

Annex III

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

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.

I. Summary of Product Characteristics

Section 4.2 - Posology and method of administration

This section should be amended to reflect the following wording:

[Product name] should be used at the lowest effective dose and for the shortest possible duration.

In adults and children over 40 kg in weight, the maximum daily dose is 100 mg per day.

In the elderly, the maximum daily dose is 50 mg per day (see section 4.4).

In children up to 40 kg in weight, the maximum daily dose is 2 mg/kg/day.

Section 4.3 Contraindications

The following wording should be added to this section:

Patients with a known acquired or congenital QT interval prolongation.

Patients with a known risk factor to QT interval prolongation including a known cardiovascular disease, significant electrolytes imbalance (hypokalaemia, hypomagnesaemia), family history of sudden cardiac death, significant bradycardia, concomitant use with drugs known to prolong the QT interval and/or induce Torsade de Pointes (see sections 4.4 and 4.5).

Section 4.4 Special warnings and precautions for use

The following wording should be added to this section:

Cardiovascular effects

Hydroxyzine has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, there have been cases of QT interval prolongation and torsade de pointes in patients taking hydroxyzine. Most of these patients had other risk factors, electrolyte abnormalities and concomitant treatment that may have been contributory (see section 4.8).

Hydroxyzine should be used at the lowest effective dose and for the shortest possible duration.

Treatment with hydroxyzine should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and the patients should seek immediate medical attention.

Patients should be advised to promptly report any cardiac symptoms.

Elderly patients

Hydroxyzine is not recommended in elderly patients because of a decrease of hydroxyzine elimination in this population as compared to adults and the greater risk of adverse reactions (e.g. anticholinergic effects) (see sections 4.2 and 4.8).

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

The following wording should be added to this section:

Associations contraindicated

Co-administration of hydroxyzine with drugs known to prolong the QT interval and/or induce Torsade de Pointes e.g. class IA (e.g. quinidine, disopyramide) and III antiarrhythmics (e.g. amiodarone, sotalol), some antihistamines, some antipsychotics (e.g. haloperidol), some antidepressants (e.g. citalopram, escitalopram), some antimalarial drugs (e.g. mefloquine), some antibiotics (e.g. erythromycin, levofloxacin, moxifloxacin), some antifungal agents (e.g. pentamidine), some gastro-intestinal medicines (e.g. prucalopride), some medicines used in cancer (e.g., toremifene, vandetanib), methadone, increase the risk of cardiac arrhythmia. Therefore, the combination is contra-indicated (see section 4.3).

Associations requiring precaution of use

Caution with bradycardia and hypokalaemia-inducing drugs.

The following wording should be present in this section:

Associations requiring precaution of use

Hydroxyzine is metabolized by alcohol dehydrogenase and CYP3A4/5 and an increase in hydroxyzine blood concentrations may be expected when hydroxyzine is co-administered with drugs known to be potent inhibitors of these enzymes.

Section 4.8 Undesirable effects

The following wording should be added to this section:

Not known: ventricular arrhythmias (e.g. Torsade de Pointes), QT interval prolongation (see section 4.4).

II. Package leaflet

The following wording should be included in the specified sections:

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

Do not <take> <use> X

- if your ECG (electrocardiogram) shows a heart rhythm problem called "QT interval prolongation"
- if you have or had a cardiovascular disease or if your heart rate is very low
- if you have low salt levels in your body (e.g. low level of potassium or of magnesium)
- if you are taking certain medicines for heart rhythm problems or medicines that may affect the heart rhythm (see "Other medicines and X")
- if anyone in your close family has died suddenly of heart problems

Warnings and precautions

X may be associated with an increased risk of heart rhythm disorder which may be life threatening. Therefore, tell your doctor if you have any heart problems or are taking any other medicines, including medicines obtained without prescription.

While taking X, seek immediate medical attention if you experience heart problems such as palpitations, trouble breathing, loss of consciousness. Treatment with hydroxyzine should be stopped.

Other medicines and X

<Tell your <doctor> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used> or might <take> <use> any other medicines.> This includes any medicines obtained without prescription. X can affect or be affected by other medicinal products.

Do not take X if you are taking medicine to treat:

- bacterial infections (e.g. the antibiotics erythromycin, moxifloxacin, levofloxacin)
- fungal infections (e.g. pentamidine)
- heart problems or high blood pressure (e.g., amiodarone, quinidine, disopyramide, sotalol)
- psychoses (e.g. haloperidol)
- depression (e.g. citalopram, escitalopram)
- gastro-intestinal disorders (e.g. prucalopride)
- allergy
- malaria (e.g. mefloquine)
- cancer (e.g. toremifene, vandetanib)
- drug abuse or severe pain (methadone)

Section 3 “How to <take> <use> X”

<Always <take> <use> this medicine exactly as your doctor <or pharmacist> has told you. Check with your <doctor> <or> <pharmacist> if you are not sure.>

X should be used at the lowest effective dose and the treatment period should be as short as possible.

In adults and children over 40 kg in weight, the maximum daily dose is 100 mg per day in all indications.

In the elderly, the maximum daily dose is 50 mg per day.

In children up to 40 kg, the maximum daily dose is 2 mg/kg/day.

If you <take> <use> more X than you should

If you have used or taken too much X, immediately contact [to be completed nationally], in particular if a child has taken too much. In the event of overdose, symptomatic treatment could be implemented. An ECG monitoring could be undertaken, because of the possibility of a heart rhythm problem such as QT interval prolongation or Torsade de Pointes.

Section 4 “Possible side effects”

Not known (frequency cannot be estimated from the available data)

Stop taking the medicine and seek immediate medical attention if you experience any problems with the heart rhythm such as palpitations, trouble breathing or loss of consciousness.