Institut national d'excellence en santé et en services sociaux
Québec

QUÉBEC'S NATIONAL MEDICAL PROTOCOL

No. 888029

Initiating pharmacological treatment for oropharyngeal mucositis in a patient receiving cancer therapy

Developed in collaboration with an advisory committee consisting of Québec clinicians and experts.

CLINICAL SITUATION OR TARGET POPULATION

Person 14 years of age or older who is receiving or has received cancer therapy and has one or more of the following signs or symptoms in the mouth or pharynx:

- Pain;
- Irritation or inflammation with erythema;
- Ulcers;
- Mucosal thickening;
- Thickening or absence of saliva;
- Cracks, fissures or bleeding;
- Difficulty opening the mouth (trismus);
- Difficulty drinking, eating or swallowing.

OR

Person between the ages of 6 and 13 years inclusive who is able to express their pain and rinse their mouth, who is receiving or has received cancer therapy[1] and who has one or more of the following signs and symptoms in the mouth or pharynx:

- Pain;
- Irritation or inflammation with erythema;
- Isolated ulcers;
- Difficulty drinking, eating or swallowing.

CONTRAINDICATIONS TO THE APPLICATION OF THIS PROTOCOL

- A contraindication or a history of allergic reaction to the use of the recommended medications;
- The presence of fever (suggestive of febrile neutropenia or a bacterial infection);
- The presence of signs and symptoms suggestive of oral candidiasis, such as white patches that peel off more or less easily and that can be scraped off with a tongue depressor, a cottony sensation or a metallic taste in the mouth[2].
- **Person under 14 years of age**:
  - The inability to visually assess the oral cavity;
  - The presence of a foul odour in the oral cavity suggestive of a bacterial infection;
  - Signs of dehydration, lethargy;
  - The presence of at least one of the following signs and symptoms suggestive of advanced mucositis in the mouth or pharynx:
    - Cracks, fissures or bleeding;
    - Confluent ulcers (i.e., touching one another);
    - Mucosal thickening;
    - Thickening or absence of saliva;
    - Difficulty opening the mouth (trismus).

[1] In this protocol, the term "cancer therapy" refers to any treatment administered for cancer (e.g., chemotherapy, radiotherapy or targeted therapy).
[2] Refer to the NMP on oral candidiasis in adults.

INSTRUCTIONS

1. ASSESSMENT OF MEDICAL CONDITION

1.1 Signs and symptoms

Check for the following signs and symptoms suggestive of mucositis in the mouth or pharynx:

- Pain;
- Irritation or inflammation with erythema;
- Ulcers;
- Mucosal thickening;
- Thickening or absence of saliva;
- Cracks, fissures or bleeding;
- Difficulty opening the mouth (trismus);
- Difficulty drinking, eating or swallowing.

Check for signs and symptoms consistent with other clinical conditions:

- Fever (suggestive of febrile neutropenia or a bacterial infection);
- A foul odour in the mouth (suggestive of a bacterial infection);
- White patches in the mouth that peel off more or less easily and that can be scraped off with a tongue depressor, a cottony sensation or a metallic taste (suggestive of oral candidiasis).

1.2 Medication history

Check for and document:

- Any history of allergic reaction or hypersensitivity to any of the ingredients of the treatment recommended in Section 2;
- The cancer treatment received and the type of cancer treated.

1.3 Health history

Check for and document any risk factors that can promote the development of oropharyngeal mucositis:

- Malnutrition or nutritional deficiencies;
- Poor oral hygiene;
- Poorly fitted dentures or braces;
- Persistent use of alcohol, tobacco or illicit drugs.

Check for any history of the following (see precautions in Section 2.2):

- Renal failure;
- Bradycardia or impaired cardiovascular function.

2. TREATMENT APPROACH

2.1 Treatment objective

Alleviate and eliminate, with the use of a topical treatment, the signs and symptoms suggestive of oropharyngeal mucositis.

2.2 General information on pharmacological treatment

The general information on pharmacological treatments for oropharyngeal mucositis presented below is not exhaustive.

General information on pharmacological treatment with the use of mouthwashes

	Magnesium/ aluminium hydroxide	Nystatin	Hydrocortisone	Lidocaine hydrochloride	Diphenhydramine hydrochloride
Available forms covered[1]	Oral suspension 200-200 mg/5 ml Tablet 200-200 mg	Oral suspension 100,000 U/ml	Powder 5 g Tablet 10 mg, 20 mg	Topical gel[2] 2%	Elixir 12.5 mg/5 ml Capsule 25 mg Tablet 25 mg, 50 mg
Contraindications	Known hypersensitivity to any ingredient of the formulation or any component of the container	Known hypersensitivity to nystatin or to any ingredient of the formulation or any component of the container	Known hypersensitivity to corticosteroids or to any ingredient of the formulation or any component of the container	Known hypersensitivity to local amide anesthetics or other ingredients of the solution, such as methylparaben and/or propylparaben or to their metabolite, para-aminobenzoic acid (PABA)	Known hypersensitivity to diphenhydramine, to other antihistamines with a similar chemical structure, or to any ingredient of the formulation or any component of the container
If oncology mouthwash is swallowed					
Precautions	Increased monitoring in patients with renal failure	Diabetes and dental caries (oral suspension: contains 50% sucrose)	Increases the risk of oral fungal infections	Risk of arrhythmia or heart block	Increased surveillance in children, the elderly, and pregnant or breastfeeding women
Most common adverse effects	• Nausea • Vomiting • Diarrhea	• Diarrhea • Nausea • Vomiting • Irritation • Local sensitivity	• None	• Swallowing reflex inhibition • Perioral paresthesia	• Sedation • Drowsiness • Dizziness • Coordination disorders • Epigastric distress • Thickening of bronchial secretions

1. Injectable solutions are not covered by the RPAM when used for compounding.
2. For further details on the coverage conditions for this drug, consult RAMQ newsletter No. 170-8.

2.3 Choice of pharmacological treatment

Treatment of oropharyngeal mucositis			
Treatment Adult and pediatric	**Composition (final concentration)**[1]	**Dosage**[2]	**Duration**
First-line treatment			
Oncology mouthwash containing a corticosteroid	Diphenhydramine (1.25 mg/ml) Hydrocortisone (0.2 mg/ml) Magnesium/aluminium hydroxide (13-13 mg/ml) Nystatin (12,500 U/ml)	Rinse mouth with 15 to 30 ml QID for at least 2 minutes, then **spit out or swallow if pharyngeal lesions.**	Until signs and symptoms resolve
! Not to be swallowed by pregnant or breastfeeding women, the elderly and individuals under 14 years of age, unless recommended by the oncology care team.			

Another treatment option in the event of severe pain ! *In the case of ENT cancer, this treatment is reserved for use by an authorized prescriber.*			
Oncology mouthwash containing lidocaine	Diphenhydramine (0.8 mg/ml) Viscous lidocaine (6.7 mg/ml) Magnesium/aluminium hydroxide (13-13 mg/ml)	Rinse mouth with 15 to 30 ml QID for at least 2 minutes, then **spit out**.	Until signs and symptoms resolve
! Can be swallowed if the patient has pharyngeal lesions, on the oncology care team's recommendation, except by persons under 14 years of age **or** with ENT cancer.			

1 See Appendix I for some formulation suggestions.

2 Use a volume of 15 ml for children. If this amount is felt to be too high, split it into 2 successive rinses.

3. INFORMATION TO BE PROVIDED

Discuss the following with the patient, their caregiver or the cancer care team.

General

- Store mouthwash in the refrigerator (for a maximum of 14 days) and shake well before use.
- Respect the recommended minimum contact time of 2 minutes during each rinse to ensure effectiveness.
- Avoid drinking and eating:
  - To the extent possible, for 30 minutes after each rinse with the oncology mouthwash containing a corticosteroid;
  - For 30 minutes after each rinse with the oncology mouthwash containing lidocaine.
- Inform the oncology care team when starting a treatment for oropharyngeal mucositis.
- Remind the patient to follow their oncology care team's instructions if their condition rapidly deteriorates.
- Consult the oncology care team if difficulty drinking or eating persists or develops after the start of treatment.
- **For patients under 14 years of age:**
  - Review with the parent or the person responsible the signs and symptoms of dehydration;
  - Schedule a telephone consultation, a teleconsultation or an appointment with the oncology care team within the next 24 hours.

Orodental hygiene

- Maintain good orodental hygiene in accordance with the recommendations provided before the start of the cancer treatment.
- Do not use a commercial mouthwash containing alcohol, dental floss or other interdental cleaners.
- **For patients with dentures or braces**
  - Remove dentures:
    - Before using the mouthwash;
    - For the night or for a period of at least 8 hours a day.
  - Wear dentures only during meals if mouth is sensitive.
  - Do not wear braces during an episode of oropharyngeal mucositis.

Diet

- Avoid eating dry, hard, spicy, hot or highly acidic foods.
- Drink plenty of fluids.
- Limit or stop your alcohol, tobacco and coffee consumption.
- Suck on an ice cube or other frozen item between treatments with the oncology mouthwash to ease the pain, unless you are receiving treatment with oxaliplatin.

If necessary, optimize with the oncology care team the management of modifiable risk factors that promote the development of oropharyngeal mucositis.

4. FOLLOW-UP

- At least once during the first 48 to 72 hours of treatment or during the first 24 hours if the patient has difficulty drinking or eating, or for patients under 14 years of age, inquire about and document:
    - The treatment's effectiveness (including the appearance of new signs or symptoms suggestive of oropharyngeal mucositis)
    - The occurrence of adverse effects related to the treatment;
    - The ability to eat or drink;
    - Dehydration.

Note: For individuals treated on an outpatient basis, this follow-up can be done by telephone or teleconsultation.

5. SITUATIONS REQUIRING SPECIAL ATTENTION, REASSESSMENT OR FURTHER INVESTIGATION

- The occurrence of a fever;
- The occurrence of an allergic reaction or intolerance to the treatment;
- No improvement in the signs or symptoms suggestive of oropharyngeal mucositis within 48 hours after the start of treatment;
- A worsening of the signs or symptoms suggestive of oropharyngeal mucositis;
- A deterioration in the patient's overall health[3];
- Difficulty swallowing or the inability to eat or drink for more than 24 hours;
- Signs of dehydration (excluding dry mouth);
- The presence of at least one of the following signs and symptoms suggestive of an advanced stage of oral or pharyngeal mucositis:
    - Unbearable pain;
    - Bleeding lasting more than 2 minutes;
    - Cracks or fissures.

REFERENCES

This protocol is based on the latest scientific data and best practice recommendations, which were supplemented with contextual information and the experiential knowledge of Québec clinicians and experts. For details on the process used to develop this national medical protocol and to consult the references, see the report in support of this protocol.

[3] Can manifest as irritability or lethargy in children.

APPENDIX I

Formulation suggestions

Oncology mouthwash containing a corticosteroid

Ingredient (concentration)	Quantity
Diphenhydramine elixir (12.5 mg/5 ml)	250 ml
or	**or**
capsule (50 mg/cap)	12.5 capsules
Hydrocortisone powder	100 mg
or	**or**
tablets (10 mg/comp)	10 tablets
or	**or**
tablets (20 mg/comp)	5 tablets
Magnesium/aluminium hydroxide oral suspension (200-200 mg/5 ml)	165 ml
Nystatin oral suspension (100,000 U/ml)	62 ml
Sterile water	q.s. to 500 ml

Oncology mouthwash containing lidocaine

Ingredient	*Quantity*
Diphenhydramine elixir (12,5 mg/5 ml)	200 ml
or	**or**
capsule (50 mg/cap)	10 capsules
2% topical lidocaine oral gel	200 ml
Magnesium/aluminium hydroxide oral suspension (200-200 mg/5 ml)	200 ml
Sterile water	q.s. to 600 ml, if necessary