



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): zonisamide

Procedure No. EMEA/H/C/PSUSA/00003152/201603

Period covered by the PSUR: 1 April 2015 to 31 March 2016



## Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for zonisamide, the scientific conclusions of CHMP are as follows:

An article published during the interval reported on a case of angle closure and myopic shift secondary to zonisamide where the author noted the association with this type of reaction and other sulphonamide derivatives such as topiramate. Following a review of the literature and cumulative reports of ocular related terms, the MAH concluded that a causal association between secondary angle closure glaucoma and zonisamide is possible.

Five cases were presented by the MAH where the time to onset was within hours/days of zonisamide initiation or dose increase, most of the patients were young (20s-40s plus one 7 year old child) without a history of eye disorders and resolution/improvement occurred shortly after discontinuation of zonisamide. The paediatric patient was also taking another sulfa containing medicine (trichlormethiazide). These five cases did not include the original literature report which concerned a 39-year-old woman who presented with sudden vision loss with a concurrent bilateral frontal headache. No changes in health were reported other than initiating zonisamide for refractory migraines 2 weeks prior. Ocular history was significant only for low myopia. With discontinuation of zonisamide, the patient experienced full recovery.

An overview of all terms reported within the Eye Disorders SOC (n = 114 reports) included reports which may be related symptoms of this reaction such as vision blurred (n=22), visual impairment (n=16), visual acuity reduced (n=7), ocular discomfort (n=2), ocular hyperaemia (n=2) and myopia (n=4).

Zonegran is a benzisoxazole derivative, which contains a sulfonamide group. Angle closure glaucoma secondary to sulfa derived medicines is acknowledged in the literature and it is thought that the mechanism relates to choroidal swelling that pushes the iris or ciliary body forward or deforms the iris so that it is retracted into the angle. The product information for topiramate and other sulfa derived medicines includes a warning in SmPC section 4.4 and listed terms in SmPC section 4.8.

Information is available on six well documented cases suggestive of a causal association between zonisamide and angle closure glaucoma while other reports have been received with terms possibly relating to this reaction. Although these numbers are small given the post-marketing exposure of zonisamide (1.7 million patient years cumulatively), the cases are sufficiently well documented and the association is also supported by the literature regarding sulfonamide derived medicines.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considers that changes to the product information of medicinal products containing zonisamide are warranted. The CHMP agrees with the scientific conclusions made by the PRAC.

## Grounds for the variation to the terms of the marketing authorisation

On the basis of the scientific conclusions for zonisamide the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing zonisamide is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation should be varied.