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DIVISION OF JANSSEN-CILAG LTD.

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Ny Indikation II/56

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26th February 2010

Medical Products Agency (MPA)
Uppsala Science Park
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SE – 751 03 UPPSALA
Sweden

02-0309-II
08-0049

Subject: Submission of Variation Application Dossier(s) for CONCERTA, UK/H/544/001-004/II/056

UK/H/544/001-004/II/056: Clinical type II variation nr C.I.6. "Addition of a new therapeutic indication": ADHD in adults

+ SEPP 2010: 2265-2342

+ CD 2010: 2350

Dear Sirs,

We are pleased to submit our Variation Application Dossier for this Type II Procedure to add a new indication, which details are as below.

Name of the medicinal product(s) (in the RMS): CONCERTA XL

Pharmaceutical form(s) and strength(s): Prolonged-release tablet. 18, 27, 36 and 54 mg strengths

INN/active substance(s): Methylphenidate hydrochloride ..... **ATC Code(s):** N06BA04

[1]**National Marketing Authorisation Number(s):** See attached Annex I (List of the names, pharmaceutical forms, strengths of the medicinal products, route of administration, marketing authorisation holders in the Member States). Please note that the letter of authorisation is specific for the MR variation procedure. Issues regarding national translations at the end of the procedure can be addressed to the 'Contact person for national issues' provided in Annex I.

Type of the Variation Application(s): ..... VIT

When appropriate, please indicate type of change:

- ☐ Quality
- ☒ Indication
- ☐ Paediatric Indication
- ☐ Other SmPC related changes
- ☐ Change following Urgent Safety Restriction
- ☐ Annual variation for human influenza vaccine composition

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[1] Letters of Authorisation (LoA) have been obtained from the national CONCERTA Marketing Authorisation holders (all sister companies and subsidiaries of Johnson and Johnson) and listed in Annex I to allow Johnson & Johnson Product Research and Development (hereafter referred to as the 'Company') to represent them in this variation procedure.

If the submission dossier is provided electronically,
☒ eCTD if eCTD: ☒ Comprehensive model ☐ National parallel model

☐ Non-eCTD electronic Submission (NeeS)

☒ History of the sequences (Sequence Tracking Table) is attached

This application uses eCTD as the submission format. All CONCERTA applications were previously provided in (NeeS) format. This application is therefore submitted to MHRA (RMS) and all CMSs as the single eCTD with the starting sequence 0000 and contains all documentation for all National Competent Authorities (NCAs) on the single common CD. Paper based submissions are also provided where required.

The submission is checked with an up-to-date and state-of-the-art virus checker Microsoft ForeFront Client Security, version 1.5 with up-to-date virus definitions.

The relevant fees have been paid, where relevant. Please see Application form for further information.

☐ The dispatch list is appended (to RMS only).
☒ The dispatch list will be forwarded to the RMS as soon as the application has been submitted to all CMS.

BACKGROUND

A Type II MR variation (code C.I.6(a)) is submitted to add a new indication to the CONCERTA Marketing Authorisation to include the treatment of ADHD in adults whose ADHD diagnosis was established before the age of 18 years and whose symptoms persist into adulthood, at doses ranging from 18 mg to 72 mg per day.

This application contains safety and efficacy data from 3 randomised, double-blind, placebo-controlled studies of CONCERTA in adults with ADHD: Study 42603ATT3002, Study 02-159, and Study 42603ATT3013. Maintenance of effect was evaluated in the double-blind randomised withdrawal phase of Study 42603ATT3004. A pre-submission meeting took place between the Company and the MHRA on 1st October 2009 to discuss the clinical program results and to obtain guidance on the submission of this Type II variation. Minutes from the meeting are provided in Module 5.4.

There are six nonclinical safety pharmacology studies and one nonclinical pharmacokinetics study in this application. There is incremental pharmacokinetic information, new data for single and multiple doses of CONCERTA in healthy adult volunteers at doses up to 144 mg/day, included in this application.

This indication will be supported with currently marketed dosage strengths and therefore, this application does not include new chemistry, manufacturing and control (CMC) information.

Module 1.3 – Product Information

Proposed SmPC and PIL to support the new indication are provided in English in module 1.3.1. Due to the minor nature of changes to the PIL no consultation with target patient groups was undertaken (module 1.3.4). The relevant product information translations into national languages will be provided at the end of the procedure.

Please be aware that in addition to the changes made to support the new indication, the side effect 'stomach pain, diarrhoea, feeling sick, stomach discomfort and being sick' under the 'common side effects' is proposed to be deleted. This common ADR is only applicable for non-modified release formulations (as indicated in the CHMP core SmPC for methylphenidate) and was included in the CONCERTA SmPC during the article 31 referral in error.

The current and proposed SmPC and PIL for CONCERTA 27 mg has not been provided as the proposed changes will be identical to those of CONCERTA 18, 36 and 54 mg strengths. Finalised CONCERTA 27 mg package leaflet will be provided during the national phase of the procedure.

Module 1.5 - Specific requirements for different types of applications: Data exclusivity

According to Article 10(5) of Directive 2001/83/EC a non-cumulative period of one year of data exclusivity may be granted for a new indication for a well-established substance. Module 1.5.3 is therefore provided to request that period of data exclusivity with this application.

Module 1.8 – Information relating to Pharmacovigilance: Risk Management System

The EU CONCERTA Risk Management Plan (RMP) has been updated for the adult sub-population. The current CONCERTA RMP (version 1, dated 16th October 2008) was updated (version 2, 23 November 2009) and submitted for assessment as part of the PSUR work-sharing procedure (UK/H/PSUR/0068/001). The proposed RMP (version 2) has been used as a basis for the RMP used to support this submission, version 3, dated 17th December 2009.

The previous RMPs (versions 1 and 2) were limited to the paediatric population for the currently approved indication in children and adolescents, with the exception of the post-marketing data and some of the referenced literature that included an adult population. For version 3, exposure, demographic, and important identified and potential risk data from double-blind and open-label clinical trials in adults with ADHD have been used for this update, including information from the literature pertaining to adults with ADHD.

Module 1.10 - Information relating to paediatrics

As CONCERTA is not protected by a Supplementary Patent Certificate (SPC) or patent which qualifies for an SPC, this application is not subject to the requirements of Articles 7 and 8 of the Paediatric Regulation (EC 1901/2006). As such, compliance with a paediatric investigation plan (PIP) or the need for a PIP waiver is not required with this variation application. A short justification explaining this is provided in module 1.10.

We trust that the application is in order for your assessment. Please let me know if you have any questions.

We hereby certify that the dossiers submitted to the RMS and CMS(s) are identical.

We also hereby certify that the content of the electronic submission is identical to the paper version.

Yours sincerely,

D. Nickless

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