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רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

נובמבר 2020

FENTANYL -PIRAMAL

חברת פארמה מדיס מבקשת להודיע על עדכון בעלון לרופא של התכשיר שבנדון.
ההתוויה הרשומה של התכשיר בישראל:

For analgesic action of short duration during anesthtic periods (premedication dinduction and maintenance) and in the immediate postoperative period as need arises.
As a narcotic analgesic supplement in general or regional anesthesia.
For administration with neuroleptics (such as droperidol) as an anesthetic premedication for the induction of anesthesia and as an adjunct in the maintenance of general or regional anesthesia.
For use as an anesthetic agent with oxygen in selected high-risk patients (open heart surgery or certain neurological or orthopedic procedures).
By the epidural route for the postoperative management of pain following general surgical procedures and cesarean sections and as adjunct to general anesthesia.

צורת המתן של התכשיר : **solution for injection**
מרכיב פעיל:
FENTANYL (AS CITRATE) 0.05 MG/ML

בהודעה זו מצוינים סעיפים בהם נעשה עדכון המהווה החמרה - מודגש בצהוב.
בעלון נעשו עדכונים נוספים על העדכונים המפורטים כאן.

4.4 Special warnings and precautions for use

Warnings:

Drug dependence, tolerance and potential for abuse

For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over-the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction.

The clinical need for analgesic treatment should be reviewed regularly.

Drug withdrawal syndrome

Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with fentanyl.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

If women take this drug during pregnancy, there is a risk that their new-born infants will experience neonatal withdrawal syndrome.

Hyperalgesia

Hyperalgesia may be diagnosed if the patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

Respiratory Depression

As with all potent opioids, profound analgesia is accompanied by marked respiratory depression, which may persist into or recur in the early postoperative period. Care should be taken after large doses or infusions of fentanyl to ensure that adequate spontaneous breathing has been established and maintained before discharging the patient from the recovery area.

Significant respiratory depression will occur following the administration of fentanyl in doses in excess of 200 mcg. This, and the other pharmacological effects of fentanyl, can be reversed by specific opioid antagonists, but additional doses may be necessary because the respiratory depression may last longer than the duration of action of the opioid antagonist.

Precautions:

Fentanyl should be given only in an environment where the airway can be controlled and by personnel who can control the airway.

Bile duct

As with other opioids, due to the anticholinergic effects, administration of fentanyl may lead to increases of bile duct pressure and, in isolated cases, spasms of the Sphincter of Oddi might be observed.

Risk from concomitant use of Central Nervous System (CNS) depressants, especially benzodiazepines or related drugs

Concomitant use of fentanyl and CNS depressants especially benzodiazepines or related drugs in spontaneous breathing patients, may increase the risk of profound sedation, respiratory depression, coma and death. If a decision is made to administer fentanyl concomitantly with a CNS depressant, especially a benzodiazepine or a related drug, the lowest effective dose of both drugs should be administered, for the shortest period of concomitant use. Patients should be carefully monitored for signs and symptoms of respiratory depression and profound sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see Interactions).

Paediatric population

Techniques that involve analgesia in a spontaneously breathing child should only be used as part of an anaesthetic technique, or given as part of a sedation / analgesia technique, with experienced personnel in an environment that can manage sudden chest wall rigidity requiring intubation, or apnoea requiring airway support.

Fentanyl-Piramal contains 3.5 mg sodium per ml. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Central Nervous System (CNS) depressants

The use of opioid premedication, barbiturates, benzodiazepines or related drugs, neuroleptics, general anaesthetics and other non-selective CNS depressants (e.g. alcohol) may enhance or prolong the respiratory depression of fentanyl.

When patients have received other CNS-depressants, the dose of fentanyl required may be less than usual.

Concomitant use with Fentanyl-Piramal in spontaneously breathing patients may increase the risk of respiratory depression, profound sedation, coma, and death (see warnings and precautions).

Cytochrome P450 3A4 (CYP3A4) inhibitors

Fentanyl, a high clearance drug, is rapidly and extensively metabolised mainly by CYP3A4. When Fentanyl-Piramal is used, the concomitant use of a CYP3A4 inhibitor may result in a decrease in fentanyl clearance. With single-dose Fentanyl-Piramal administration, the period of risk for respiratory depression may be prolonged, which may require special patient care and longer observation. With multiple-dose Fentanyl-Piramal administration, the risk for acute and/or delayed respiratory depression may be increased, and a dose reduction of Fentanyl-Piramal may be required to avoid accumulation of fentanyl.

Effect of fentanyl on other drugs

Following the administration of Fentanyl-Piramal, the dose of other CNS depressant drugs should be reduced. This is particularly important after surgery, because profound analgesia is accompanied by marked respiratory depression, which can persist or recur in the postoperative period. Administration of a CNS depressant, such as a benzodiazepine or related drugs, during this period may disproportionally increase the risk for respiratory depression (see warnings and precautions).

4.6 Fertility, pregnancy and lactation

Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate.

If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

Breast-feeding

Administration to nursing women is not recommended as fentanyl may be secreted in breast milk and may cause respiratory depression in the infant. The risk/benefit of breast-feeding following fentanyl administration should be considered.

4.7 Effects on ability to drive and use machines

This medicine can impair cognitive function and can affect a patient's ability to drive safely. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you

העלון לרופא מפורסם במאגר התרופות שבאתר משרד הבריאות:
https://data.health.gov.il/drugs/index.html#!/byDrug
ניתן לקבל עלון מודפס ע"י פנייה לבעל הרישום: חברת פארמה מדיס בע"מ, רחוב פיירברג 4, ת.ד 2820, חולון.

בברכה,
אבנר דור- רוקח ממונה