European Medicines Agency
Evaluation of Medicines for Human Use

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CHMP ASSESSMENT REPORT

FOR

Tadalafil Lilly

International Nonproprietary Name: Tadalafil

Procedure No. EMEA/H/C/001021

Assessment Report as adopted by the CHMP with
all information of a commercially confidential nature deleted.

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1. BACKGROUND INFORMATION ON THE PROCEDURE

1.1 Submission of the dossier

The applicant Eli Lilly Nederland B.V. submitted on 8 May 2008 an application for Marketing Authorisation to the European Medicines Agency (EMEA) for Tadalafil Lilly, through the centralised procedure under Article 3 (2) (a) of Regulation (EC) No 726/2004. The eligibility to the centralised procedure was agreed upon by the CHMP on 24 January 2008.

The legal basis for this application refers to Article 10(c) of Directive 2001/83/EC, as amended – relating to informed consent from a marketing authorisation holder Eli Lilly Nederland B.V. for the authorised medicinal product Cialis (EU/1/02/237).

Scientific Advice
The applicant did not seek scientific advice at the CHMP.

Licensing status:

The initial product, Cialis, has been given a Community Marketing Authorisation on 12 November 2002.

The Rapporteur and Co-Rapporteur appointed by the CHMP were:

Rapporteur: **Concepción Prieto Yerro** Co-Rapporteur: **Cristina Sampaio**

1.2 Steps taken for the assessment of the product

- The application was received by the EMEA on 8 May 2008.
- The procedure started on 28 May 2008.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 1 July 2008. The Co-Rapporteur's first Assessment Report was circulated to all CHMP members on 3 July 2008.
- The Rapporteurs circulated a Joint Assessment Report to all CHMP members on 15 July 2008.
- During the meeting on 21-24 July 2008, the CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a Marketing Authorisation to Tadalafil Lilly on 24 July 2008. The applicant provided the letter of undertaking on the follow-up measure to be fulfilled post-authorisation on 24 July 2008.
- The CHMP opinions were forwarded, in all official languages of the European Union, to the European Commission, which adopted the corresponding Decisions on 1 October 2008.

2 SCIENTIFIC DISCUSSION

2.1 Introduction

This application has been submitted as an informed consent application in accordance with Article 10c of Directive 2001/83/EC as amended.

The MAH for Cialis provided consent to make use of the pharmaceutical, preclinical and clinical documentation contained in the file of Cialis, assessed and approved.
As a consequence, quality, safety and efficacy of Tadalafil Lilly are identical to the up to date quality, safety and efficacy profile of Cialis. The application for Tadalafil Lilly concerns the strength of 20mg film-coated tablets and consists only of Module 1 information.

As a consequence, quality, safety and efficacy of Tadalafil Lilly medicinal product are identical to the up-to-date quality, safety and efficacy profile of Cialis.
Information on the scientific discussions can be found in the Cialis CHMP assessment reports and in the European Public Assessment Report (EPAR).

The Tadalafil Lilly informed consent application concerns only the 20 mg strength of Cialis. The Summary of Product Characteristics for Tadalafil Lilly appropriately reflects this.

The approved indication is:

Treatment of erectile dysfunction.
In order for tadalafil to be effective, sexual stimulation is required.
Tadalafil Lilly is not indicated for use by women.

Tadalafil is an orally administered phosphodiesterase type 5 (PDE5) inhibitor that has been developed as a treatment for erectile dysfunction. When sexual stimulation causes the local release of nitric oxide, which plays a central role in the vasodilation of erectile tissues by stimulating guanylyl cyclase activity, consequently raising intracellular concentrations of cyclic guanosine monophosphate (cGMP) and relaxing vascular smooth muscle. This results in smooth muscle relaxation and inflow of blood into the penile tissues, thereby producing an erection.

Thus, tadalafil is indicated for the treatment of erectile dysfunction. Tadalafil has no effect in the absence of sexual stimulation.

Tadalafil should not be used in individuals below 18 years of age.

2.2 Quality aspects

Since this application is an informed consent of the Cialis application, the quality data in support of the Tadalafil Lilly application are identical to the up-to-date quality data of the Cialis dossier , which have been assessed and approved (including all post-marketing procedures).

2.3 Non-clinical aspects

Since Tadalafil Lilly application is an informed consent of the Cialis application, the non-clinical data in support of the Cialis application are identical to the up-to-date non-clinical data of the Cialis dossier, which have been assessed and approved (including all post-marketing procedures).

2.4 Clinical aspects

Since this application is an informed consent of the Cialis application, the clinical data in support of the Tadalafil Lilly application are identical to the up-to-date clinical data of the Cialis dossier, which have been assessed and approved (including all post-marketing procedures). No additional clinical studies are provided.

2.5 Pharmacovigilance

Detailed description of the Pharmacovigilance system

The CHMP considered that the Pharmacovigilance system (version 2.2) as described by the applicant fulfils the legislative requirements.

Risk Management Plan

The MAA submitted a risk management plan (version 3) identical with that for Cialis.

The CHMP, having considered the data submitted in the application, is of the opinion that no additional risk minimisation activities are required beyond those included in the product information.

PSUR

The PSUR cycle of Tadalafil Lilly will correspond to the one of the cross-referred product, Cialis, until otherwise specified. Therefore, as of 15 December 2007, the MAH will continue to submit yearly PSURs unless otherwise specified by the CHMP.

2.6 Overall conclusions, risk/benefit assessment and recommendation

Since this application is an informed consent of the Cialis application, the CHMP considered that the risk-benefit balance of Tadalafil Lilly was favourable and therefore recommended the granting of the marketing authorisation for the following indication:

"Treatment of erectile dysfunction.
In order for tadalafil to be effective, sexual stimulation is required.
Tadalafil Lilly is not indicated for use by women."

- User consultation

A justification for not conducting a user testing for this application was provided, in view of the fact that the company has no intention to market this product in the current indication. However, a user consultation in accordance with Articles 59(3) and 61(1) of Directive 2001/83 is requested during the upcoming Type II variation procedure for Tadalafil Lilly to change the indication to PAH. This is included as a follow up measure.