Annex III

Amendments to relevant sections of the product information

Note:

These amendments to the relevant sections of the product information are the outcome of the referral procedure.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

Amendments to relevant sections of the product information

{For all products in Annex I, the existing product information shall be amended (insertion, replacement or deletion of the text, as appropriate) to reflect the agreed wording as provided below}

Summary of product characteristics

- *All methotrexate-containing medicinal products with at least one indication requiring once weekly dosing:*

Any recommendations to split the dose should be deleted from the SmPC.

4.2 Posology and method of administration

- *All methotrexate-containing medicinal products with at least one indication requiring once weekly dosing:*

{This section should be amended as follows (new text underlined, deleted text strikethrough):}

~~Only physicians with experience in the various properties of the medicinal product and its mode of action should prescribe methotrexate.~~

Methotrexate should only be prescribed by physicians with expertise in the use of methotrexate and a full understanding of the risks of methotrexate therapy.

- *All oral formulations of methotrexate-containing medicinal products with at least one indication requiring once weekly dosing:*

{The following wording should be reflected:}

The prescriber should ensure that patients or their carers will be able to comply with the once weekly regimen.

- *All parenteral formulations of methotrexate-containing products with at least one indication requiring treatment once a week (e.g. rheumatologic/dermatological diseases or Crohn's disease)*

{This section should include the following wording:}

Important warning about the dosage of <product name> (methotrexate)

In the treatment of <indication(s) requiring dosing once a week, e.g. rheumatoid arthritis, psoriasis, etc.)>, <product name> (methotrexate) **must only be used once a week.** Dosage errors in the use of <product name> (methotrexate) can result in serious adverse reactions, including death. Please read this section of the summary of product characteristics very carefully.

Labelling

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

7. OTHER SPECIAL WARNING(S), IF NECESSARY

A framed warning should be placed at the front of the outer package in a clearly visible place, e.g. after the information on the name and the active substance; the letters should be of appropriate size; the respective wording and frame should be in red colour on a white background, but ensuring that it contrasts with the rest of the packaging. The warning should read as follows:

- *Oral formulations of methotrexate-containing medicinal products only with indications requiring treatment once a week:*

{The following wording should be included on the outer packaging}

[...]

Take only once a week on ……(include weekday of intake in full)

[...]

- *Oral formulations of methotrexate-containing medicinal products with at least one indication requiring treatment once a week:*

[...]

For [indication*] Take only once a week on …….. (include weekday of intake in full)

**[Indication] should be inserted by the MAHs in grouped terms, e.g. colitis, arthritis psoriasis, where applicable.*

[...]

- *Parenteral formulations of methotrexate-containing medicinal products only with indications requiring treatment once a week:*

[...]

Use only once a week on …….. (include weekday of use in full)

[...]

- *Parenteral formulations of methotrexate-containing medicinal products with at least one indication requiring treatment once a week and oncologic indication:*

[...]

For [indication*] Use only once a week

on ……(include weekday of use in full)

**[Indication] should be inserted by the MAHs in grouped terms, e.g. colitis, arthritis, psoriasis, where applicable.*

[…]

PARTICULARS TO APPEAR ON THE INTERMEDIATE PACKAGING

7. OTHER SPECIAL WARNING(S), IF NECESSARY

{For parenteral formulations, a warning e.g. in red should be implemented once in a prominent place on the intermediate packaging. The warning should read as follows:}

- *Methotrexate-containing products only with indications requiring treatment once a week:*

Use only once a week

- *methotrexate-containing products with at least one indication requiring treatment once a week:*

For [indication*] use only once a week

**[Indication] should be inserted by the MAHs in grouped terms, e.g. colitis, arthritis psoriasis, where applicable.*

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

7. OTHER SPECIAL WARNING(S), IF NECESSARY

{For oral formulations, a warning e.g. in red should be implemented on the immediate packaging. On blisters the wording should be printed repeatedly in one or more (e.g. on multilingual packages) rows depending on readability. On other immediate packaging it should be implemented once only in a prominent place.}

{For parenteral formulations (solution for injection in prefilled syringes or pens), the warning should be implemented once in a prominent place of the immediate packaging if space allows.}

- *All methotrexate-containing products only with indications requiring treatment once a week:*

{The warning should read as follows:}

Take/Use [depending on formulation] only once a week

- *All methotrexate-containing products with at least one indication requiring treatment once a week:*

{The warning should read as follows:}

For [indication*] take/use [depending on formulation] only once a week

**[Indication] should be inserted by the MAHs in grouped terms, e.g. colitis, arthritis psoriasis, where applicable.*

Patient card text

- *Oral formulations of methotrexate-containing medicinal products with at least one indication requiring treatment once a week:*

{This section should include the following wording:}

THIS PATIENT CARD IS ONLY INTENDED FOR PATIENTS WHO USE A METHOTREXATE-CONTAINING MEDICINE FOR <INDICATIONS INSERTED BY THE MAHS IN GROUPED TERMS, E.G. COLITIS, ARTHRITIS, PSORIASIS, AS PER INDICATIONS LISTED IN PACKAGE LEAFLET>.

IF YOU USE METHOTREXATE FOR ONE OF THE ABOVE MENTIONED INDICATIONS, YOU SHOULD ONLY TAKE METHOTREXATE ONCE A WEEK

Write here in full the day of the week for intake: _____

Do not take more than the prescribed dose.

Overdose could lead to serious adverse effects and may be fatal. Symptoms of overdose are e.g. sore throat, fever, mouth ulcers, diarrhoea, vomiting, skin rashes, bleeding or unusual weakness. If you think you have taken more than the prescribed dose, consult a physician immediately.

Always show this card to health care professionals not familiar with your methotrexate treatment to alert them about your once weekly use (e.g. on hospital admission, change of care).

For more information, please read the patient leaflet inserted in the package.

Package leaflet

- *All methotrexate-containing medicinal products with at least one indication requiring treatment once a week (e.g. rheumatologic/dermatological diseases or Crohn's disease):*

{Any reference to dividing the dose for indications requiring treatment once a week should be removed from the package leaflet.}

- *Parenteral formulations of methotrexate-containing products with at least one indication requiring treatment once a week (e.g. rheumatologic/dermatological diseases or Crohn's disease)*

Section 3: How to use <product name>

{A boxed warning should be included in this section as follows:}

Important warning about the dose of <product name> (methotrexate):

Use <product name> **only once a week** for the treatment of <indication(s) requiring dosing once a week, e.g. rheumatoid arthritis, psoriasis etc.>. [Using] too much of <product name> (methotrexate) may be fatal. Please read section 3 of this leaflet very carefully. If you have any questions, please talk to your doctor or pharmacist before you take this medicine.