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(IN REPLY PLEASE QUOTE THIS FILE REF.)

14 Apr 2023

Dear Healthcare Professionals,

FDA updates prescribing information for all opioid pain medicines to provide additional guidance for safe use

Your attention is drawn to the United States Food and Drug Administration's (FDA) announcement that it is requiring several updates to the prescribing information for both immediate-release (IR) and extended release/long acting (ER/LA) opioid pain medicines. This includes stating for all opioid pain that the risk of overdose increases as the dose increases.

- The updates to IR opioids state these products should not be used for an extended period unless the pain remains severe enough to require them and alternative treatments continue to be inadequate, and that many acute pain conditions treated in the outpatient setting require no more than a few days of an opioid pain medicine. This may include pain occurring with a number of surgical conditions or musculoskeletal injuries.
- The FDA is also updating the approved use for ER/LA opioid pain medicines to recommend they be reserved for severe and persistent pain that requires an extended treatment period with a daily opioid pain medicine and for which alternative treatment options are inadequate.
- The FDA is also adding a new warning about opioid-induced hyperalgesia (OIH) for both IR and ER/LA opioid pain medicines. This includes information describing the symptoms that differentiate OIH from opioid tolerance and withdrawal.
- Information in the Boxed Warning, FDA's most prominent warning, for all IR and ER/LA opioid pain medicines will be updated and reordered to elevate the importance of warnings concerning life-threatening respiratory depression, and risks associated with using opioid pain medicines in conjunction with benzodiazepines or other medicines that depress the central nervous system (CNS).
- Other changes are also being required to several sections of the prescribing information, including to the Indications and Usage, Dosage and Administration, and Warnings and Precautions sections. The FDA is also requiring updates to the existing patient Medication Guides to help educate patients and caregivers about these risks.

Recommendations to healthcare professionals:

- In assessing the severity of pain, discuss with the patient the impact of the pain on their ability to function and their quality of life. Assessment of pain should consider both the cause of pain and individual patient factors.
- If the patient's pain is severe enough to require an opioid pain medicine and alternative treatment options are insufficient, prescribe the lowest effective dose of an IR opioid for the shortest duration of time to reduce the risks associated with these products.
- Reserve ER/LA opioid pain medicines only for severe and persistent pain that requires an extended treatment period with a daily opioid pain medicine and for which alternative treatment options are inadequate.
- For all patients prescribed opioid pain medicines, discuss the availability of naloxone, and consider prescribing it to those at increased risk of overdose.
- Be aware that the symptoms of OIH, a condition where opioids cause an increase in pain (called hyperalgesia) or an increased sensitivity to pain (called allodynia), are distinct from opioid tolerance and withdrawal and can be difficult to recognize.
- If a patient is suspected to be experiencing OIH, carefully consider an appropriate decrease in dose of the current opioid pain medicine or safely switching them to a different opioid product, if tolerated. Advise patients about the risk of OIH and tell them to never increase the opioid dosage without first consulting a health care professional, because this could worsen the pain and increase the risk of respiratory depression.

Please refer to the following website in FDA for details:
https://www.fda.gov/safety/medical-product-safety-information/all-opioid-pain-medicines-drug-safety-communication-fda-updates-prescribing-information-provide

In Hong Kong, there are registered pharmaceutical products containing buprenorphine (7 products), codeine (356 products), fentanyl (16 products), morphine (16 products), oxycodone (18 products), and tramadol (42 products). These products are drugs under supervised sales or prescription-only medicines. There is no registered pharmaceutical product containing hydrocodone, hydromorphone, and oxymorphone. So far, the Department of Health (DH) has received adverse drug reaction related to codeine (4 cases), fentanyl (3 cases), morphine (10 cases), oxycodone (4 cases), and tramadol (7 cases). The DH has not received any case of adverse drug reaction related to buprenorphine.

Related news on the safe and appropriate use of opioid analgesics was previously issued by various overseas drug regulatory authorities, and was posted on the Drug Office website since 11 Sep 2013, with the latest update posted on 3 Oct 2020. Letters to inform local healthcare professionals were issued by the DH on 11 Sep 2013. In Feb 2015, the Registration Committee of the Pharmacy and Poisons Board discussed the matter, and decided that pharmaceutical products which are controlled-release, extended-release or long-acting opioid analgesics (containing hydromorphone, morphine, oxycodone,

oxymorphone, tapentadol, fentanyl, buprenorphine and methadone) should include safety information about the risks of addiction, abuse, misuse, overdose and death, and limitations of use in patients with severe pain for which alternative treatment options are inadequate.

The risk of tolerance, dependence, withdrawal symptoms, respiratory depression associated with the use of opioid analgesics, and the risks associated with using opioid analgesics in conjunction with benzodiazepines or other medicines that depress the central nervous system (CNS) are documented in overseas reputable drug references such as the "Martindale: The Complete Drug Reference" and "AHFS Drug Information". The DH will remain vigilant on safety update of the drugs issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Adverse Drug Reaction Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

pp (Terence MAN)
for Assistant Director (Drug)