



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public statement

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# Interaction between clopidogrel and proton-pump inhibitors

## CHMP updates warning for clopidogrel-containing medicines

Following an analysis of new data concerning the possible interactions between clopidogrel<sup>1</sup> and proton-pump inhibitors (PPIs)<sup>2</sup>, the European Medicines Agency has recommended an amendment to the existing warning over the concomitant use of clopidogrel-containing medicines and PPIs.

Clopidogrel is an antiplatelet medicine that is used to prevent problems with blood clots such as heart attacks or strokes. Clopidogrel is converted in the body to its active form by an enzyme called CYP2C19. PPIs are medicines that are used to prevent and treat heartburn and stomach ulcers and may be available without a prescription. As heartburn and stomach ulcers can occur as side effects of clopidogrel, patients taking clopidogrel often take PPIs to prevent or ease their symptoms.

Following the publication of observational studies suggesting that PPIs may reduce the effectiveness of clopidogrel by reducing its conversion into the active form, the Agency's Committee for Medicinal Products for Human Use (CHMP) recommended in May 2009 that the product information for all clopidogrel-containing medicines be amended to discourage the concomitant use of PPIs and clopidogrel unless absolutely necessary.

Since then, the CHMP has become aware of the results of a number of new studies, some of which put in question the clinical relevance of interactions between PPIs as a class and clopidogrel. However, two studies, completed at the end of August 2009, looked into the effect of omeprazole on the blood levels of the active form of clopidogrel. The studies confirmed that omeprazole can reduce the levels of the active form of clopidogrel in the blood and reduce its antiplatelet effects, therefore supporting the conclusion that there is an interaction between clopidogrel and omeprazole and esomeprazole.

Taking all of the currently available data into account, the CHMP and its Pharmacovigilance Working Party have concluded that there are no solid grounds to extend the warning to other PPIs. The class warning for all PPIs has been replaced with a warning stating that only the concomitant use of clopidogrel and omeprazole or esomeprazole should be discouraged. The Committee also recommended that a description of the results of the two recent studies that show the interaction between clopidogrel and omeprazole be added to the product information.

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<sup>1</sup> Available in the European Union under the trade names Plavix and Iscover, and as generic medicines.

<sup>2</sup> Omeprazole and its S-isomer esomeprazole, lansoprazole, pantoprazole and rabeprazole.

