Date: January 15, 2021

Subject: Important Prescribing Information About PrRALIVIA® (Tramadol Hydrochloride Extended-Release Tablets) concerning Risks in relation to Opioid-related Harms

Dear Healthcare Professional:

PrRALIVIA® (Tramadol Hydrochloride Extended-Release Tablets) is indicated for the management of moderate to moderately severe pain in adults who require continuous treatment for several days or more.

In order to make tramadol the subject to the same regulatory requirements in Canada, already in place for other opioid analgesics, regulations to amend the *Schedule I to the Controlled Drugs and Substances Act and the Schedule to the Narcotic Control Regulations* are proposed.

In line with the initiative of the Government of Canada to address the growing number of overdoses and deaths caused by opioids in Canada we would like to reiterate the importance of the following steps to be taken when prescribing Tramadol Hydrochloride Extended-Release Tablets:

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, PrRALIVIA® should only be used in patients for whom alternative treatment options are ineffective or not tolerated (e.g., non-opioid analgesics), or would be otherwise inadequate to provide sufficient management of pain (e.g., immediate-release opioids) (see DOSAGE AND ADMINISTRATION).

Tramadol Hydrochloride Extended-Release Tablets poses risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Each patient's risk should be assessed prior to prescribing Tramadol Hydrochloride Extended-Release Tablets, and all patients should be monitored regularly for the development of these behaviour or conditions (see WARNINGS AND PRECAUTIONS).

Patients should be instructed not to give Tramadol Hydrochloride Extended-Release Tablets to anyone other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death. Tramadol Hydrochloride Extended-Release Tablets should be stored securely to avoid theft or misuse.

Serious, life-threatening, or fatal respiratory depression may occur with use of Tramadol Hydrochloride Extended-Release Tablets. Infants exposed in-utero or through breast milk are at risk of life-threatening respiratory depression upon delivery or when nursed. Patients should be monitored for respiratory depression, especially during initiation of Tramadol Hydrochloride Extended-Release Tablets or following a dose increase. Tramadol Hydrochloride Extended-Release Tablets must be swallowed whole; crushing, chewing, or dissolving Tramadol Hydrochloride Extended-Release Tablets can cause rapid release and absorption of a potentially fatal dose of tramadol hydrochloride (see WARNINGS AND PRECAUTIONS). Further, instruct patients of the hazards related to taking opioids including fatal overdose.

Accidental consumption of even one dose of Tramadol Hydrochloride Extended-Release Tablets, especially by children, can result in a fatal overdose of tramadol hydrochloride (active opioid) (see DOSAGE AND ADMINISTRATION Disposal, for instructions on proper disposal).

Prolonged maternal use of Tramadol Hydrochloride Extended-Release Tablets during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening (see WARNINGS AND PRECAUTIONS).

DOSAGE AND ADMINISTRATION

All doses of opioids carry an inherent risk of fatal or non-fatal adverse events. This risk is increased with higher doses. For the management of chronic non-cancer, non-palliative pain, it is recommended that a maximum daily dosage of 300 mg (50 morphine milligram equivalent) of PrRALIVIA® not be exceeded. Each patient should be assessed for their risk prior to prescribing PrRALIVIA®, as the likelihood of experiencing serious adverse events can depend upon the type of opioid, duration of treatment, level of pain as well as the patient's own level of tolerance. In addition, the level of pain should be assessed routinely to confirm the most appropriate dose and the need for further use of PrRALIVIA® (see DOSAGE AND ADMINISTRATION, Adjustment or reduction of Dosage).

REPORTING SUSPECTED ADVERSE REACTIONS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected adverse reaction of drugs. If you suspect a serious or unexpected reaction to PrRALIVIA®, you may notify Canada Vigilance:

By toll-free telephone: 1-866-234-2345

By toll-free fax: 1-866-678-6789

Online: https://hpr-rps.hres.ca/static/content/form-formule.php?lang=en

By email: hc.canada.vigilance.sc@canada.ca

Should you have any medical inquiries regarding PrRALIVIA®, please do not hesitate to contact our Medical Information service at 1-800-361-4261. We will be pleased to answer any questions and address any concerns.

We appreciate your time and consideration.

Sincerely,

Maxime Barakat, MD, Ph D, MBA
Canada/EMEA Head, VP Medical & Clinical Affairs
VP Global Medical Devices/Clinical Evaluation Group

For the full product monograph and any additional information please contact the toll-free number 1-800-361-4261