

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

4.1 Therapeutic indications

[This section should be read as follows]

Treatment of symptoms in patients with osteoarthritis of the hip or knee, with delayed effect.

Treatment with diacerein is not recommended in patients with rapidly progressive hip osteoarthritis, as they may have a weaker response to diacerein.

4.2 Posology and method of administration

[The wording below should be added at the top of this section]

The treatment should be initiated by specialists experienced in the treatment of osteoarthritis.

Posology

[The dose recommendation for adults should be as follows]

As some patients may experience loose stools or diarrhoea, the recommended starting dose is 50 mg once daily with evening meal for the first 2 to 4 weeks of treatment, after which the recommended daily dose is 50mg twice daily.

The treatment should be taken with food, one with breakfast and the other with evening meal. The capsules must be swallowed intact, without opening them, together with a glass of water.

[The following wording should also be reflected in this section]

Diacerein is not recommended in patients older than 65 years.

[In addition, any existing dose recommendation in case of hepatic impairment should be deleted from this section as diacerein is now contraindicated in patients with liver disease.]

4.3. Contraindications

[The following contraindication should be added in this section and replace any existing wording on hepatic insufficiency]

- Current and/or history of liver disease

4.4 Special warnings and precautions for use

[The wording on diarrhoea and hepatotoxicity in this section should be presented and read as follows]

Diarrhoea

Intake of diacerein frequently leads to diarrhoea (see section 4.8) that can consequently lead to dehydration and hypokalaemia.

Patients should be advised to stop diacerein treatment in case of diarrhoea and contact their physician to discuss treatment alternatives.

Caution should be exercised in patients receiving diuretics, because dehydration and hypokalaemia may occur. Particular caution should also be exercised in case of hypokalaemia in patients treated with cardiac glycosides (digitoxin, digoxin) (see section 4.5).

Concomitant intake of laxatives should be avoided.

Hepatotoxicity

Elevated serum hepatic enzyme levels and symptomatic acute hepatic injury have been reported with diacerein in the post-marketing phase (see section 4.8).

Before treatment with diacerein is initiated, the patient should be questioned about possible comorbid conditions and past or concurrent liver disease and screened for major causes of active hepatic disease. A diagnosis of liver disease is a contraindication to diacerein use (see section 4.3).

Signs of hepatic injury should be monitored and caution should be exercised when diacerein is used concomitantly with other medicinal products associated with hepatic injury. Patients should be advised to limit their alcohol intake while on treatment with diacerein.

Treatment with diacerein should be stopped if elevation of hepatic enzymes or suspected signs or symptoms of liver damage are detected. Patients should be advised about the signs and symptoms of hepatotoxicity and must be advised to immediately contact their physician in case of appearance of symptoms suggestive of liver damage.

4.5 Interaction with other medicinal products and other forms of interaction

[The following wording should be reflected in this section]

Intake of diacerein can lead to diarrhoea and hypokalaemia. Caution must be exercised in the concomitant administration of diuretics (high-ceiling loop and thiazides) and/or cardiac glycosides (digitoxin, digoxin), as the risk of arrhythmia is increased (see section 4.4).

4.8 Undesirable effects

[The following text should be reflected in this section]

GASTROINTESTINAL DISORDERS

Very common (> 1/10): diarrhoea, abdominal pain.

Common (> 1/100 and < 1/10): frequent bowel movements, flatulence.

As a rule, these effects abate with continuing treatment. In some cases, diarrhoea was severe with complications such as dehydration and disorders of fluid and electrolyte balance.

HEPATOBIILIARY DISORDERS

Uncommon ($\geq 1/1000$ and < 1/100): Cases of elevated hepatic enzymes in serum.

SKIN AND SUBCUTANEOUS TISSUE DISORDERS

Common (> 1/100 and < 1/10): pruritus, rash, eczema.

From post-marketing surveillance

[...]

HEPATOBIILIARY DISORDERS

Cases of acute liver injury, including elevated serum hepatic enzymes and cases of hepatitis have been reported in the post-marketing phase with diacerein. Most of them occurred during the first months of treatment. Patients should be monitored for signs and symptoms of hepatic injury (see section 4.4).

B. Package Leaflet

1. What [Invented Name] is and what it is used for

[This section should be read as follows]

[Invented Name] contains diacerein and is used to relieve symptoms of osteoarthritis of the hip or knee.

It takes some time for [Invented Name] to have its effect. Treatment with [Invented Name] is therefore not recommended for a specific form of hip osteoarthritis called rapidly progressive (worsening) hip osteoarthritis. Patients with such form of the disease may derive less benefit from treatment.

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

Do not take [Invented Name]:

[The following contraindication should be added here and replace any existing wording on hepatic insufficiency]

- if you have any liver problems or a history of liver problems

Warnings and precautions

[The following wording should be reflected in this section]

Talk to your doctor before taking [Invented Name] if you have ever suffered from liver disease.

Some patients may experience loose stools or diarrhoea after the intake of [Invented Name]. If you have diarrhoea while taking this medicine, stop taking [Invented Name] and contact your doctor to discuss which other treatments you can take.

You should not take laxatives during your treatment with [Invented Name].

Liver problems including raised liver enzymes in the blood and hepatitis (inflammation in the liver) have been reported in some patients taking diacerein. Your doctor may ask you to undergo blood tests to check your liver function.

Other medicines and [Invented Name]

[The following wording should be reflected in this section]

Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

[Invented Name] with food, drink and alcohol

[The following wording should be reflected in this section]

Drinking alcohol while taking [Invented Name] may increase the risk of liver damage. You should limit your alcohol consumption while you are undergoing treatment with [Invented Name].

3. How to take [Invented Name]

[The following wording should be reflected in this section]

It is recommended that you start treatment with one capsule in the evening for the first 2-4 weeks, after which the dose can be increased to two capsules per day.

[Invented Name] should be taken with food, one with breakfast and the other with the evening meal. The capsules must be swallowed intact, without opening them, with a glass of water.

[The following wording should also be reflected in this section]

Diacerein is not recommended in patients older than 65 years.

[In addition, any existing dose recommendation for patients with hepatic impairment should be deleted from this section as diacerein is now contraindicated in patients with liver disease.]

4. Possible side effects

[The following text should be reflected in this section]

Tell your doctor immediately and stop taking [Invented Name] if you experience unusually frequent liquid or watery stools.

[The following text should be reflected in this section]

Tell your doctor immediately if you have abdominal pain, jaundice (yellow discolouration of the eyes or skin), impaired consciousness or itching of the skin, as these may indicate serious conditions such as liver disease.

[The following side effects should be inserted in this paragraph]

Very common side effects (may affect more than 1 in 10 people treated):

- diarrhoea,
- abdominal pain

[The following side effects should be inserted in this paragraph]

Common side effects (may affect up to 1 in 10 people treated):

- frequent bowel movements,
- flatulence
- pruritus (itching), rash, eczema (itchy, red rash).

[The following side effects should be inserted in this paragraph]

Uncommon side effects (may affect up to 1 in 100 people):

- increase in liver enzymes levels in blood tests.

[The following wording should be reflected in this section]

In some cases, diarrhoea can be severe with life threatening complications such as fluid loss and electrolyte disturbances.