

FENTANİL İÇEREN İLAÇLAR-ACIL GÜVENLİLİK KISITLAMASI- GÖRÜŞ KATKI İNG

Turkish Ministry of Health Turkish Medicines and Medical Devices Agency

Number: E-24931227-510.01.04-5575642 28.01.2025 Subject: Fentanyl-containing medicinal products / Emergency Safety Restriction / Opinion-Contribution

FILE

Regarding all fentanyl-containing medicinal products (transdermal patches, solutions for injection and medicinal products with transmucosal administration), the European Medicines Agency (EMA) Pharmacovigilance Assessment Committee (PRAC) notices regarding the request to include more information on "Opioid Use Disorder (OUD)" in the product information have been evaluated by our Agency and accordingly, the statements specified in the attached document should be added to the summary of product characteristics (KÜB) and patient information leaflet (KT) of the medicinal products in question. Please be informed and take necessary actions to submit your opinions, suggestions and contributions, if any, regarding the decision taken to the Pharmacovigilance and Controlled Substances Department Pharmacovigilance Risk Management Unit until 10.02.2025 and not to apply to the Pharmacological Evaluation Unit until this date.

Eray KAPLAN Acting Agency Head

Attached: KÜB/KT text (6 pages)

To be distributed to:

Turkish Pharmaceutical Industry Association Association of Research-Based Pharmaceutical Companies Pharmaceutical Industry Employers' Association Health Products Association

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The following revisions should be made to the corresponding sections of the Summary of Product Characteristics (KÜB) (new text is underlined and in bold font, deleted text is strikethrough).

KÜB

4.2 Posology and route of administration

The following statements about the duration and goals of treatment should be added. The following statement should be added before the treatment discontinuation section.

Treatment duration and goals

Before starting treatment with <medicinal product name>, a treatment strategy including duration of treatment, treatment goals and a plan for the end of treatment should be agreed with the patient in accordance with pain control guidelines. During the course of treatment, there should be frequent communication between the physician and the patient to assess the need for continued treatment, to consider stopping treatment and to adjust the dose if necessary. In the absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered (see Section 4.4). <Medicinal product name> should not be used for longer than necessary.

Discontinuation of treatment with <Medicinal product name>

[...]

4.4 Special warnings and precautions for use

The following statements should be deleted (if applicable):

Iatrogenic dependence is known to occur following therapeutic use of opioids.

Tolerance and opioid use disorder (abuse and dependence)

Repeated administration of opioids such as <medicinal product name> may lead to the development of tolerance, physical and/or physiological dependence. In addition, iatrogenic

dependence is known to occur following therapeutic use of opioids in the treatment of cancer-related pain.

Repeated use of <Medicinal product name> may lead to Opioid Use Disorder (OUD). Higher doses and longer duration of opioid treatment may increase the risk of developing Opioid Use Disorder (OUD). Abuse or intentional misuse of <medicinal product name> may result in overdose and/or death. The risk of developing OUD is increased in patients with a personal or family history (parents or siblings) of substance use disorders (including alcohol use disorder), current smokers or patients with a history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

Before initiating treatment with <medicinal product name> and during treatment, treatment goals and a treatment discontinuation plan should be agreed with the patient (see Section 4.2). Before and during treatment, the patient should be informed about the risks and symptoms of OUD. Patients should be advised to contact their physician if these symptoms occur.

Patients will need to be monitored for signs of drug-seeking behaviour (e.g. too early requests for prescription renewal). This monitoring includes co-administered opioids and psychoactive drugs (such as benzodiazepines). Consultation with an addiction specialist should be considered for patients with signs and symptoms of OUD.

4.8 Undesirable effects

The following statements should be added to the adverse reaction tables for all fentanyl-containing medicinal products:

“Drug tolerance” should be included in the adverse reaction summary table (SOC ‘General Disorders and Administration Site Conditions’, frequency ‘unknown’).

The following information should be added to the subsection “Description of selected adverse reactions” (if the subsection does not already exist, it should be added):

Tolerance

Tolerance may develop with repeated use.

Drug Dependence

Repeated use of <medicinal product name> may lead to drug dependence even at therapeutic doses. The risk of drug dependence may vary depending on the patient's individual risk factors, dose and duration of treatment with opioids (see Section 4.4).

Patient Information Leaflet (KT)

2. Things to consider before using <medicinal product name>

The following statements should be deleted (if present)

[...]

Repeated use may result in the medicine becoming less effective (getting used to the medicine) or becoming dependent on the medicine.

[...]

Repeated use of <medicinal product name> can lead to dependence and abuse, resulting in a life-threatening overdose. It is important to talk to your doctor if you suspect that you may be dependent on <medicinal product name>.

[...]

Your doctor may need to monitor you more closely if, • you or someone in your family has ever been dependent on (“addicted to”) or abused alcohol, prescription drugs or illegal substances • you smoke • you have ever had mood problems (depression, anxiety or personality disorder) or have been treated by a psychiatrist for another mental illness

The new statements on tolerance, OUD and accidental overdoses should be included underlined as follows, preferably immediately after the bulleted list: <Consult your doctor when using <medicinal product name>, if you are taking <medicinal product name>, tell your doctor or dentist that you are taking this medicine, if:

Prolonged use and tolerance

This medicine contains fentanyl, an opioid. Repeated use of opioid painkillers can make the medicine less effective (getting used to the medicine, known as drug tolerance). You may also be more sensitive to pain while taking <medicinal product name>. This is known as hyperalgesia. Increasing the dose of <medicinal product name> may give you more pain relief for a while, but it may also be harmful. Talk to your doctor if you think your medicine is becoming less effective. Your doctor will decide whether it is better for you to increase or gradually decrease the dose of <medicinal product name>.

Dependence

Repeated use of <medicinal product name> may also lead to dependence and abuse, resulting in life-threatening overdose. Higher doses and longer use may increase the risk of these side effects. Dependence can make you feel that you are no longer in control of how much or how often you take your medicine. You may feel that you need to keep taking your medicine even if it does not relieve your pain. The risk of becoming dependent varies from person to person.

You may be at higher risk of becoming dependent on <medicinal product name>, if:

- If you or someone in your family has ever been dependent on ("addicted to") or abused alcohol, prescription drugs or illegal substances
- If you smoke
- If you have ever had mood problems (depression, anxiety or personality disorder) or have been treated by a psychiatrist for another mental illness.

If you notice any of the following symptoms while taking <medicinal product name>, it may mean that you are dependent,

- If you need to take the medicine for a longer period than your doctor has recommended,
- If you need to use more than the recommended dose,
- If you are taking the medicine for non-prescribed reasons, such as 'to stay calm' or 'to help you sleep',
- If you have made repeated unsuccessful attempts to stop taking the medicine or to get it under control,
- If you feel unwell when you stop taking the medicine (e.g. nausea, vomiting, diarrhoea, anxiety, chills, shivering and sweating) and feel better when you take it again ('withdrawal effects')

If you notice any of these symptoms, talk to your doctor to discuss the best course of treatment for you, including how and when best to stop taking the medicine safely.

3. How to take <medicinal product name>

Before you start treatment and regularly during treatment, your doctor will talk to you about what you can expect from taking <medicinal product name>, when and how long you should take it, when to contact your doctor and when to stop taking it (see also Section 2).

4. Possible side effects

Add a cross-reference "see Section 2" after the adverse reaction of dependence and drug abuse in the list of adverse reactions with "unknown" frequency (if adverse reactions are individually bulleted, the cross-reference should be added at each bullet point).

Unknown: Frequency cannot be estimated from the available data

[...]

- Drug tolerance, drug dependence, drug abuse (see Section 2)

These changes should be included in the corresponding sections of the Product Information (new text is underlined and in bold font, deleted text is strikethrough).

KÜB

4.4 Special warnings and precautions for use

A warning should be added as follows (preferably directly at the beginning of the section)

Because of the risks including fatal consequences associated with accidental exposure, misuse and abuse, patients and their caregivers should be advised to keep <medicinal product name> in a safe and secure place out of the reach of others.

KT

2. Things to consider before using <Medicinal product name>

Warnings / precautions

The following information should be added directly above the bulleted list “< Talk to > < Tell > < Check with > your doctor or pharmacist before using < Medicinal product name> If [.....]:”

Keep this medicine in a safe and secure place out of the reach of others (see Section 5 for more information. How to store <Medicinal product name>.

5. How to store <Medicinal product name>

Where to store < Medicinal product name >

[...]

The following information should be added. If there is existing text on storage recommendations (e.g. regarding temperature or locked area), add the new text directly above or below the existing text as appropriate.

Keep this medicine in a safe and secure place out of the reach of others. When this medicine is not prescribed, it can cause serious harm and can be fatal to people who may accidentally or intentionally take it.

These changes should be included in the corresponding sections of the Product Information (new text is underlined and in bold font, deleted text is strikethrough).

KÜB

To all fentanyl-containing drugs for transmucosal administration

• 4.9 Overdose and treatment

Symptoms and signs

[...]

The following symptom of overdose should be added:

Toxic leukoencephalopathy has also been observed with fentanyl overdose.

KT

• 3. How to use <Medicinal product name>

The following statement should be added to the subsection <If you <take> <use> more <medicinal product name> than you should, you should>):

[...]

Overdose can also cause a brain disorder known as toxic leukoencephalopathy.