This material was developed by sanofi-aventis Canada Inc., as part of the Canadian Specific Opioids targeted Risk Management Plan (CSO-tRMP) for DEMEROL® TABLETS. It is not intended for promotional use.

DEMEROL® Tablets
Educational Material for Healthcare Professionals on Opioid-Related Harm

Dear Healthcare Professional:

This educational material is intended for healthcare professionals who are prescribing, dispensing or administering DEMEROL® Tablets for the relief of acute episodes of moderate to severe pain. This material is designed to highlight the importance of the risks of fatal or non-fatal adverse events (such as addiction, abuse, and misuse, which can lead to overdose and death). It can also assist you with counseling patients and/or caregivers on the safe use, serious risks and proper storage and disposal of DEMEROL® Tablets.

Your patients should receive the Information Handout title "**OPIOID MEDICINES – INFORMATION FOR PATIENTS AND FAMILIES**" at the time of dispensing of DEMEROL® Tablets. In addition, the Patient Package Insert (PPI) should be provided to the patient/caregiver. These documents are designed to help patients and caregivers understand the potential for opioid-related harm.

KEY POINTS TO CONSIDER WHEN PRESCRIBING DEMEROL® TABLETS

Patient selection

- Consider whether DEMEROL® Tablets are an appropriate treatment option. DEMEROL® Tablets should only be used in patients for whom alternative treatment options (e.g. non-opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide appropriate management of pain.
- **DEMEROL® Tablets are for use only in adults.** Safety in patients under the age of 18 years has not been studied and therefore DEMEROL® Tablets are not recommended in this patient population. Adolescents report higher rates of nonmedical opioid use and intentional poisonings and suffer a disproportionately higher rate of opioid-related deaths than the general adult population.
- DEMEROL® Tablets are not recommended for use in pregnant or nursing women as infants exposed to meperidine *in-utero* or through breast milk are at risk of life-threatening respiratory depression upon delivery or when nursed. Prolonged maternal use of DEMEROL during pregnancy can also result in neonatal opioid withdrawal syndrome, which may be life-threatening.
- Life-threatening respiratory depression is more likely to occur in the elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients.

Each patient should be assessed for their risk prior to being prescribed DEMEROL® Tablets. The likelihood of experiencing serious adverse events can depend upon the type of opioid, duration of treatment, level of pain, the patient's own level of tolerance as well as risk factors for opioid

use disorder (OUD). The risk factors include patient or family history of alcohol or drug abuse or psychiatric conditions, age, and a history of preadolescent sexual abuse.

Prescribing

DEMEROL® Tablets are contraindicated for patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy). Therapeutic doses of DEMEROL® have occasionally precipitated severe, unpredictable, and sometimes fatal reactions in patients who have received MAOIs within the previous 14 days.

Dosing

- Instruct patients to swallow DEMEROL® Tablets whole. Cutting, breaking, crushing, chewing, or dissolving DEMEROL® Tablets can lead to dangerous adverse events including death.
- As with other opioids, tolerance and physical dependence may develop upon repeated administration of DEMEROL® Tablets and there is a potential for development of psychological dependence.
- Prescribe DEMEROL® Tablets for “as needed” use every 3 to 4 hours and not at scheduled intervals.
- Prescribe an appropriate amount **for two days or less** for the relief of acute pain and instruct the patient to seek physician’s advice if effective pain relief is not achieved after 2 days of treatment.
- The total daily dose of DEMEROL® Tablets should not exceed 600 mg.To reduce the risk of respiratory depression, proper dosing and titration of DEMEROL® are essential. Overestimating the DEMEROL® dose when converting patients from another opioid product can result in a fatal overdose with the first dose.
- Reserve concomitant prescribing of DEMEROL® Tablets and benzodiazepines or other CNS depressants (including alcohol) to patients for whom alternative treatment options are inadequate as such concomitant use may result in sedation, respiratory depression, coma, and death.
- Use DEMEROL® Tablets with caution within 12 hours pre-operatively and within the first 12-24 hours post-operatively.
- DEMEROL® Tablets should be given with caution and the initial dose should be reduced in elderly patients and patients with severe impairment of hepatic and renal function Patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control. Withdrawal symptoms may occur following abrupt discontinuation of therapy or upon administration of an opioid antagonist. Tapering should be individualized and carried out under medical supervision.

Monitoring

All patients receiving DEMEROL® Tablets should be monitored for signs of opioid addiction, misuse and abuse and their level of pain should be assessed routinely to determine the most appropriate dose and the need for further use of DEMEROL® Tablets.

- Adjust/reduce dosage or discontinue DEMEROL® Tablets accordingly.
- Assess your patient's compliance with the prescribed dosage and identify any signs and symptoms of opioid misuse, abuse and OUD. Be familiar with the available screening tools for risk of abuse.

  Access the resources that are available to you in your province of practice to understand the provincial clinical guidelines on the management of OUD. Additional resources on the treatment of OUD are available and include the Canadian Research Initiative on Substance Misuse National Guideline for the Clinical Management of the OUD (https://crismprairies.ca/wp-content/uploads/2018/03/CRISM_NationalGuideline_OUD-ENG.pdf).

- Monitor patients for signs and symptoms of respiratory depression, especially during initiation of DEMEROL® or following a dose increase.
- Monitor for the potential occurrence of medication error(s) in your patients by asking detailed questions regarding dosage and administration of the product.

Patient/Caregiver Counselling

- Emphasize the potential risk of opioid-related harm and advise your patient/caregiver to read the Information Handout titled "**OPIOID MEDICINES – INFORMATION FOR PATIENTS AND FAMILIES"** provided at the time of dispensing and the PPI.
- Remind patient/caregiver to report any adverse events to you or to their other healthcare professional.
- Provide clear dosing instructions to your patient/caregiver including the daily maximum dose and the duration of treatment.
- Discuss the safe storage and disposal of DEMEROL® Tablets with your patient/caregiver, to reduce risk of accidental exposure/ingestion by household contacts, especially children/teens and to reduce risk of theft. Accidental exposure, especially by children, can result in a fatal overdose of meperidine.
- Inform patient/caregiver of the availability of "free take-home naloxone kits" in their respective provinces: Refer to: https://www.canada.ca/en/health-canada/services/substance-use/problematic-prescription-drug-use/opioids/naloxone.html

Adverse Events Reporting

To report any suspected adverse events associated with the use of DEMEROL® Tablets:

- Visit the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffectcanada.html) for information on how to report online, by mail or by fax; or call toll-free at 1-866-234-2345.

- Contact sanofi-aventis Canada Inc. by phone at 1-800-265-7927 or by visiting the "contact us" page on Sanofi's website at www.sanofi.ca.

CONTINUING OPIOID TRAINING

Maintain your knowledge concerning the risks of opioid-related harm, weighing these risks before prescribing an opioid, and properly managing patients who are prescribed opioids, both for short and long-term use. Always be aware of the current conditions of use for DEMEROL® Tablets, as detailed in the Canadian Product Monograph.

Please refer to the links below for examples of the available Opioid Online Training.

- Ontario Pharmacies Association : https://www.opatoday.com/Tags/Addictions
- McMaster University: https://machealth.ca/programs/opioids_clinical_primer/
- Centre for Addiction and Mental Health: https://www.camh.ca/en/education/continuing-education
- British Columbia Centre on Substance Abuse: http://www.bccsu.ca/provincial-opioid-addiction-treatment-support-program/
- University of British Columbia: https://ubccpd.ca/course/provincial-opioid-addiction-treatment-support-program
- University of Calgary: https://ecme.ucalgary.ca/program-listing/

This educational material is not an exhaustive description of the risks associated with the use of DEMEROL® Tablets. Refer to the full Prescribing Information of DEMEROL® Tablets posted on the company website or contact Sanofi Medical Information (1-800-265-7927 or SanofiMedInfoCA@sanofi.com) for complete prescribing information.

Regards,

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