect Canada.

For Health Professionals and Consumers

December

Multaq (dronedarone) - Information on Important Revisions to Product Monograph - Sanofi-aventis Canada Inc.

For Health Professionals [2011-12-08]
For the Public [2011-12-08]

AVASTIN (bevacizumab) - Reports of Cases of Severe Eye Inflammation Leading to Blindness Following Use in the Eye - Hoffmann-La Roche Ltd.

For Health Professionals [2011-12-07]
For the Public [2011-12-07]

Ursodiol (ursodeoxycholic acid, UDCA) - Association of High-Dose with Serious Liver Side Effects - Aptalis Pharma Canada Inc., Dominion Pharmacal, Pharmascience Inc., Pharmel Inc., Teva Canada Ltd.

For Health Professionals [2011-12-05]
For the Public [2011-12-05]

Sublinox (zolpidem tartrate) - Association with complex sleep behaviours - Meda Valeant Pharma Canada Inc.

For Health Professionals [2011-12-05]
For the Public [2011-12-05]

November

"Stiff One Hard 169" Recalled From the Canadian Market: May Pose Serious Health Risks to Canadians [2011-11-30]

Supplement to The Manitoba Pharmaceutical Association Newsletter December, 2011
Retain a copy for reference.
Avastin (bevacizumab) - Health Canada has Suspended Approval for Use in Metastatic Breast Cancer - Hoffmann-La Roche Ltd.

For Health Professionals [2011-11-29]

CooperVision Expands List of Contact Lenses [2011-11-16]

Avastin (bevacizumab) - Higher Incidence of New Cases of Ovarian Failure Observed in Premenopausal Women - Hoffmann-La Roche Limited

For Health Professionals [2011-11-14]

For the Public [2011-11-14]

Pradax (dabigatran etexilate) and Plavix (clopidogrel bisulfate) - Risk of Potential Patient Harm Associated with Brand Name Confusion - Boehringer Ingelheim (Canada) Ltd. and sanofi-aventis Canada Inc.

For Health Professionals [2011-11-08]

For the Public [2011-11-08]

Fluoroquinolone antibiotics: patients with myasthenia gravis may risk increased muscle weakness [2011-11-07]

October

Xigris (drotrecogin alfa [activated]) - Worldwide Withdrawal - Eli Lilly Canada Inc.

For Health Professionals [2011-10-28]

Notice to Hospitals [2011-10-28]

For the Public [2011-10-28]

SynchroMed II Implantable Drug Infusion Pumps - Urgent Medical Device Correction Letter - Medtronic of Canada Ltd.

For Health Professionals [2011-10-26]

Xigris (drotrecogin alfa) withdrawn worldwide [2011-10-25]

STRATTERA (atomoxetine) - Association with Increased Blood Pressure and Increased Heart Rate - Eli Lilly Canada Inc.

For Health Professionals [2011-10-24]

For the Public [2011-10-24]

Citalopram: Health Canada reviewing dose-related heart risk [2011-10-13]

September

Plavix (blood thinner): New recommendations for use with PPIs (antacids) [2011-09-22]

Trasylol (aprotinin) - Important New Safety Information - Bayer Inc.

Notice to Hospitals [2011-09-21]

For the Public [2011-09-21]

Health Canada decision on Trasylol (aprotinin) [2011-09-21]

GnRH Agonists: Heart-related Risk in Men Treated for Prostate Cancer [2011-09-08]

Mesna (Uromitexan), Multi-Dose Vials - Association with Fatal Gasping Syndrome in Neonates and Infants - Baxter Corporation
August

Sprycel (dasatinib) - Safety Information Regarding Pulmonary Arterial Hypertension (PAH) - Bristol-Myers Squibb Canada
  For Health Professionals [2011-08-30]
  For the Public [2011-08-30]

Central Vascular Access Devices - Complications of Catheter Pinch-off
  Notice to Hospitals [2011-08-23]

Certain Injectable and Inhalational Sterile Drugs Imported from Ben Venue Laboratories Inc. - Potential Supply Shortage
  Notice to Hospitals [2011-08-18]

Recent Advisories Warnings and Recalls

Multaq (dronedarone) - Information on Important Revisions to Product Monograph - Sanofi-aventis Canada Inc.
  For Health Professionals [2011-12-08]
  For the Public [2011-12-08]

AVASTIN (bevacizumab) - Reports of Cases of Severe Eye Inflammation Leading to Blindness Following Use in the Eye - Hoffmann-La Roche Ltd.
  For Health Professionals [2011-12-07]
  For the Public [2011-12-07]

Yasmin and Yaz (drospirenone): Updated information on increased risk of blood clots
  [2011-12-05]

Ursodiol (ursodeoxycholic acid, UDCA) - Association of High-Dose with Serious Liver Side Effects - Aptalis Pharma Canada Inc., Dominion Pharmacal, Pharmascience Inc., Pharmel Inc., Teva Canada Ltd.
  For Health Professionals [2011-12-05]
  For the Public [2011-12-05]

Sublinox (zolpidem tartrate) - Association with complex sleep behaviours - Meda Valeant Pharma Canada Inc.
  For Health Professionals [2011-12-05]
  For the Public [2011-12-05]

Three Additional Unauthorized Health Products Tested: May Pose Serious Health Risks
  [2011-12-02]

"Stiff One Hard 169" Recalled From the Canadian Market: May Pose Serious Health Risks to Canadians [2011-11-30]

Avastin (bevacizumab) - Health Canada has Suspended Approval for Use in Metastatic Breast Cancer - Hoffmann-La Roche Ltd.
  For Health Professionals [2011-11-29]

For Health Professionals [2011-09-06]
For the Public [2011-09-06]
Health Canada directs Hoffmann-La Roche to remove use of Avastin (bevacizumab) for the treatment of metastatic breast cancer from the product label  [2011-11-29]

CooperVision Expands List of Contact Lenses  [2011-11-16]

Avastin (bevacizumab) - Higher Incidence of New Cases of Ovarian Failure Observed in Premenopausal Women - Hoffmann-La Roche Limited

  For Health Professionals  [2011-11-14]
  For the Public  [2011-11-14]

Foreign Product Alert - Zhui Feng Bao Wei San  [2011-11-09]

Foreign Product Alert - Metabolic Advantage  [2011-11-09]

Foreign Product Alert - Majun Dua Istimewa, Raja Maajun-Jerat Dan Seret Angin, and Horkut Chooi Foong Hor Lok Tan  [2011-11-09]

Foreign Product Alert - Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al, and Pao Ni Kang  [2011-11-09]

Foreign Product Alert - Slimming Kapsul  [2011-11-09]

Foreign Product Alert - Pancre-Plus  [2011-11-09]

Foreign Product Alert - Maxidus capsules, Chao Jimengnan SuperPowerful Man tablets, Fu Yuan Chun capsules, and Qing Tian Zhu tablets  [2011-11-09]

Advisories, Warnings and Recalls for the Public - 2011

December

Multaq (dronedarone) - Information on Important Revisions to Product Monograph - Sanofi-aventis Canada Inc.

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  For the Public  [2011-12-05]

Sublinox (zolpidem tartrate) - Association with complex sleep behaviours - Meda Valeant Pharma Canada Inc.

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Pradax (dabigatran etexilate) and Plavix (clopidogrel bisulfate) - Risk of Potential Patient Harm Associated with Brand Name Confusion - Boehringer Ingelheim (Canada) Ltd. and sanofi-aventis Canada Inc.

For Health Professionals [2011-11-08]

For the Public [2011-11-08]

Fluoroquinolone antibiotics: patients with myasthenia gravis may risk increased muscle weakness [2011-11-07]

Colgate Motion Electric Toothbrush Recall [2011-11-02]

October

Xigris (drotrecogin alfa [activated]) - Worldwide Withdrawal - Eli Lilly Canada Inc.

For Health Professionals [2011-10-28]

Notice to Hospitals [2011-10-28]

For the Public [2011-10-28]

Brewer's Yeast Tablets: May Pose Serious Health Risks to Canadians with Milk Allergies [2011-10-25]

Xigris (drotrecogin alfa) withdrawn worldwide [2011-10-25]

STRATTERA (atomoxetine) - Association with Increased Blood Pressure and Increased Heart Rate - Eli Lilly Canada Inc.
For Health Professionals [2011-10-24]
For the Public [2011-10-24]

Foreign Product Alert - SXL Sexcellence sachets [2011-10-17]
Foreign Product Alert - OxyELITE Pro capsules and Pure Fat Three Days Reduce Weight capsules [2011-10-17]
Foreign Product Alert - Huo Li Bao and Ren Sem Tu Chon Chin Kuo Pill [2011-10-17]

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Unlicensed HIV Home Test Kit: Accu-HIV 1 & 2 Saliva Test [2011-09-12]
GnRH Agonists: Heart-related Risk in Men Treated for Prostate Cancer [2011-09-08]
Mesna (Uromitexan), Multi-Dose Vials - Association with Fatal Gasping Syndrome in Neonates and Infants - Baxter Corporation
   For Health Professionals [2011-09-06]
   For the Public [2011-09-06]
Bi Yan Pian Recalled Due to Excessive Amount of Mercury [2011-09-01]

August

Sprycel (dasatinib) - Safety Information Regarding Pulmonary Arterial Hypertension (PAH) - Bristol-Myers Squibb Canada
   For Health Professionals [2011-08-30]
   For the Public [2011-08-30]
Potential Dangers of Using Donor Semen from Questionable Sources [2011-08-29]
New Emergency Compounding Instructions for Pharmacists for Oral Suspension of TAMIFLU (oseltamivir phosphate)

New Strength for Tamiflu for Oral Suspension
6 mg/mL Now Available
- 6mg/mL harmonizes concentration for both emergency compounding and pre-manufactured concentration
- FDA has approved simplified steps for emergency compounding
- Simple syrup has been added as an additional vehicle option

*The new oral suspension will help simplify prescribing, dosing and administration.*

Rx only
(Directions are included in the Prescribing Information)

Emergency Compounding of an Oral Suspension from TAMIFLU 75 mg Capsules (Final Concentration 6 mg/mL).

The following directions are provided for use only during emergency situations. These directions are not intended to be used if the FDA-approved, commercially manufactured TAMIFLU for oral suspension is readily available from wholesalers or the manufacturer.

Compounding an oral suspension with this procedure will provide one patient with enough medication for a 5-day course of treatment or a 10-day course of prophylaxis.

Commercially manufactured TAMIFLU for oral suspension (6 mg/mL) is the preferred product for pediatric and adult patients who have difficulty swallowing capsules or where lower doses are needed. In the event that TAMIFLU for oral suspension is not available, the pharmacist may compound a suspension (6 mg/mL) from TAMIFLU 75 mg capsules using one of these vehicles: Cherry Syrup (Humco®), Ora-Sweet® SF (sugar-free) (Paddock Laboratories), or simple syrup. Other vehicles have not been studied. This compounded suspension should not be used for convenience or when the FDA-approved TAMIFLU for oral suspension is commercially available.

First, calculate the total volume of an oral suspension needed to be compounded and dispensed for each patient. The total volume required is determined by the weight of the patient (see Table 2 in Prescribing Information).

Second, determine the number of capsules and the amount of water and vehicle (Cherry Syrup, Ora-Sweet® SF, or simple syrup) that are needed to prepare the total volume (determined from Table 2 in PI: 75 mL, 100 mL, 125 mL, or 150 mL) of compounded oral suspension (6 mg/mL) (see Table 3 in PI).

<p>| Volume of an Oral Suspension (6 mg/mL) Needed to be Compounded Based Upon the Patient’s Body Weight |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|</p>
<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Weight (lbs)</th>
<th>Total Volume to Compound per Patient (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 kg or less</td>
<td>33 lbs or less</td>
<td>75 mL</td>
</tr>
<tr>
<td>16 thru 23 kg</td>
<td>34 thru 51 lbs</td>
<td>100 mL</td>
</tr>
<tr>
<td>24 thru 40 kg</td>
<td>52 thru 88 lbs</td>
<td>125 mL</td>
</tr>
<tr>
<td>41 kg or more</td>
<td>89 lbs or more</td>
<td>150 mL</td>
</tr>
</tbody>
</table>
Third, follow the procedure below for compounding the oral suspension (6 mg/mL) from TAMIFLU capsules 75 mg:

1. Place the specified amount of water into a polyethyleneterephthalate (PET) or glass bottle (see Table 3 in PI).

2. Carefully separate the capsule body and cap and pour the contents of the required number of TAMIFLU 75 mg capsules into the PET or glass bottle. Weighing paper may also be used to hold capsule contents for transfer into bottle.

3. Gently swirl the suspension to ensure adequate wetting of the TAMIFLU powder for at least 2 minutes.

4. Slowly add the specified amount of vehicle to the bottle.

5. Close the bottle using a child-resistant cap and shake well for 30 seconds to completely dissolve the active drug and to ensure homogeneous distribution of the dissolved drug in the resulting suspension. (Note: The active drug, oseltamivir phosphate, readily dissolves in the specified vehicles. The suspension is caused by inert ingredients of TAMIFLU capsules which are insoluble in these vehicles.)

6. Put an ancillary label on the bottle indicating “Shake Well Before Use.”

7. Instruct the parent or caregiver that any unused suspension remaining in the bottle following completion of therapy must be discarded by either affixing an ancillary label to the bottle or adding a statement to the pharmacy label instructions.

8. Place an appropriate expiration date on the label according to storage conditions below.

Storage of the Emergency Compounded Suspension

- Refrigeration: Stable for 5 weeks (35 days) when stored in a refrigerator at 2° to 8°C (36° to 46°F).
- Room Temperature: Stable for five days (5 days) when stored at room temperature, 25°C (77°F).

Note: The storage conditions are based on stability studies of compounded oral suspensions, using the above mentioned vehicles, which were placed in glass and polyethyleneterephthalate (PET) bottles. Stability studies have not been conducted with other vehicles or bottle types.

Place a pharmacy label on the bottle that includes the patient’s name, dosing instructions, and drug name and any other required information to be in compliance with all State and Federal Pharmacy Regulations.
Oral Dosing Device

Consider dispensing the suspension with an oral dosing device (a graduated oral syringe or spoon) suitable for measuring the suspension. If possible, mark or highlight the graduation corresponding to the appropriate dose (5 mL, 7.5 mL, 10 mL, or 12.5 mL) on the oral syringe or spoon for each patient.

For further information, please visit http://www.Tamiflu.com/HCP or refer to the Pharmaceutical Insert.

Indications and Limitations of Use

TAMIFLU is indicated in patients 1 year and older for the treatment of uncomplicated influenza caused by viruses types A and B who have been symptomatic for no more than 2 days and for the prophylaxis of influenza. Efficacy of TAMIFLU in patients who begin treatment after 48 hours of symptoms has not been established.

TAMIFLU is not a substitute for early and annual vaccination as recommended by the Centers for Disease Control’s Advisory Committee on Immunization Practices (ACIP).

There is no evidence for efficacy of TAMIFLU in any illness caused by agents other than influenza viruses Types A and B.

Influenza viruses change over time. Emergence of resistance mutations could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefits of antiviral drugs. Consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use TAMIFLU.

Table 1 Below from Prescribing Information for Dosing of the Compounded Suspension by Indication

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Weight (lbs)</th>
<th>Treatment Dosing for 5 days</th>
<th>Prophylaxis Dosing for 10 days‡</th>
<th>Volume of Oral Suspension (6 mg/mL) for each Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 kg or less</td>
<td>33 lbs or less</td>
<td>30 mg <strong>twice</strong> daily</td>
<td>30 mg <strong>once</strong> daily</td>
<td>5 mL</td>
</tr>
<tr>
<td>16 kg thru 23 kg</td>
<td>34 lbs thru 51 lbs</td>
<td>45 mg <strong>twice</strong> daily</td>
<td>45 mg <strong>once</strong> daily</td>
<td>7.5 mL</td>
</tr>
<tr>
<td>24 kg thru 40 kg</td>
<td>52 lbs thru 88 lbs</td>
<td>60 mg <strong>twice</strong> daily</td>
<td>60 mg <strong>once</strong> daily</td>
<td>10 mL</td>
</tr>
<tr>
<td>41 kg or more</td>
<td>89 lbs or more</td>
<td>75 mg <strong>twice</strong> daily</td>
<td>75 mg <strong>once</strong> daily</td>
<td>12.5 mL</td>
</tr>
</tbody>
</table>

† Treatment should begin within 2 days of onset of symptoms and prophylaxis should begin within 2 days of exposure to an infected individual. Please see the Prescribing Information for dosing in patients with renal impairment.

‡ Prophylaxis for adults following close contact with an infected individual for at least 10 days. Duration of prophylaxis in both adults and pediatric patients during a community outbreak is up to 6 weeks in immunocompetent patients.

Please see accompanying Full Prescribing Information.
Please see next page for Important Safety Information.
**Important Safety Information**

TAMIFLU is contraindicated in patients who have had severe allergic reactions such as anaphylaxis or serious skin reactions such as toxic epidermal necrolysis, Stevens-Johnson syndrome, or erythema multiforme to any component of TAMIFLU. Cases of these events have been reported in postmarketing experience with TAMIFLU. TAMIFLU should be stopped and appropriate treatment instituted if an allergic-like reaction occurs or is suspected.

There have been postmarketing reports of delirium and abnormal behavior leading to injury, and in some cases resulting in fatal outcomes, in patients with influenza who were receiving TAMIFLU. These events were reported primarily among pediatric patients and often had an abrupt onset and rapid resolution. The contribution of TAMIFLU to these events has not been established. Patients with influenza should be closely monitored for signs of abnormal behavior. If neuropsychiatric symptoms occur, the risks and benefits of continuing treatment should be evaluated for each patient.

Serious bacterial infections may begin with influenza-like symptoms or may co-exist with or occur as complications during the course of influenza. TAMIFLU has not been shown to prevent such complications.

Efficacy in subjects with chronic cardiac and/or respiratory disease or in immunocompromised patients has not been established. No information is available regarding treatment of influenza in patients at imminent risk of requiring hospitalization.

The concurrent use of TAMIFLU with live attenuated influenza vaccine (LAIV) intranasal has not been evaluated. However, because of the potential for interference between these products, LAIV should not be administered within 2 weeks before or 48 hours after administration of TAMIFLU, unless medically indicated.

Adverse events that occurred more frequently in patients treated with TAMIFLU than in patients taking placebo and occurred in ≥2% of patients were (TAMIFLU%, placebo %):

- **Treatment in adults** – nausea (10%, 6%), vomiting (9%, 3%), bronchitis (2%, 2%)
- **Treatment in pediatrics** – vomiting (15%, 9%), abdominal pain (5%, 4%), epistaxis (3%, 3%), ear disorder (2%, 1%)
- **Prophylaxis of adults** – headache (18%, 18%), nausea (7%, 3%), diarrhea (3%, 2%), vomiting (2%, 1%), abdominal pain (2%, 1%)
- **Prophylaxis of pediatrics** – vomiting (10%, 2%), abdominal pain (3%, 0%), nausea (4%, 1%)
CONTRAINDICATIONS

Patients with known serious hypersensitivity to oseltamivir or any of the components of TAMIFLU® (oseltamivir phosphate) capsules should not be administered TAMIFLU.

Other conditions for which TAMIFLU should not be administered include:

- Community outbreak: 75 mg once daily for up to 6 weeks

Treatment of influenza (2.2)

Consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use TAMIFLU.

2.2 Use in Specific Populations

1.6 Pregnancy

3.3 DOSAGE FORMS AND STRENGTHS

The recommended oral dose of TAMIFLU for pediatric patients 1 year and older is 75 mg once daily. Safety and efficacy have been demonstrated for up to 6 weeks in pediatric patients 1 year and older. The recommended oral dose of TAMIFLU for adults and adolescents is 75 mg twice daily for 10 days.

NSAIDS, aspirin, or other medications that may increase the risk for serious bleeding should be used with caution in patients taking TAMIFLU.

4.1 Pregnancy

TAMIFLU is not indicated for use in women who are or may become pregnant. If a woman becomes pregnant while taking TAMIFLU, she should stop taking it and contact her healthcare professional immediately.

4.2 Lactation

It is not known whether TAMIFLU is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TAMIFLU is administered to a nursing woman.

4.3 Pediatric Use

Efficacy of TAMIFLU in patients who begin treatment after 48 hours of symptoms is not established. TAMIFLU was consistent with that previously observed in other TAMIFLU prophylaxis studies, with the exception that the difference in incidence between TAMIFLU and placebo for these events was less than 1% in the clinical trials for pediatric patients 7 to 17 years of age.

Additional adverse events occurring in <1% of patients receiving TAMIFLU for treatment or prophylaxis of influenza have included:

- Abdominal pain (2.1%)
- Diarrhea (1.7%)
- Headache (1.1%)
- Nervousness (1.1%)
- Seizure (1.1%)

The following adverse reactions are also possible:

- Nausea
- Vomiting
- Diarrhea
- Headache
- Fatigue
- Sleep disturbances
- Irritability
- Respiratory infections
- Sinusitis
- Bronchitis
- Acute otitis media
- Urinary tract infections

5.1 Drug Interactions

No studies have been conducted to directly assess drug interaction with TAMIFLU. However, drug interactions have been well characterized with ribavirin and zidovudine, two antiviral agents with similar mechanisms of action to oseltamivir.

6.1 Laboratory Tests

Laboratory tests should be performed before and after treatment with TAMIFLU, especially in the elderly, in patients with renal or hepatic impairment, and in those with pre-existing neuropsychiatric disorders.

7.7 Breastfeeding

It is not known whether TAMIFLU is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TAMIFLU is administered to a nursing woman.

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Shake the bottle well for about 5 seconds before inserting the oral dispenser into the bottle.
When Metformin Is Not Enough: Choosing the Optimal Second- and Third-Line Therapy for Type 2 Diabetes

When metformin monotherapy becomes insufficient for managing blood glucose levels, most adults with type 2 diabetes should have a sulfonylurea added to the metformin. Once this combination therapy becomes insufficient, most adults with type 2 diabetes should have neutral protamine Hagedorn (NPH) insulin added to the metformin and sulfonylurea therapy.

These are the recent recommendations developed through projects conducted by the Canadian Agency for Drugs and Technologies in Health (CADTH) that involved systematic reviews of clinical evidence and analyses of cost-effectiveness for a wide range of antidiabetes drugs:

- Sulfonylureas*
- Meglitinides
- Alpha-glucosidase inhibitors
- Thiazolidinediones (TZDs)
- Dipeptidyl peptidase-4 (DPP-4) inhibitors
- Glucagon-like peptide-1 (GLP-1) analogues
- Insulins (basal, bolus, biphasic).

*Reviewed for second-line use only.

The clinical-effectiveness reviews involved examining how well specific antidiabetes drug combinations were able to lower blood glucose levels, as measured by glycated hemoglobin (A1C). Other outcomes of interest included changes to patient body weight, incidence of hypoglycemia, long-term complications of diabetes, mortality, quality of life, and serious adverse effects.

**Second-line therapy**

When added to metformin, all the reviewed drugs were able to significantly reduce A1C levels (by 0.6% to 1.0% compared with metformin monotherapy), and there were no statistically significant differences between drug classes. Severe hypoglycemia was rare for all drugs; however, the insulins, sulfonylureas, and meglitinides were associated with a higher risk for overall hypoglycemia than the other drugs. Compared with metformin alone, sulfonylureas, meglitinides, TZDs, and insulins were all associated with a modest increase in body weight (1.8 kg to 3 kg); DPP-4 inhibitors and alpha-glucosidase inhibitors were weight-neutral; while GLP-1 analogues were associated with weight loss (about 1.8 kg). There was insufficient evidence on how second-line antidiabetes drugs affect long-term complications of diabetes.

The cost-effectiveness analysis showed that adding a sulfonylurea to metformin is the most cost-effective second-line therapy, primarily because sulfonylureas cost less than insulin and newer drugs.
Third-line therapy

When added to metformin and sulfonylurea combination therapy, DPP-4 inhibitors, GLP-1 analogues, TZDs, and insulins produced statistically and clinically significant reductions in A1C (0.9% to 1.2% compared with metformin and sulfonylurea second-line therapy), and there were no statistically significant differences between these drug classes. Meglitinides and alpha-glucosidase inhibitors did not reduce A1C.

Using insulin as third-line therapy was typically associated with a greater risk of overall hypoglycemia relative to other active comparators; however, severe hypoglycemic events were rare across all treatments. The insulins and TZDs were associated with weight gain (2 kg to 5 kg), DPP-4 inhibitors and alpha-glucosidase inhibitors were weight-neutral, while GLP-1 analogues were associated with weight loss (about 1.6 kg). There was insufficient evidence to evaluate the comparative efficacy of third-line antidiabetes drugs in reducing clinically important long-term complications of diabetes.

The cost-effectiveness analysis showed that adding NPH insulin to metformin and sulfonylurea combination therapy is the most cost-effective third-line therapy. The findings also showed that long-acting insulin analogues at prices similar to insulin NPH would also be an option for patients with blood glucose levels inadequately controlled on metformin and a sulfonylurea.

What does this mean in the real world?

The CADTH recommendations aim to guide health care professionals who have to make decisions about how to adjust therapy for their patients with type 2 diabetes when metformin alone becomes insufficient for managing blood glucose levels. It is a decision that physicians face often — because type 2 diabetes is a progressive disease. Choosing a second- and third-line therapy for patients can be challenging because recently, new, often more expensive drugs have entered the market, while information to guide prescribing varies. Also, prescribing insulin can be challenging because patients require access to adequate education, support, and monitoring.

CADTH developed the recommendations in collaboration with experts across Canada, including endocrinologists, internists, family physicians, health economists, pharmacists, epidemiologists, and with input from public members and other stakeholders. Rooted in evidence from the systematic reviews and economic evidence, the recommendations promote the optimal use and prescribing of antidiabetes agents to benefit patients, while helping to ensure the sustainability of Canada’s health care system.

For additional information, please contact Barbara McCannell, CADTH Liaison Officer for Manitoba, at 204-788-6644 or barbaram@cadth.ca. Detailed reports and tools are available online at www.cadth.ca/2nd-3rd-line.
Custom-Pak Ophthalmic Surgery Procedure Pack: contamination with foreign bodies and risk of related complications

Key points

- Health Canada received 28 reports of incidents suspected of being associated with contamination of the surgical pack with lint, fibre or particles.
- Fourteen patients required removal of fibre particles from their eye by a surgeon.
- Health professionals are reminded to examine the pack and its contents before use.

The Custom-Pak Ophthalmic Surgery Procedure Pack is a surgical tray consisting of single-use devices and accessories for specific ophthalmic procedures such as cataract surgery. It is regulated as a class IV medical device (highest risk class). Its licence was first issued in Canada in October 1999. The pack is customized for each type of procedure to meet the specific needs of the surgeon and the facility. The contents of the pack are grouped based on their intended use and include components such as procedure cassettes and accessories, barrier products, plastics, gloves, knives, sutures, absorbing products, self-adhesive products, eye protection products and electrosurgical devices. Once assembled, the packs are placed in plastic pouches with a content label and sealed. The pouches are sterilized and then placed in cardboard shipping boxes.

As of Apr. 30, 2011, Health Canada received 28 reports of incidents suspected of being associated with the contamination of the surgical pack with lint, fibre or particles. The foreign bodies were either discovered in the packs or found by the surgeon during surgery or the postoperative examination of the patient’s eye. In 14 cases, the reporter described that the foreign body was removed by the surgeon. In 10 of these cases, a second surgery was required to do this, and in 3 cases the surgeon removed the foreign body from the eye during the initial surgery (information not specified in 1 report). In several of the reports, physicians expressed a concern for the potential risk of infection. Also, in many of these reports, the exact source of the foreign body could not be conclusively determined.

Some of the reports described that the manufacturer had identified the particles as cotton, polyethylene, paper, polyurethane foam, polyester fibre, polystyrene, poly 3-methylcaprolactam and cardboard. It was also reported that the particles may have originated from...
the components of the surgical pack itself. The cardboard particles may have entered the product at the supplier’s, in the Custom-Pak warehouse or during the assembly process.

Any foreign substance has the potential to induce an inflammatory response.2 In cases where a foreign body, such as a cotton fibre, has been inadvertently implanted inside the eye during surgery and left there, the evidence relating to the long-term clinical consequences is limited.3 A foreign body that penetrates the eye as a result of an ocular trauma can cause infection, among other complications. In such cases, prompt diagnosis and appropriate treatment, including antimicrobial therapy, can help prevent the risk of infection and endophthalmitis.4

Health professionals are reminded to examine the Custom-Pak Ophthalmic Surgery Procedure Pack and its contents before use. Health Canada continues to monitor adverse incidents suspected of being associated with this product and is working with the manufacturer to update the product label.

Ilhemme Djeloahah, RPh, BScPhm, DIS Medical Biology (University of Paris V), Health Canada

References

Case presentation

Recent Canadian cases are selected based on their seriousness, frequency of occurrence or the fact that the reactions are unexpected. Case presentations are considered suspicions and are presented to stimulate reporting of similar suspected adverse reactions.

Dental/surgical rotary handpieces and patient burns

Rotary handpieces used in dental and surgical procedures consist primarily of an engine and a chuck mechanism that secures burs (drill bits) into place. Handpieces may be classified as either pneumatic (use of a turbine driven by compressed air) or electric (powered by an electric motor). These devices are used to cut, shape, drill, abrade, burnish, finish and polish tissue and restorative materials. In Canada, surgical rotary handpieces are typically regulated as class II medical devices (IV being the highest risk class).

Health Canada received a report of a patient who experienced a burn to the cheek area during restorative work on an upper tooth with a dental handpiece. As a result, there was pain and swelling in the area and the patient was prescribed an analgesic. After 2 weeks, some scarring was noted at the burn site. Post-incident analysis by the manufacturer revealed that the handpiece in question had worn bearings and had been inadequately maintained overall. This possibly contributed to increased internal friction and heat production. Furthermore, the reported use of the back of the head of the handpiece as a cheek retractor, and the presence of a dent along the back cap edge of the device, may have also affected the operation of the handpiece and contributed to the device overheating. Health Canada has received similar reports of patient burns involving different handpiece models from several device manufacturers.

Health Canada encourages the reporting of patient burns and other adverse incidents suspected of being associated with the use of dental or surgical handpieces to the Health Products and Food Branch Inspectorate through the toll free hotline (1-800-267-9675).

Reference
CARN’s 20th anniversary

Celebrating a milestone anniversary is an opportunity to remember what has been accomplished in past years and to look ahead to new challenges. The Canadian Adverse Reaction Newsletter (CARN) was first published in 1991. Although its appearance and Editorial Team have changed over the last 20 years, its primary goal remains the same: to be a reliable source of information on adverse reactions (ARs) suspected of being associated with health products in Canada.

CARN is an example of an early-stage risk communication tool, one of many risk communication vehicles that Health Canada uses to issue health product safety information. It features articles and data related to serious or unexpected adverse reactions (ARs) reported to Health Canada by industry, health professionals and consumers. Spontaneous AR reports continue to be an important component in monitoring the safety of health products. These reports provide the backbone of CARN and make it relevant to the reader. Its intent is not only to raise awareness, but also to stimulate reporting of similar ARs by health professionals and consumers.

The information published in CARN about Canadian AR reports can enhance the global understanding of a health product safety issue. For example, in a recent review of the interaction between rosiglitazone and fenofibrate published in Endocrine Practice, an AR report from the July 2005 issue of CARN was included as evidence in the clinical understanding of the interaction. In April 2011, CARN published an update on rosiglitazone–fenofibrate interactions, with details of the most recent Canadian cases reported to Health Canada. This is not the only time CARN has been cited in the literature. The Editorial Team conducted an analysis of the number of citations to CARN in the scientific literature as an indirect measure of its impact. As of March 31, 2011, there have been 140 citations in more than 70 journals internationally.

The Editorial Team would like to take this opportunity to thank its readers for their continued interest.

CARN Editorial Team

References


Did you know? Medical devices and incidents

This issue of the Canadian Adverse Reaction Newsletter is dedicated to incidents with medical devices.

The term “medical device” covers a wide range of products used in the treatment, mitigation, diagnosis or prevention of a disease or abnormal physical condition. In Canada, all medical devices are categorized into 4 classes based on the level of risk associated with their use:

**Class I:** Lowest risk (e.g., reusable surgical scalpel, bandages, culture media)

**Class II:** Low risk (e.g., contact lenses, epidural catheters, pregnancy test kits)

**Class III:** Moderate risk (e.g., orthopedic implants, glucose monitors, dental implants)

**Class IV:** High risk (e.g., HIV test kits, pacemakers, angioplasty catheters)


Editor’s note

After 20 years, CARN will be undergoing changes to its Editorial Team. I am pleased to introduce the new Editor-in-Chief, Patricia Carruthers-Czyzewski. I have had the privilege of serving as Editor-in-Chief since 1996. I have witnessed first-hand how AR reports published in CARN contributed to the understanding of emerging safety issues. This underscores the vital role you play in reporting ARs that you witness in your professional practice. It also highlights the importance of promoting a reporting culture where health professionals, consumers and industry have a shared responsibility. I am convinced that CARN will continue to disseminate this valuable information. The challenge for CARN over the next decade will be to leverage the reach of new tools such as social media to further its goal of prompting AR reporting and increasing awareness.

Ann Sztuke-Fournier, BPharm, Former Editor-in-Chief

Adverse reactions (ARs) to health products are considered to be suspicious, as a definite causal association often cannot be determined. Spontaneous reports of ARs cannot be used to estimate the incidence of ARs because ARs remain underreported and patient exposure is unknown.
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*Date of issuance. This date may differ from the posting date on Health Canada’s Web site.*