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 the 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.

If the current SmPC and package leaflet includes corresponding information in any other sections, it should be deleted in order to avoid repeated information.]

Summary of product characteristics

Section 4.2 Posology and method of administration (and/or any other section as applicable)

[Removal of any recommendation on regular blood count monitoring of patients.]

[Removal of any text suggesting that the risk of agranulocytosis is increased after one week or on long-term use.]

Section 4.3 Contraindications

[The following contraindications should be inserted]

- **Agranulocytosis in the medical history induced by metamizole, other pyrazolones or pyrazolidines**
- **Impaired bone marrow function or diseases of the hematopoietic system**

Section 4.4 Special warnings and precautions for use

[The following text should be added as a boxed warning at the top of section 4.4]

Agranulocytosis

Treatment with metamizole can cause agranulocytosis, which may be fatal (see section 4.8). It may occur even after metamizole has previously been used without complications.

Metamizole-induced agranulocytosis is an idiosyncratic adverse reaction. It is not dose-dependent, and may occur at any time during treatment, even shortly after treatment discontinuation.

Patients must be instructed to discontinue their treatment and seek immediate medical attention in case any symptoms suggestive of agranulocytosis appear (e.g. fever, chills, sore throat and painful mucosal changes, especially in the mouth, nose and throat or in the genital or anal region).

If metamizole is taken for fever, some symptoms of emerging agranulocytosis may go unnoticed. Similarly, symptoms may also be masked in patients receiving antibiotic therapy.

If signs and symptoms suggestive of agranulocytosis occur, a complete blood cell count (including differential blood count) should be performed immediately, and treatment must be stopped while waiting for the results. If confirmed, treatment must not be reintroduced (see section 4.3).

Package leaflet

[Removal of any recommendation on regular blood count monitoring of patients.]

[Any text suggesting that the risk is increased after one week or on long-term use should be removed]

[The following text should be added as a boxed warning at the top of the package leaflet]

<X> may cause abnormally low white blood cell count (agranulocytosis), which can lead to serious and life-threatening infections (see section 4).

You must stop taking the medicine and contact your doctor immediately if you experience any of the following symptoms: fever, chills, sore throat, painful sores in your nose, mouth and throat, or in the genital or anal region.

If you ever had agranulocytosis with metamizole or similar medicines, you must never take this medicine again (see section 2).

Section 2: What you need to know before you <take> <use> <X>

Do not <take><use> <X>

- **If you previously had a significant decrease in a type of white blood cells called granulocytes, which was caused by metamizole or any similar medicines called pyrazolones or pyrazolidines.**
- **If you have problems with your bone marrow or have a condition that affects how your blood cells are made or work.**

Warnings and precautions

Talk to your doctor or pharmacist before <taking><using><X>

Abnormally low white blood cell count (agranulocytosis)

<X> can cause agranulocytosis, a very low level of a type of white blood cells called granulocytes, which are important for fighting off infection (see section 4). You must stop taking metamizole and see a doctor immediately if you experience the following symptoms, as this may indicate possible agranulocytosis: chills, fever, sore throat and painful sores in mucosa (moist body surfaces) especially in the mouth, nose and throat or in the genital or anal region. Your doctor will perform laboratory test to check the level of your blood cells.

If metamizole is taken for fever, some symptoms of emerging agranulocytosis may go unnoticed. Similarly, symptoms may also be masked if you are receiving antibiotic therapy.

Agranulocytosis may develop anytime during the use of <X> and even shortly after you have stopped taking metamizole.

You may get agranulocytosis even if you have used metamizole without problems in the past.