Inconsistency between the Prazepam innovator and generics on contraindication in glaucoma

Final SmPC and PL wording agreed by PhVWP in July 2012

Doc.Ref.: CMDh/PhVWP/055/2012
July 2012

SUMMARY OF PRODUCT CHARACTERISTICS/PACKAGE LEAFLET

Section 4.3 Contraindication/Section 2

Glaucoma/if you suffer from glaucoma
Annex 8

Summary Assessment Report of the PhVWP July 2012

Prazepam – Not contraindicated in glaucoma

Key message

Product information for prazepam should be updated to delete contraindication in glaucoma.

Safety concern and reason for current safety review

The PhVWP was informed by its member from the French competent authority about inconsistent information in the product information of prazepam-containing medicinal products across Member States regarding the contraindication of glaucoma, which was included in the product information in some, but not all Member States. The PhVWP therefore agreed to review the risk of glaucoma with benzodiazepines and prazepam in particular.

Clinical setting

Prazepam is a benzodiazepine, indicated in the treatment of anxiety. Benzodiazepines act by stimulating the gamma-aminobutyric acid (GABA) receptor complex.

Glaucoma is a disease in which damage to the optic nerve leads to progressive and irreversible vision loss. It is normally associated with increased fluid pressure in the eye called intraocular hypertension. Glaucoma can be divided into two main categories, open angle and closed angle glaucoma.

Intraocular hypertension is a known adverse reaction reported for medicines with anticholinergic effects such as antipsychotic medicines. This could lead to serious consequences in patients with underlying glaucoma. Furthermore, glaucoma is also a known adverse reaction of some selective serotonin reuptake inhibitors (SSRIs). The mechanism is related to the presence of serotonin receptors on the ciliary corpus of the eye.

Information on the data assessed

The PhVWP reviewed data from the medical literature related to the risk of glaucoma with benzodiazepines [1-7]. Additionally, spontaneously reported cases of glaucoma with a benzodiazepine as a suspected medicine collected in the agency’s adverse reaction database EudraVigilance and in the French adverse reaction database were reviewed.

Outcome of the assessment

The PhVWP considered that three publications were case reports showing an association between benzodiazepines and glaucoma [1-3] and four publication articles did not show a link [4-7].

In the French adverse reaction database and in EudraVigilance, very few cases of glaucoma were reported in association with the use of benzodiazepines. Furthermore, in most of these few cases patients had received concomitantly other medicines with known risk of glaucoma, such as antipsychotics or SSRIs. These risk factors being present in the reported cases, together with the absence of evidence suggesting a biologically plausible role for prazepam or any benzodiazepine in the development of glaucoma lead the PhVWP to the conclusion that a causal relationship between benzodiazepines and glaucoma is unlikely.
On this basis, the PhVWP considered that there was insufficient evidence to require a contraindication for glaucoma in the summary of product characteristic (SmPC) of any benzodiazepine, and therefore the PhVWP recommended deleting the glaucoma contraindication from the SmPC for prazepam-containing medicinal products authorised in the EU.

References


