

Annex III

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

Note:

The amendments to the Summary of Product Characteristics and package leaflets 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

4.2 Posology and method of administration

[Replaces current sentence 'The recommended daily dose for adults is 10 mg']

The treatment should be taken in a single intake and not be re-administered during the same night.

The recommended daily dose for adults is 10 mg to be taken immediately at bedtime. The lowest effective daily dose of zolpidem should be used and must not exceed 10 mg.

[...]

4.4 Special warnings and precautions for use

[The wording below should be inserted in this section]

[...]

Next-day psychomotor impairment

The risk of next-day psychomotor impairment, including impaired driving ability, is increased if:

- zolpidem is taken within less than 8 hours before performing activities that require mental alertness (see section 4.7);
- a dose higher than the recommended dose is taken;
- zolpidem is co-administered with other CNS depressants or with other drugs that increase the blood levels of zolpidem, or with alcohol or illicit drugs (see section 4.5).

Zolpidem should be taken in a single intake immediately at bedtime and not be re-administered during the same night.

[...]

Amnesia

[...]

In order to reduce the risk, patients should ensure that they will be able to have an uninterrupted sleep of 8 hours (see section 4.8).

[...]

4.5 Interaction with other medicinal products and other forms of interaction

[The wording below should be inserted in this section under the following headings]

[...]

Combination with CNS depressants

Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, antiepileptic drugs, anaesthetics and sedative antihistamines. Therefore, concomitant use of zolpidem with these drugs may increase drowsiness and next-day psychomotor impairment, including impaired driving ability (see section 4.4 and section 4.7). Also, isolated cases of visual hallucinations were reported in patients taking zolpidem with antidepressants including bupropion, desipramine, fluoxetine, sertraline and venlafaxine.

Co- administration of fluvoxamine may increase blood levels of zolpidem, concurrent use is not recommended.

[...]

CYP450 inhibitors and inducers

Co- administration ciprofloxacin may increase blood levels of zolpidem, concurrent use is not recommended.

[...]

Other drugs

[When present in the current SmPC, the following sentence should be modified to remove reference to cimetidine]

When zolpidem was administrated with ranitidine ~~or cimetidine~~, no significant pharmacokinetic interactions were observed.

[...]

4.7 Effects on ability to drive and use machines

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

[Invented name] has major influence on the ability to drive and use machines.

Vehicle drivers and machine operators should be warned that, as with other hypnotics, there may be a possible risk of drowsiness, prolonged reaction time, dizziness, sleepiness, blurred/double vision and reduced alertness and impaired driving the morning after therapy (see section 4.8). In order to minimise this risk a resting period of at least 8 hours is recommended between taking zolpidem and driving, using machinery and working at heights.

Driving ability impairment and behaviours such as 'sleep-driving' have occurred with zolpidem alone at therapeutic doses.

Furthermore, the co-administration of zolpidem with alcohol and other CNS depressants increases the risk of such behaviours (see section 4.4 and 4.5). Patients should be warned not to use alcohol or other psychoactive substances when taking zolpidem.

5.1 Pharmacodynamic properties

[The wording below should be inserted in this section]

[...]

The randomized trials only showed convincing evidence of efficacy of 10mg zolpidem.

In a randomized double-blind trial in 462 non-elderly healthy volunteers with transient insomnia, zolpidem 10mg decreased the mean time to fall asleep by 10 minutes compared to placebo, while for 5mg zolpidem this was 3 minutes.

In a randomized double-blind trial in 114 non-elderly patients with chronic insomnia, zolpidem 10mg decreased the mean time to fall asleep by 30 minutes compared to placebo, while for 5mg zolpidem this was 15 minutes.

In some patients, a lower dose of 5mg could be effective.

B. Package Leaflet

2. What you need to know before you are given [Invented Name]

[The wording below should be inserted in this section under the following headings]

Warnings and precautions

Next-day psychomotor impairment (see also Driving and using machines)

The day after taking [Invented Name], the risk of psychomotor impairment, including impaired driving ability may be increased if:

- You take this medicine less than 8 hours before performing activities that require your alertness
- You take a higher dose than the recommended dose
- You take zolpidem while you are already taking another central nervous system depressants or another medicines that increase zolpidem in your blood, or while drinking alcohol, or while taking illicit substances

Take the single intake immediately at bedtime.

Do not take another dose during the same night.

Other medicines and [Invented name]

[...]

While taking zolpidem with the following medicines, drowsiness and next-day psychomotor impairment effects, including impaired driving ability, may be increased.

- Medicines for some mental health problems (antipsychotics)
- Medicines for sleep problems (hypnotics)
- Medicines to calm or reduce anxiety
- Medicines for depressions
- Medicines for moderate to severe pain (narcotic analgesics)
- Medicines for epilepsy
- Medicines used for anesthesia
- Medicines for hay fever, rashes or other allergies that can make you sleepy (sedatives antihistamines)

While taking zolpidem with antidepressants including bupropion, desipramine, fluoxetine, sertraline and venlafaxine, you may see things that are not real (hallucinations)

It is not recommended to take zolpidem with fluvoxamine or ciprofloxacin.

Driving and using machines

[...]

[Invented Name] has major influence on the ability to drive and use machines such as "sleep driving". On the day after taking [Invented Name] (as other hypnotic medicines), you should be aware that:

- You may feel drowsy, sleepy, dizzy or confused

- Your quick decision-making may be longer
- Your vision may be blurred or double
- You may be less alert

A period of at least 8 hours is recommended between taking zolpidem and driving, using machinery and working at heights to minimize the above listed effects.

Do not drink alcohol or take other psychoactive substances while you are taking [Invented Name], as it can increase the above listed effects

[...]

3. How to take [product name]

[The wording below should be inserted in this section]

The recommended dose per 24 hours is 10 mg of [Invented Name]. A lower dose may be prescribed to some patients. [Invented Name] should be taken:

- as a single intake,
- just before bedtime

Make sure you have a period of at least 8 hours after taking this medicine before performing activities that require your alertness.

Do not exceed 10mg per 24 hours.