# 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 for the non-interventional imposed PASS final report for the medicinal product(s) containing the active substance methylphenidate and concerned by the PASS final report, the scientific conclusions are as follows:

The benefit-risk balance of methylphenidate-containing products remains unchanged. However, based on current available data, no conclusions can be drawn regarding a reduced risk of the previously raised concerns on cardiovascular or psychiatric safety of methylphenidate.

CMDh noted a variable pattern across the three Nordic countries where the study had been conducted, questioning a causal association between methylphenidate and psychiatric events and no increased risk for methylphenidate treatment when compared to other attention-deficit/hyperactivity disorder (ADHD) drugs.

However, given the short study follow up time (in comparison to the observation period of 5 years), methylphenidate (limited) treatment duration and data of only three Nordic European countries, further monitoring of the long-term consequences of methylphenidate therapy is required. Therefore, the MAH should continue monitoring both cardiovascular and psychiatric risks and present any new information of interest in upcoming PSURs. In light of the known limitation of spontaneous reporting, special focus should be given to published studies discussing psychiatric events in patients receiving methylphenidate.

In addition, the risk minimisation measures currently in place for methylphenidate should remain unchanged.

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 methylphenidate 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 methylphenidate concerned by the non-interventional imposed PASS final report.**

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

The MAH shall complete, within the stated timeframe, the below measures:

| ~~**Description**~~ | ~~**Due date**~~ |
|---|---|
| ~~A category 1 PASS with the following requirements~~<br>• ~~The study should be a non-interventional study in adult ADHD patients (aged ≥ 18 years).~~<br>• ~~The protocol should be submitted within 3 months after finalization of the referral procedure to PRAC. An updated RMP should be submitted along with this.~~<br>• ~~The design should be a prospective cohort study in different countries with a mean follow-up of 5 years. Interim reports should be provided yearly.~~<br>• ~~The following cardiovascular endpoints (in line with the ADDUCE study) should be studied: blood pressure, pulse rate, hypertension, left-ventricular hypertrophy, myocardial infarction and cardiomyopathy.~~<br>• ~~The psychiatric endpoints are to be determined.~~<br>• ~~A power calculation should be provided showing a sufficient sample size for these endpoints.~~<br>• ~~The final study report should be provided within 7 years after finalization of the referral procedure.~~ | ~~April 2018 (protocol submission)~~<br><br>~~April 2025 (final study report)~~ |

## Annex III

## Timetable for the implementation of this position

**Timetable for the implementation of the position**

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|---|---|
| Adoption of CMDh position: | October 2025 CMDh meeting |
| Transmission to National Competent Authorities of the translations of the annexes to the position: | 30 November 2025 |
| Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder): | 29 January 2026 |