

Product Information as approved by the CMDh on 20 May 2015.

Annex III

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

Note:

These amendments to the relevant sections of the Summary of Product Characteristics and Package Leaflet 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.

For all ibuprofen-containing products

A. Summary of Products Characteristics

Section 4.2 - Posology and method of administration

[The section should be amended to reflect the following wording]

[...]

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

[...]

Section 4.3 - Contraindications

[The section should be amended to reflect the following wording]

[...]

Severe heart failure (NYHA Class IV)

[...]

Section 4.4 - Special warnings and precautions for use

[The section should be amended to reflect the following wording]

[...]

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (2400 mg/day) should be avoided.

Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

[...]

Section 4.5 - Interactions with other medicinal products and other forms of interaction

[The section should be amended to reflect the following wording]

[...]

Acetylsalicylic acid

Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid

cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

[...]

Section 4.8 - Undesirable effects

[The section should be amended to reflect the following wording]

[...]

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

[...]

Section 5.1 - Pharmacodynamic properties

[The section should be amended to reflect the following wording]

[...]

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

[...]

B. Package Leaflet

Section 2 - What you need to know before you take [Invented name]

[...]

Warnings and precautions

[The section should be amended to reflect the following wording]

[...]

Anti-inflammatory/pain-killer medicines like ibuprofen may be associated with a small increased risk of heart attack or stroke, particularly when used at high doses. Do not exceed the recommended dose or duration of treatment.

You should discuss your treatment with your doctor or pharmacist before taking [Invented name] if you:

- have heart problems including heart failure, angina (chest pain), or if you have had a heart attack, bypass surgery, peripheral artery disease (poor circulation in the legs of feet due to narrow or blocked arteries), or any kind of stroke (including 'mini-stroke' or transient ischaemic attack "TIA").

- have high blood pressure, diabetes, high cholesterol, have a family history of heart disease or stroke, or if you are a smoker.

[...]

Other medicines and [Invented name]

[The section should be amended to reflect the following wording]

[...]

[Invented name] may affect or be affected by some other medicines. For example:

[...]

- medicines that are anti-coagulants (i.e. thin blood/prevent clotting e.g. aspirin/acetylsalicylic acid, warfarin, ticlopidine)
- medicines that reduce high blood pressure (ACE-inhibitors such as captopril, beta-blockers such as atenolol medicines, angiotensin-II receptor antagonists such as losartan)

[...]

Some other medicines may also affect or be affected by the treatment of [Invented name]. You should therefore always seek the advice of your doctor or pharmacist before you use [Invented name] with other medicines.

[...]

For all dexibuprofen-containing products

A. Summary of Products Characteristics

Section 4.2 - Posology and method of administration

[The section should be amended to reflect the following wording]

[...]

The dosage should be adjusted to the severity of the disorder and the complaints of the patient. Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

[...]

Section 4.3 - Contraindications

[The section should be amended to reflect the following wording]

[...]

Severe heart failure (NYHA Class IV)

[...]

Section 4.4 - Special warnings and precautions for use

[The section should be amended to reflect the following wording]

[...]

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg/day) is associated with an increased risk of arterial thrombotic events. Although there are limited data on the arterial thrombotic risk of dexibuprofen, it is reasonable to assume that the risk with high dose dexibuprofen (1200 mg/day) would be similar to that associated with high dose ibuprofen (2400 mg/day).

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with dexibuprofen after careful consideration and high doses (1200 mg/day) should be avoided.

Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of dexibuprofen (1200 mg/day) are required.

[...]

Section 4.5 - Interactions with other medicinal products and other forms of interaction

[The section should be amended to reflect the following wording (if sub-sections exist this wording should be included in the relevant sub-section, e.g. concomitant use not recommended)]

[...]

Acetylsalicylic acid

Concomitant administration of dexibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1). Whilst there are no data available for dexibuprofen, it is reasonable to assume that a similar interaction may exist between dexibuprofen (= S(+)-ibuprofen) (which is the pharmacologically active enantiomer of ibuprofen) and low-dose acetylsalicylic acid.

[...]

Section 4.8 - Undesirable effects

[The section should be amended to reflect the following wording]

[...]

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4). Although there are limited data on the arterial thrombotic risk of dexibuprofen, it is reasonable to assume that the risk with high dose dexibuprofen (1200 mg/day) would be similar to that associated with high dose ibuprofen (2400 mg/day).

[...]

Section 5.1 - Pharmacodynamic properties

[The section should be amended to reflect the following wording]

[...]

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5). Whilst there are no data available for dexibuprofen, it is reasonable to assume that a similar interaction may exist between dexibuprofen (= S(+)-ibuprofen) (the pharmacologically active enantiomer of ibuprofen) and low-dose acetylsalicylic acid.

[...]

B. Package Leaflet

Section 2 - What you need to know before you take [Invented name]

[...]

Warnings and precautions

[The section should be amended to reflect the following wording]

[...]

Anti-inflammatory/pain-killer medicines like dexibuprofen may be associated with a small increased risk of heart attack or stroke, particularly when used at high doses. Do not exceed the recommended dose or duration of treatment.

You should discuss your treatment with your doctor or pharmacist before taking [Invented name] if you:

- have heart problems including heart failure, angina (chest pain), or if you have had a heart attack, bypass surgery, peripheral artery disease (poor circulation in the legs of feet due to narrow or blocked arteries), or any kind of stroke (including 'mini-stroke' or transient ischaemic attack "TIA").
- have high blood pressure, diabetes, high cholesterol, have a family history of heart disease or stroke, or if you are a smoker.

[...]

Other medicines and [Invented name]

[The section should be amended to reflect the following wording]

[...]

[Invented name] may affect or be affected by some other medicines. For example:

[...]

- medicines that are anti-coagulants (i.e. thin blood/prevent clotting e.g. aspirin/acetylsalicylic acid, warfarin, ticlopidine)
- medicines that reduce high blood pressure (ACE-inhibitors such as captopril, beta-blockers such as atenolol medicines, angiotensin-II receptor antagonists such as losartan)

[...]

Some other medicines may also affect or be affected by the treatment of [Invented name]. You should therefore always seek the advice of your doctor or pharmacist before you use [Invented name] with other medicines.

[...]