Annex III

Amendments to relevant sections of the summary of product characteristics and package leaflet

Note:

The summary of product characteristics and package leaflet may need to be subsequently updated by the national competent authorities, in liaison with the reference Member State, if appropriate

A. Summary of Product Characteristics (SmPC)

< ▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.>

Section 4.1 Therapeutic indications

[The currently approved indications should be deleted and replaced by the following:]

*[**Oral pharmaceutical forms and suppositories**]*
Treatment of acute pain in adults.
< Product Name > must only be used if treatment with other analgesics (e.g. non-steroidal anti-inflammatory drugs, weak opioids) is contraindicated.

[***Solution for injection (i.m.)***]
For single dose application in adults with postoperative pain. If a longer duration of use is required, other pharmaceutical forms are available.
< Product Name > must only be used if treatment with other analgesics (e.g. non-steroidal anti-inflammatory drugs, weak opioids) is contraindicated.

Section 4.2 Posology and method of administration

[The wording below should be inserted in this section]

[…]

[***100 mg IR pharmaceutical form, suppositories***]
Flupirtine should be administered at the lowest effective dose for the shortest duration necessary to achieve adequate analgesia.
The duration of treatment must not exceed 2 weeks.
[…]

Paediatric population
The safety and efficacy of flupirtine in children and adolescents have not been established.
<Product Name> should not be used in children and adolescents under the age of 18 years.

[***400 mg MR pharmaceutical form***]
Flupirtine should be administered for the shortest duration necessary to achieve adequate analgesia.
The duration of treatment must not exceed 2 weeks.
[…]

Paediatric population
The safety and efficacy of flupirtine in children and adolescents have not been established.
<Product Name> should not be used in children and adolescents under the age of 18 years.

[***Solution for injection (i.m.)***]
Paediatric population
The safety and efficacy of flupirtine in children and adolescents have not been established.
<Product Name> should not be used in children and adolescents under the age of 18 years.
[…]

Section 4.3 Contraindications

[The wording below should be inserted in this section]

[…]
[***Oral pharmaceutical forms and suppositories***]
Patients with pre-existing liver disease or alcohol abuse must not take <Product Name>.
Concomitant use of flupirtine with other drugs known to cause drug induced liver injury must be avoided (see Section 4.5).

[***Solution for injection (i.m.)]***
<Product Name> should not be used in patients with pre-existing liver disease or alcohol abuse.
Concomitant use of flupirtine with other drugs known to cause drug induced liver injury must be avoided (see Section 4.5).
[…]

Section 4.4 Special warnings and precautions for use

[The wording below should be inserted in this section]

[…]
[***All pharmaceutical forms***]
Liver function tests must be performed at weekly intervals during treatment with <Product Name> because increased liver enzyme levels, hepatitis and liver failure have been reported in association with flupirtine therapy.
If abnormal liver function tests or clinical symptoms consistent with liver disease occur, treatment with <Product Name> must be discontinued.

Patients should be advised to remain vigilant for any symptoms compatible with hepatic damage during treatment with <Product Name> (e.g. loss of appetite, nausea, vomiting, abdominal pain, fatigue, dark urine, jaundice, pruritus) and to discontinue intake of <Product Name> and to seek medical advice immediately if any such symptoms occur.
[…]

Section 4.5 Interaction with other medicinal products and other forms of interaction

[The wording below should be inserted in this section]

[…]
[***All pharmaceutical forms***]
Concomitant use of flupirtine with other drugs known to cause drug induced liver injury must be avoided (see Section 4.3).
[…]

Section 4.8 Undesirable effects

[The wording below should be inserted in this section]

[…]

*[**All pharmaceutical forms**]*
Hepatobiliary disorders:
Very common: Transaminases increased.
Not known: Hepatitis, liver failure.
[…]

[The wording below should be inserted at the end of this section]

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*.

*[*For the printed materials: No reference to the Appendix V should be included in the printed materials. The above grey-shaded terms will only appear in the published version of the approved product information annexes on EMA's website. The actual details of the national reporting system (as listed within the Appendix V) of the concerned Member State(s) shall be displayed on the printed version. Linguistic adjustments may also be necessary depending on the grammatical rules of the languages used.]*

B. Package Leaflet

< ▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects. >

1. What < product name > is and what it is used for

[This section should replace any existing one and should read as follows:]

[Oral pharmaceutical forms and suppositories]

Treatment of acute pain in adults.
<Product name> must only be used if treatment with other analgesics is contraindicated.

[Solution for injection (i.m.)]

For single dose application in adults with postoperative pain. If a longer duration of use is required, other pharmaceutical forms are available.
<Product name > must only be used if treatment with other analgesics is contraindicated.

2. What you need to know before you use < product name >

[The wording below should be inserted in the relevant sections]

[Oral pharmaceutical forms and suppositories]

Do not <take><use><Product name> if you:

- suffer from pre-existing liver disease
- suffer from alcoholism
- concomitantly use other medicinal products known to cause drug induced liver injury.

[Solution for injection (i.m.)]

Do not use <Product name> if you:

- suffer from pre-existing liver disease
- suffer from alcoholism
- concomitantly use other medicinal products known to cause drug induced liver injury.

[…]

Warnings and precautions

[All pharmaceutical forms]

Your doctor will test liver function every week during treatment with <Product Name> because increased liver enzyme levels, hepatitis and liver failure have been reported in association with flupirtine therapy. If liver function tests show pathological results your doctor will ask you to discontinue intake/use of <Product Name> immediately.

If you observe any symptoms that may indicate hepatic damage during treatment with <Product Name> (e.g. loss of appetite, nausea, vomiting, abdominal discomfort, fatigue, dark urine, jaundice, pruritus) you have to discontinue intake/use of <Product Name> and to seek medical advice immediately if any such symptoms occur.
[…]

3. How to take < product name >

[the wording below should be inserted in the relevant sections]

[…]

[**100 mg IR pharmaceutical form, suppositories**]

Flupirtine should be used at the lowest effective dose for the shortest duration necessary to achieve adequate pain relief.

The duration of treatment must not exceed 2 weeks.

[…]

Use in children and adolescents

The safety and efficacy of flupirtine in children and adolescents have not been established.

<Product Name> should not be used in children and adolescents under the age of 18 years.

[***400 mg MR pharmaceutical form***]

Flupirtine should be used for the shortest duration necessary to achieve adequate pain relief.

The duration of treatment must not exceed 2 weeks.

[…]

Use in children and adolescents

The safety and efficacy of flupirtine in children and adolescents have not been established.

<Product Name> should not be used in children and adolescents under the age of 18 years.

[***Solution for injection (i.m.)]***

Use in children and adolescents

The safety and efficacy of flupirtine in children and adolescents have not been established.

<Product Name> should not be used in children and adolescents under the age of 18 years.

[…]

4. Possible side effects

[…]

[***All pharmaceutical forms***]

Liver disorders:

Very common: Liver enzymes increased

Frequency not known: Hepatitis, liver failure

[…]

[The wording below should be inserted at the end of this section]

Reporting of side effects

If you get any side effects, talk to your <doctor> <or> <,> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

*[*For the printed materials:*

No reference to the Appendix V should be included in the printed materials. The above grey-shaded terms will only appear in the published version of the approved product information annexes. The actual details of the national reporting system (as listed within the Appendix V) of the concerned Member State(s) shall be displayed on the printed version.]