

Annex I

Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for paroxetine, the scientific conclusions are as follows:

Bruxism can be part of extrapyramidal symptoms which are known for paroxetine as well as for other SSRIs / SNRIs (i.e. citalopram, escitalopram, fluoxetine, sertraline, venlafaxine) and included as ADR in section 4.8 of the SmPC.

Between December 1986 and June 2017, the Netherlands Pharmacovigilance Centre Lareb received 12 case reports of bruxism with the use of paroxetine. The case reports concerned 7 female and 5 male. The time to onset for bruxism varied from 6 hours to 13 years, with a median of 4 days. Four reports showed a positive dechallenge of which one case also reported a positive rechallenge. Lareb also identified a literature case of paroxetine induced bruxism with significant reduction of the bruxism event after switching to a lower paroxetine dosage (Romanelli et al. 1996). Case reports of bruxism with paroxetine are also present in the WHO and EudraVigilance database with respectively 139 reports, ROR (95% CI) 11.6 (9.8-13.8) and 43 reports, ROR (95% CI) 9.2 (6.8-12.5). A more recent article, Milanlioglu et al., 2012, also describes a case of paroxetine-induced severe sleep bruxism and other authors (Lavigne et al, 2003 & Jaffee and Bostwick 2000) have postulated the mechanism of action of this ADR involving a dopaminergic deficit in the meso-cortical tract which causes a specific form of akathisia and akathisia-like movement of the jaw muscles, thereby leading to bruxism.

Based on the above, it is considered that bruxism should be included as an adverse drug reaction in the product information of paroxetine containing products

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for paroxetine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing paroxetine is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing paroxetine are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

Annex II

Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike through~~)

Summary of Product Characteristics

- Section 4.8

The following adverse reaction should be added under the SOC Psychiatric disorders with a frequency not known:

Bruxism

Package leaflet

The following adverse reaction should be added under section 4. Possible side effects with a frequency not known:

Tooth grinding

Annex III

Timetable for the implementation of this position

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Adoption of CMDh position:	July CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	8 September 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 November 2018