European Medicines Agency
Evaluation of Medicines for Human Use

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ASSESSMENT REPORT

FOR

Clopidogrel Winthrop

International Nonproprietary Name: clopidogrel

Procedure No. EMEA/H/C/000975

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 Sanofi Pharma Bristol-Myers Squibb SNC submitted on 8 January 2008 an application for Marketing Authorisation to the European Medicines Agency (EMEA) for Clopidogrel Winthrop, 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 EMEA/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 Sanofi Pharma Bristol-Myers Squibb SNC for the authorised medicinal product Plavix (EU/1/98/069/001a to 007b and EU/1/98/069/008-010).

Licensing status:
The initial product, Plavix, has been given a Community Marketing Authorisation on 15 July 1998.

The Rapporteur and Co-Rapporteur appointed by the CHMP were:
Rapporteur: Cristina Sampaio Co-Rapporteur:Pieter Neels

1.2 Steps taken for the assessment of the product

- The application was received by the EMEA on 8 January 2008.
- The procedure started on 24 February 2008.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 1 April 2008. . The Co-Rapporteur's first Assessment Report was circulated to all CHMP members on 25 March 2008.
- During the meeting on 21-24 April 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 Clopidogrel Winthrop on 24 April 2008. The applicant provided the letter of undertaking on the follow-up measures to be fulfilled post-authorisation on 22 April 2008.
- The CHMP opinions were forwarded, in all official languages of the European Union, to the European Commission, which adopted the corresponding Decisions on 16 July 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.
Therefore, consent from the MAH of the Plavix application, which was submitted within the scope of Part B of the Annex of the Council Regulation (EEC) 2309/93, of the 22 July 1993, has been given allowing access to Module 2 to Module 5 of the initial dossier of this authorised product and any subsequent post-marketing procedures submitted, assessed and approved. The application for Clopidogrel Winthrop consists only of Module 1 information.

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

The approved indication is:

Clopidogrel is indicated in adults for the prevention of atherothrombotic events in:

- Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.
- Patients suffering from acute coronary syndrome:
  - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA).
  - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.

Clopidogrel should be given as a single daily dose of 75 mg with or without food. In patients suffering from non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction) clopidogrel treatment should be initiated with a single 300-mg loading dose and then continued at 75 mg once a day (with acetylsalicylic acid (ASA) 75 mg-325 mg daily). Since higher doses of ASA were associated with higher bleeding risk it is recommended that the dose of ASA should not be higher than 100 mg.
In patients suffering from ST segment elevation acute myocardial infarction clopidogrel should be given as a single daily dose of 75 mg initiated with a 300-mg loading dose in combination with ASA and with or without thrombolytics. For patients over 75 years of age clopidogrel should be initiated without a loading dose. Combined therapy should be started as early as possible after symptoms start and continued for at least four weeks.

Clopidogrel Winthrop contains clopidogrel, which is a prodrug. The active metabolite, a thiol derivative, is formed by oxidation of clopidogrel to 2-oxo-clopidogrel and subsequent hydrolysis.

2.2 Quality aspects

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

2.3 Non-clinical aspects

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

An environmental risk assessment was provided. No further request of information is considered necessary.

2.4 Clinical aspects

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

2.5 Pharmacovigilance

Detailed description of the Pharmacovigilance system

The CHMP considered that the Pharmacovigilance system as described by the applicant fulfils the legislative requirements.

Risk Management Plan

The CHMP did not require the MAA to submit a risk management plan because the aim of this submission is to obtain a duplicate form of the available clopidogrel brand Plavix, under the name of Clopidogrel Winthrop, using the same current summary of product characteristics (SPC). In this context, this application does not represent a significant change in the marketing authorisation of clopidogrel, and therefore it is not considered that any specific Risk Management measures are necessary.

The current SPC for clopidogrel appropriately describes the safety profile and recommendations for the safe use of this medicinal product, for which no additional risk minimization activities beyond appropriate labelling statements have been deemed necessary since its first marketing authorisations.

2.6 Overall conclusions, risk/benefit assessment and recommendation

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

“Clopidogrel is indicated in adults for the prevention of atherothrombotic events in:

- Patients suffering from myocardial infarction (from a few days until less than 35 days), ischaemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease.

- Patients suffering from acute coronary syndrome:
    - Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA).
    - ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy.”