

2.5 Clinical overview

Introduction

Axsain (capsaicin 0.075% cream) is currently licensed in the UK for the symptomatic relief of neuralgia associated with and following Herpes Zoster infections (post-herpetic neuralgia) after open skin lesions have healed, and for the symptomatic management of painful diabetic peripheral polyneuropathy.

Zacin® (Capsaicin Cream 0.025%) is currently licensed in the UK for the symptomatic relief of pain associated with osteoarthritis.

Although the precise mechanism of action of capsaicin is not fully understood, current evidence suggests that capsaicin renders skin insensitive to pain by depleting and preventing re-accumulation of substance P in peripheral sensory neurons. Substance P is thought to be the principal chemo-mediator of pain impulses from the periphery to the Central Nervous System.

Following the production of a 5-year Periodic Safety Update Report (PSUR) covering the period 20 March 2003 to 19 March 2009 for Axsain® (Capsaicin Cream 0.075%) and Zacin® (Capsaicin Cream 0.025%) a review was performed to determine whether additional irritant effects, such as nasal irritation and throat irritation should be added to the summary of product characteristics (SmPCs).

2.5.1 Product Development Rationale

Not applicable for this application.

2.5.2 Overview of Biopharmaceutics

Not applicable for this application.

2.5.3 Overview of Clinical Pharmacology

Not applicable for this application.

2.5.4 Overview of Efficacy

Not applicable for this application.

2.5.5 Overview of Safety

2.5.5.1 Review of additional irritant effects

Review of the Cephalon Pharmacovigilance database identified a total of 32 non-serious cases mapping to the Preferred Terms of Nasal Discomfort (8 cases) and Throat Irritation (24 cases) for the active ingredient capsaicin. Of the 8 cases of nasal discomfort, the reported verbatim term was either nasal irritation or irritation of the nose. Of the 24 cases of throat irritation, the majority of verbatim reports were of *throat irritation, irritated throat or burning sensation in the throat*.

The SmPCs for both products currently include in section 4.8 the following statement:

Irritation of the mucous membranes of the eyes and respiratory tract (such as coughing, sneezing, runny eyes) on application of Axsain[Zacin] cream has been reported rarely.

The nasal and throat irritant effects fall under the respiratory tract irritation stated above. However, only symptoms are referred to, and in view of the number of reports of anatomically defined (i.e. nasal and throat) mucous membrane irritation, Cephalon proposes to include these as examples of mucous membrane irritation, replacing the reference to symptoms alone. The proposed wording for this statement in section 4.8 of the SmPC for both Axsain and Zacin is now:

*Irritation of the mucous membranes of the eyes and respiratory tract (such as **nasal and throat irritation** ~~coughing, sneezing, runny eyes~~) on application of Axsain[Zacin] cream has been reported rarely, **resulting in symptoms such as coughing, sneezing and runny eyes.***

The patient information leaflets (PILs) for both products already include the following warning regarding the inhalation of vapours in section 4 (possible side effects):

Rarely when Axsain[Zacin] cream is applied the vapour can cause brief irritation of the eyes, nose, and throat, such as runny nose, cough or sneezing, breathlessness or worsening of asthma.

This information is considered sufficient and no changes to the leaflets are proposed.

2.5.5.2 Consequential update to section 4.4 for Zacin

Section 4.4 of the Axsain SmPC contains the following warning in relation to the inhalation of vapours:

Patients and carers should avoid inhalation of vapours from the cream, as transient irritation of the mucous membranes of the eyes and respiratory tract (including exacerbation of asthma) has been reported.

This warning is not present in section 4.4 of the Zacin SmPC and, as a consequence of updating the related wording in section 4.8 (see above), Cephalon proposes adding the same sentence to section 4.4 of the Zacin SmPC. As outlined above the PIL already contains adequate warnings regarding the inhalation of vapours so no changes are proposed.

2.5.6 Benefits and Risks Conclusions

The proposed changes to the product information outlined in this document are in line with the most recent pharmacovigilance data and are designed to improve the information provided to Healthcare Professionals. The information provided in this document does not alter the benefit/risk profile for Axsain or Zacin.

2.5.7 Literature References

Not applicable for this application.