

# Narcotic drugs used for pain treatment

Version 4.3

Strategy to restrict the pack sizes or the type of packaging available in public pharmacies.

## 1. Introduction

The document describing the strategy of the FAMHP regarding the delivery status of medicinal products indicates that products with the same active substance, same strength and same pharmaceutical form should in general have the same delivery status.

Exceptions are foreseen for therapeutic classes where the pack sizes or the type of packaging can include an important risk. Those exceptions should be described in an FAMHP guideline that should be published on the website.

The objective of this document is to restrict for narcotic analgesics the pack sizes or the type of packaging that can be available in public pharmacies. Larger pack sizes and container packages can still be accepted for hospital use.

Drugs involved are all opioids that belong to step III of the WHO pain ladder:

- ✓ Morphine
- ✓ Diacetylmorphine (heroin)
- ✓ Oxycodone
- ✓ Fentanyl
- ✓ Hydromorphone
- ✓ Buprenorphine
- ✓ Methadone
- ✓ Nalbuphin
- ✓ Piritramide
- ✓ Pentazocine
- ✓ Pethidine (= meperidine)
- ✓ Tapentadol

Some of those molecules are also used in substitution treatment of opioid addiction. However, those are out of the scope of this document.

## **2. Pack form**

To reduce the risk of accidental or intentional intoxication, oral solid dosage forms of opioids that belong to step III of the WHO pain ladder are reserved for hospital use if packed in containers.

## **3. Justification to restrict pack sizes in public pharmacies**

The literature describes abuse for all opioids that belong to step III of the WHO pain ladder, with potential risk of overdoses. Restricting pack sizes available in public pharmacies and avoiding unnecessary residues of unused drugs are one of the measures in the control of the abuse of these products.

Restricting the pack size can also be seen as one of the measures to avoid accidental overdosage with this type of products.

Apart from those safety considerations, adjustment of the pack size also contributes to the necessary follow up by health care professionals for this type of products.

Reference is made to the recommendations of the Guideline on Risk Management Systems for Medicinal Products for Human Use (EMA/CHMP/96268/2005, annex B, 1.4): "by limiting the number of units the patient will need to see a healthcare professional at defined intervals increasing the opportunity for testing and reducing the length of time a patient is without review...A small pack size can also be useful, especially if over dose is thought to be a major risk or if the potential for drugs to get into the general population needs to be controlled.

## **4. Recommendations**

### **4.1. Prolonged release forms**

All opioids listed in the introduction are used for the treatment of severe and most severe chronic pain. For the treatment of continuous pain, the opioids are presented in prolonged release dosage forms such as prolonged release tablets, prolonged release capsules or transdermal patches.

Patients suffering from severe chronic pain should be followed on a very regular base, as well as their analgesic treatment should be consequently adapted/titrated. It is recommended that maximal pack sizes should not allow treating patients beyond the recommended periods of follow-up.

The patient who suffers from severe chronic pain should be followed twice to four times during the month, in order to evaluate the pain and the other symptoms accompanying the cancer, and to adapt or titrate the different

treatments. Potential interactions between drugs should also be frequently assessed.

For chronic pain, it is sometimes needed to switch between pharmaceutical forms (e.g. from a transdermal to an oral system or inversely) and/or between molecules (opioid rotation). The purpose of this switching is to overcome tolerance development and to decrease adverse effects to the drug. In case of a switch, the amount of residual material should be limited.

For non-cancer pain, the use of WHO step III opioids should also be followed by the physician regularly, in order to prevent over dosage.

It is proposed to restrict the maximal pack size available in public pharmacies for this type of products to one month of treatment. This enables the physician to follow the patient adequately and gives sufficient flexibility.

#### **4.2. Immediate release oral dosage forms**

Immediate release oral dosage forms such as immediate release tablets and capsules and oral solutions are used for dose titration and in the treatment of severe acute pain where nonnarcotic analgesics or step II opioids are insufficiently effective.

When the product is used for titration, the immediate-release formulation is used to find the dose which gives adequate pain control. Thereafter, the patient is transferred to the same daily dose using prolonged-release tablets.

Based on those considerations, it is proposed to restrict the maximal pack size available in public pharmacies for immediate release oral dosage forms to one week of treatment.

Multidose oral solutions are considered to include an additional risk for accidental overdosage. As a consequence, further restrictions may be applied.

#### **4.3. Products developed for systemic absorption through buccal or nasal mucosa**

This type of products is developed to obtain a rapid absorption through buccal mucosa (e.g. as a compressed lozenge, sublingual tablet, buccal tablet) in the management of breakthrough pain.

Breakthrough pain is a transient exacerbation of otherwise controlled chronic background pain. The patient can use the products specifically developed for breakthrough pain maximum 4 times daily. Using it more frequently indicates that the dose of long-acting opioid should be increased.

As their onset of action is very rapid (a few minutes), these agents are the most dangerous and can kill a naïve patient (or a child) within a few minutes after having taken only one tablet.

Therefore pack sizes should be "as small as possible". It is proposed that the largest pack size in public pharmacies should not exceed 10 units. . This rather limited size enables the patient to have enough tablets for a week-end without need to call back the physician.

#### **4.4. Parenteral forms**

To avoid abuse, for example due to residues of unused products, the maximum pack size in public pharmacies of parenteral forms is limited to 10 units.

### **5. Practical application**

For new marketing authorisation applications, the delivery status is evaluated during the procedure using the recommendations described in section 2 and 4.

Below, it is illustrated how those recommendations can be applied for products with an existing MA. The posology is based on what is described in the approved SPC.

Pack sizes for individual pack forms that can be delivered in public pharmacies (containers are reserved for hospital use):

- Morphine

Prolonged release tablets/capsules:	
- Maximum posology 2 per day	60 units
- Maximum posology 1 per day	30 units
Immediate release tablets/capsules:	50 units
Monodose oral solution:	50 units
Multidose oral solution:	
- 2 mg/ml	100 ml
- 20 mg/ml	20 ml
Parenteral:	10 units

- Oxycodone
 

Prolonged release tablets/capsules:	
- Maximum posology 2 per day	60 units
Immediate release tablets/capsules:	50 units
Multidose oral solution:	
- 1mg/ml	250 ml
- 10mg/ml	50 ml
- Fentanyl
 

Transdermal patch:	
- Maximum posology every 3 days	10 units
Buccal tablet:	10 units
Compressed lozenge:	10 units
Sublingual tablet:	10 units
Nasal spray:	10 units
Parenteral:	10 units
- Hydromorphone
 

Prolonged release tablets/capsules:	
- Maximum posology 2 per day	60 units
Immediate release tablets/capsules:	50 units
Parenteral:	10 units
- Buprenorphine (where used for pain treatment)
 

Transdermal patch:	
- Maximum posology every 7 days	5 units
- Maximum posology 2 x / week	10 units
Parenteral:	10 units
Sublingual tablet	50 units

- Methadone (where used for pain treatment)
  - Parenteral: 10 units
- Piritramide
  - Parenteral: 10 units
- Pethidine
  - Parenteral: 10 units
- Tapentadol
  - Prolonged release tablets/capsules:
    - Maximum posology 2 per day 60 units
  - Immediate release tablets/capsules: 50 units
  - Multidose oral solution:
    - 4 mg/ml 250 ml
    - 20 mg/ml 100 ml
- Nalbuphin
  - Parenteral: 10 units
- Pentazocine
  - Immediate release tablets/capsules: 50 units
  - Suppositories: 50 units