Fenhuma®

(fentanyl citrate) sublingual tablet

Prescriber Guide

Important risk minimisation information for prescribing physicians

Glenmark
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Introduction

Physician's guide to prescribing Fenhuma® (fentanyl citrate) sublingual tablet

This brochure will provide you with information on how to properly prescribe Fenhuma® to your patients. Before prescribing Fenhuma®, please read and take note of the following important safety information and retain it for future reference. Patients must be carefully selected according to the therapeutic indication which is for the treatment of cancer breakthrough pain (CBTP) in patients who are already receiving maintenance opioid therapy for chronic cancer pain. For accurate patient selection, a prescribing checklist is also provided.

Note, Fenhuma® should only be prescribed by physicians who are experienced, knowledgeable and competent in the management of opioid therapy in cancer patients. The following documents are also available for download at medicines.org.uk:

- A patient guide
- A pharmacist's guide to dispensing Fenhuma®, including a dispensing checklist
- Summary of Product Characteristics (SmPC).

A digital copy of this brochure, as well as other educational materials are available and downloadable by scanning this QR code:

Contents

Chapter 1

What is Fenhuma®?

- **Definition**
  Fenhuma® is a sublingual tablet containing fentanyl.

- **Indication**
  Fenhuma® is ONLY indicated for the treatment of Cancer Breakthrough Pain (CBTP) in adult patients already receiving maintenance opioid therapy. Fenhuma® is not indicated to treat any other type of pain.

- **Cancer Breakthrough Pain (CBTP)**
  CBTP is a sudden onset, transient exacerbation of pain (usually of moderate to severe intensity) experienced by cancer patients that occurs on a background of otherwise controlled persistent pain despite being on maintenance opioid therapy.[1]

- **Maintenance opioid therapy**
  Patients receiving maintenance opioid therapy are those who are taking at least 60 mg of oral morphine daily, at least 25 mcg of transdermal fentanyl per hour, at least 30 mg of oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.

Chapter 2

What are the opioid-specific risks associated with Fenhuma®?

- **Opioid use disorder (OUD):**
  OUD is defined as the problematic pattern of opioid use leading to clinically significant distress or impairment.[2] Symptoms of OUD include an overpowering desire to use opioids, increased opioid tolerance, and withdrawal syndrome when opioids are discontinued.[3] OUD is classified in DSM-4 as opioid abuse and dependence, however, in the DSM-5, these two categories were merged into a single diagnosis called "opioid use disorder".[4]
  - **Opioid abuse** is the intentional and non-therapeutic use of opioids with the aim of achieving the desired psychological or physiological effect.[5]
  - **Dependence** refers to physical or psychological dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs after abrupt discontinuation. Psychological dependence refers to a state in which individuals have impaired control over drug use based on the rewarding properties of the drug.[3]

- **Addiction:**
  A chronic and recurrent use disorder characterised by compulsive drug-seeking behaviour and continuous use despite harmful consequences.[6]

- **Off-label use:**
  The use of a drug for an unapproved indication or in an unapproved age group, dosage, or route of administration. The off-label use of Fenhuma® includes:
  - Use for all other indications (including use for other pain therapy) other than CBTP
  - Use in patients not already receiving maintenance opioid therapy
  - More frequent dosing than recommended
  - Use in persons under the age of 18 years.

Please note that different fentanyl formulations have different indications. Make sure that you are familiar with the specific indication of Fenhuma® before prescribing. The use of Fenhuma® for indications other than their approved indication increases the risk of misuse, abuse, medication error, overdose, addiction and death.

- **Overdose:**
  Intake of a dose higher than the maximal recommended dose in the SmPC or PIL of Fenhuma®. Signs of overdose are described in the warnings section below with the most serious effects being cardiorespiratory arrest and death.

- **Misuse:**
  Situations where a drug is intentionally and inappropriately used not in accordance with the authorised product information. Fenhuma® should not be used for purposes of seeking effects other than analgesic effects such as for sedation or to 'get high'. Misuse of a drug may increase the risk of drug dependence.

- **Medication error:**
  A medication error is an unintended failure in the drug treatment process that leads to or has the potential to lead to, harm to the patient. This might be related to administering the drug by a wrong dose, wrong route, wrong frequency, to a wrong person, or for a wrong duration. Medication errors are also particularly important to avoid when prescribing Fenhuma®. Types of medication errors include:
  - Unintentional errors in prescribing a drug
  - Error in administration of a drug
  - Error in dispensing a drug
  - Administration of an incorrect dose
  - Using an incorrect route of administration.

Chapter 3 Prescription guide

The objectives of an analgesic treatment for CBTP are:

- The "background pain" is absent or of low-intensity
- No more than 4 breakthrough pain episodes per day
- Regular activity achievable or not limited by pain
- No disturbance to sleep of the patient

Before treatment

- Fenhuma® is to be prescribed by a physician experienced in the management of opioid therapy for cancer patients.
- Before prescribing Fenhuma® ensure that you and all other staff are familiar with the Fenhuma® SmPC/PIL, this Brochure and the Brochure for Patients and Carers.
- Please make use of the prescribing checklist that can be found at the end of this Brochure (refer to Chapter 10) or online.
- Evaluation of the indication. Fenhuma® is only to be prescribed to cancer patients with breakthrough pain.
- After careful selection of the patients, please take patients through the comprehensive Fenhuma® Brochure for Patients and Carers and ensure that the patient understands how to use Fenhuma® correctly; make sure they take a copy with them.
- Patients should be instructed never to share their medication with anyone or use it for a different purpose.
- Provide them with updated label information including hyperalgesia, use in pregnancy, drug interactions such as with benzodiazepines, iatrogenic addiction, withdrawal and dependence.
- Explain to the patients the risks associated with Fenhuma® such as off-label use, abuse, dependence, misuse, addiction, medication error, overdose and death.
- Patients at risk of abuse and misuse before and during treatment with Fenhuma® need to be monitored for distinguishing features of opioid-related side effects versus that of OUD.
- Tools or assessment manuals such as the essential features listed in the World Health Organisation International Classification of Diseases (ICD-11) for diagnosis of opioid dependence (refer to Chapter 4), the Opioid Risk Tool (ORT) and the Prescription Opioid Misuse Index (POMI) can be used to diagnose patients with OUD.

During treatment

- As the treating physician, you need to tailor the therapy if you recognise any signs of OUD. Discuss with the patients the risk of OUD and the treatment management.
- Cases of off-label use, misuse, abuse, addiction, and overdose should be reported to responsible competent authorities.
- Patients should be instructed not to use two different short-acting formulations of fentanyl concurrently for the treatment of CBTP when switching to Fenhuma®.
- Patients should be informed about the child-resistant blisters, the different strengths of Fenhuma® which are available, and how to differentiate the strengths according to the colour-coded packaging.
- The prescribed dosing instructions must be strictly adhered to by the patient.
- Patients must be aware of the need for recurrent visits to the prescribing physician to perform periodic check-ups.
- Patients should be encouraged to report any issues they encounter during their treatment.

Chapter 4

What are the risks associated with opioid use disorder?

Who is at risk of OUD?

Repeated use of Fenhuma® may lead to opioid use disorder. 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), in current tobacco users, or in patients with a personal history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

Table 1: Essential features listed in the World Health Organisation International Classification of Diseases (ICD-11) for diagnosis of opioid dependence[7]

A pattern of recurrent episodic or continuous use of opioids plus evidence of two or more of the following:

1	Impaired control of opioid use in terms of onset, termination, or levels of use.
2	Increasing precedence of opioid use over other aspects of life, such as maintenance of health, daily activities, and responsibilities, such that opioid use continues or escalates despite harm or negative consequences.
3	Tolerance or a need to use increasing amounts of opioids to achieve the same effect.
4	Withdrawal symptoms following cessation or reduction in use of opioids.
5	Repeated use of opioids or pharmacologically similar substances to prevent or alleviate withdrawal symptoms.

How to detect adverse effects associated with OUD?

- Pay attention to patients who are exposed to significant risks: some of the risk factors for OUD include e.g. personal and family history of substance abuse, psychological stress, trauma or disease; history of substance abuse treatment, history of legal problems; young age, smokers, exaggeration of pain and unclear etiology of pain[8]. For patients with signs and symptoms of opioid addiction, a consultation with an addiction specialist should be considered.
- Review the diagnostic criteria for opioid use disorder and look for patients that meet the criteria.
- Recognise the symptoms of addiction and withdrawal.
- Communicate with your patients: ask questions about their overall well-being and determine if the problems discussed are related to primary diagnosis, pain medications or other factors.

What should you do if you think that your patient has OUD?

Patients with OUD can still be treated with opioids to relieve their cancer pain. Several treatment options can be employed such as using certain opioid drugs e.g. methadone or buprenorphine, behavioural and psychosocial intervention, rehabilitation, self-help groups and resettlement/ integration service.[9] Treatment of OUD may require a multidisciplinary approach involving a psychiatrist, addiction specialist and pain specialist. Physicians should offer or arrange treatment with evidence-based medications to treat patients with OUD, particularly if moderate or severe. Physicians unable to provide treatment themselves should arrange for patients with OUD to receive care from a substance use disorder treatment specialist.

Chapter 5

Important points to note when prescribing Fenhuma®/ side effects

Information concerning adverse reactions to Fenhuma, contraindications, special warnings and precautions, interactions, use during pregnancy, and driving may be found in the Summary of Product Characteristics.

Chapter 6

Warnings

- Unintentional exposure to Fenhuma® is considered a medical emergency and a potentially life-threatening event.
- If a child is accidentally exposed to the product, seek immediate medical attention as this is considered to be a medical emergency and may, without proper professional treatment, cause death.
- Ensure your staff are aware of the signs of Fenhuma® overdose and toxicity. Patients and carers should also be made aware of the signs of Fenhuma® overdose, understand the potential seriousness and be advised on what to do in the event of an emergency. The most common serious signs of opioid overdose are:
  - Altered mental status
  - Myosis
  - Respiratory depression potentially leading to respiratory distress and respiratory failure which could lead to death.

Other symptoms of opioid overdose include:

- Deep sedation potentially leading to loss of consciousness/coma
- Hypotension
- Convulsions
- Cases of Cheyne-Stokes respiration have been observed in cases of fentanyl overdose, particularly in patients with a history of heart failure
- Cardiorespiratory arrest.

Opioid overdose without medical intervention could lead to death.

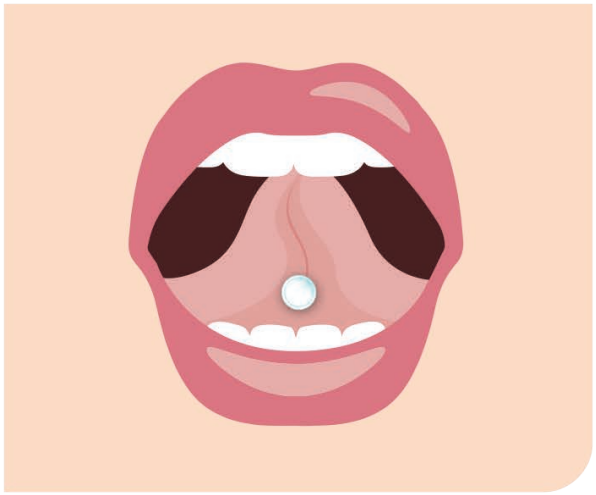
Any of the above events require immediate medical assistance.

As a prescribing physician ensure that you and your staff are trained in basic life support and call an ambulance for immediate medical assistance if necessary. Also, ensure that you and your staff have an appropriate protocol in place for opioid overdose management including the proper use of naloxone to treat opioid overdose. Patients and their caregivers should also be trained on how to use naloxone. It is important to remember that the effect of naloxone is short and the patient might still be in danger after administering naloxone. Therefore the patients should continuously be monitored for signs of relapse.

Chapter 7 Administration of Fenhuma®

Fenhuma® is a very strong opioid and must never be taken by anyone but the person it is prescribed for.

- The patient should sip some water before taking Fenhuma®, if their mouth is dry.
- Fenhuma® tablet should be placed under the tongue, as far back as possible, and allowed to dissolve completely.
- The patient should not bite, chew, suck, or swallow the tablet or it will not work properly.
- The patient should not eat or drink anything until the tablet has completely dissolved



NB. For more information on how to take Fenhuma®, please read the "Patient Information Leaflet" which can be found in the Fenhuma® pack.

Chapter 8

Dosage and Titration

Fenhuma® is available in different strengths. The different strength tablets have different shapes and come in colour-coded boxes to avoid confusion.

Initial dose

The starting dose of Fenhuma® is 100 micrograms (mcg), titrating upwards as shown in the table below. Patients should be monitored during the titration process. Fenhuma® is a generic version of the reference product of Fentanyl sublingual tablets and has demonstrated bioequivalence to the reference product. This means that Fenhuma® is considered interchangeable with the reference product. The initial dosing applies for patients switching from all other fentanyl-containing products for their cancer breakthrough pain (CBTP).

Titration

15-30 minutes*

*During titration, if adequate analgesia is not obtained within 15-30 minutes, a supplemental tablet may be administered.

Decrease dose if undesirable effects are unacceptable

Increase dose if adequate analgesia is not obtained

	First Tablet	Supplemental Tablet
Starting Dose	100mcg	100mcg
Next BTP Episode	200mcg	100mcg
Next BTP Episode	300mcg	100mcg
Next BTP Episode	400mcg	200mcg
Next BTP Episode	600mcg	200mcg
Next BTP Episode	800mcg	No supplemental tablet

Once an appropriate dose has been established, which may be more than one tablet, patients should be maintained on this dose.

Comprehensive range of tablet strengths for flexible dosing

Distinctive tablet shapes and colour-coded packs for easy dose identification.

- During titration, patients can be instructed to use multiples of 100 microgram tablets and/or 200 microgram tablets for any single dose.
- The total dose for a single episode of BTP during the titration phase includes the first tablet(s) taken plus the supplemental tablet(s), if required.
- No more than four (4) tablets should be used at any time.
- No more than 4 episodes of BTP should be treated in any 24 hour period, once the dose of Fenhuma® that controls the BTP has been reached.
- Patients should wait at least 2 hours before treating another episode of BTP with Fenhuma®.
- If adequate analgesia is achieved at the higher dose, but undesirable effects are considered unacceptable, an intermediate dose (using the 100 microgram tablet where appropriate) maybe administered.
- In order to minimise the risk of opioid-related adverse reactions and to identify the appropriate dose, it is imperative that patients be monitored closely by healthcare professionals during the titration process.

If after titration, patients do not experience relief for their BTP episodes, they should first be reassessed so that their pain management strategy can be reviewed and modified as appropriate. Following continued monitoring, patients who continue to receive inadequate pain relief should be referred to a pain or palliative care specialist.

Discontinuation

Monitor and re-evaluate the patient's pain status when renewing prescriptions or during visits. Fenhuma® should be discontinued immediately if the patient no longer experiences CBTP episodes. The treatment for the persistent background pain should be kept as prescribed. If discontinuation of all opioid therapy is required, the patient must be closely monitored to avoid the possibility of abrupt withdrawal effects. Refer to section 4.2 of the SmPC for further information about stopping treatment with Fenhuma®.

Chapter 9

Storage/Safety Information and Disposal of Fenhuma®

Storage and safety information:

Fenhuma® sublingual tablet can cause life-threatening breathing difficulties if ingested by individuals, especially children, for whom it was not prescribed. Additionally, there is a risk of the medication being stolen by individuals who misuse prescription medications. Therefore patients should be advised about the importance of correct storage/disposal of this medicine, as inappropriate storage/disposal could put someone else (not the patient) at risk of accidental opioid-naïve use, or drug diversion.

- Tablets should be stored in a safe and secure place, such as a locked storage space, out of the reach and sight of children and inaccessible to other people, to avoid risk of serious harm and/or death.
- Tablets must be kept in the original blister pack to protect them from moisture.

Please ensure patients understand that, in order to prevent theft, diversion of the drug and misuse, they should always store Fenhuma® in a suitably safe place. Fentanyl, the active ingredient of Fenhuma® sublingual tablets is a target for people who abuse narcotic medicines or other street drugs and therefore storage instructions must be closely followed. Please also see "Disposal" below.

Disposal:

It is your responsibility to highlight the correct disposal process to the patient:

- They should not dispose of unused or expired Fenhuma® through sewage or household waste.
- Any partly used or unused tablets should be returned to the pharmacy where they will be disposed of in accordance with national and local requirements.

Chapter 10 Prescribing Checklist

Please complete the following checklist before prescribing Fenhuma®:

	✓
Check that the indication is in line with the approved indication: management of cancer breakthrough pain (CBTP) in adults.	
Check that the patient is receiving maintenance opioid therapy for their chronic cancer pain.	
Supply the patient/carer with the Fenhuma® Brochure for Patients and Carers.	
Advise the patient/carer of the risks of misuse and signs of Fenhuma® overdose and the need for immediate medical assistance.	
Advise the patient/carer to read the PIL inside the Fenhuma® box or package.	
Explain the administration instructions for the use of Fenhuma®, including how to open the child-resistant blister, the different strengths of Fenhuma® that are available, and the colour-coded packaging for each strength.	
Check that the patient understands the titration steps.	
Advise the patient/carer on the risks of using more than the recommended dose of Fenhuma®	
Refer the patient/carer to the dose monitoring card found at the end of the Fenhuma® Brochure for Patients and Carers.	
Advise and show the patients/carer on how to enter the information in the dose monitoring card.	
Advise the patient/carer about safe storage and the need to keep Fenhuma® out of reach and sight of children.	
Advise the patient/carer on the correct disposal of Fenhuma®.	
Remind the patient/carer to ask their doctor or pharmacist if they have any questions or concerns about Fenhuma®, its administration or the associated risks of misuse, abuse and addiction.	

Chapter 11 Dose monitoring card

- This dose monitoring card serves to keep a record of how many Fenhuma® doses the patient has taken. Remember, it is not safe to treat more than four breakthrough pain episodes per day.
- Remind the patient/carer to fill in the correct dose strength in the dose monitoring card.
- Remind the patient/carer that the date and time Fenhuma® was taken should be documented on the card each time Fenhuma® is taken.
- Remind the patient/carer to take the card to their doctor's visit. The information recorded will help their doctor provide the best pain treatment.
- If the patient/carer cannot use the dose monitoring card, inform them to use other means to keep a record of Fenhuma® use. The patient can ask a friend or carer for help. If necessary, the patient can inform their doctor or pharmacist. This will help the patient keep track of their Fenhuma® use.
- The dose monitoring card found at the end of the Fenhuma® Brochure for Patients and Carers.

Fenhuma® Dose Monitoring Card

100/200/300/400/600/800 micrograms (mcg) sublingual tablets

Dose Monitoring Card: Below is **an example** of the first four doses taken during initial titration.

Date	Time	Amount & Strength of tablets taken
21.04.2023	10:00 am	1 x 100 mcg
21.04.2023	10:15 am	1 x 100 mcg
21.04.2023	04:00 pm	2 x 100 mcg
22.04.2023	09:00 am	2 x 100 mcg

Chapter 12

Advert event reporting

Healthcare professionals are asked to report any suspected adverse reactions. Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme. You can report via:

- the Yellow Card website www.mhra.gov.uk/yellowcard
- the free Yellow Card app available from the Apple App Store or Google PlayStore
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals.

Alternatively you can report suspected adverse drug reactions to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible. By reporting adverse drug reactions, you can help provide more information on the safety of this medicine.

Adverse events should also be reported to **medical_information@glenmarkpharma.com**.

Chapter 13 References

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