Annex I

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

Scientific conclusions

The study provides drug utilisation data on an annual basis for up to 5 years for European countries where dexamfetamine was marketed.

The objectives were to describe how dexamfetamine is prescribed by physicians including the evaluation of off-label use (in terms of indication, age, prescribed overdose) and to collect data on abuse, misuse, overdose, diversion and dependence related to individual dexamfetamine use. The marketing authorization holder presented results as two separate study reports, the first focuses on prescribing patterns and uses databases, and the second on abuse, misuse, overdose, diversion and dependence and uses a literature review. The MAH was asked to clarify some aspects and in response an updated final study report version 2.0 (dated 28 May 2021) was submitted.

This was the last of five annual reports and data is presented by year, as well as a summary for this five-year period.

Concerning drug utilization, off-label use was very common in most countries, and this result was mainly driven by the use in adult patients. The marketing authorization holder was requested to comment on the implications of this medicine being used so often and, in some countries, almost exclusively in adult patients. The MAH presented several factors contributing to the use of dexamfetamine (as well as other stimulants) in adults, including many outside their control, namely the existence of clinical guidelines for ADHD in adults with recommendations on the use of dexamfetamine, even if specified that such use is not licensed. The extensive use in adults may also be due to increased awareness of the persistence of ADHD into adulthood, and the existence of other similar products for the treatment of ADHD in adults. However, no data in the assessed study has provided new safety concerns associated with off-label use in adults that justifies such unspecified safety concern to be included in the RMP summary of safety concerns, and as such it is agreed with its removal from that list.

The use of higher than recommended doses was also frequent but after further clarification and stratification, data suggests higher doses are mostly used in adults and are not a prevalent problem among children and adolescents.

Information on abuse, misuse, overdose, diversion and dependence of dexamfetamine was scarce and often grouped with other amphetamines or other stimulants. Overall, the review suggests these are not major issues at present.

It is concluded that the benefit-risk balance of medicinal products containing the active substance dexamfetamine remains unchanged as a result of this drug utilization study.

No further measures seem needed at this stage. Therefore, the MAH should submit an updated RMP at the next regulatory opportunity in order to address that this marketing authorization condition has been fulfilled.

As a result of the fulfilment of the study, the products should be removed from the list of medicines under additional monitoring.

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 the results of the study for the medicinal product(s) containing the active substance dexamfetamine and concerned by the PASS final report , the CMDh is

of the opinion that the benefit-risk balance of the medicinal product(s) mentioned above is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of the products concerned by this PASS final report should be varied.

Annex II

Conditions to the Marketing Authorisation(s)

Changes to be made to the conditions of the marketing authorisation(s) of medicinal product(s) containing the active substance dexamfetamine concerned by the non-interventional imposed PASS final report

The marketing authorisation holder(s) shall remove the following condition(s) (new text **<u>underlined and in bold</u>,** deleted text ~~strike through~~)

~~Drug utilization study of dexamfetamine in European countries~~

Annex III

Timetable for the implementation of this position

Timetable for the implementation of the position

Adoption of CMDh position:	September 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	1 November 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	30 December 2021