Translated from *Rev Prescrire* March 2007; **27** (281): 169

clopidogrel

New Indication

In combination with aspirin: marginal additional benefits

● **In patients with myocardial infarction who are not eligible for angioplasty, adding clopidogrel to aspirin reduces the overall 15-day mortality rate, but the subsequent outcome is not known.**

NOT ACCEPTABLE

Previously approved in combination with aspirin for the treatment of acute coronary syndromes without ST depression, clopidogrel (Plavix°, Sanofi Pharma, Bristol-Myers Squibb), is now also approved for myocardial infarction with ST elevation (1).

This new indication is mainly based on the results of a single trial, the COMMIT study, which we first examined in 2006 (2). This randomised double-blind placebo-controlled trial included approximately 45 000 patients, hospitalised for suspected myocardial infarction, who did not receive coronary angioplasty as part of their first-line management. It compared aspirin + clopidogrel versus aspirin + placebo, prescribed until hospital discharge or for 4 weeks, in addition to usual treatments.

Adding clopidogrel to aspirin significantly reduced the overall mortality rate at 15 days (the median duration of treatment). There were around 5 fewer deaths per 1000 treated patients, and no increase in the incidence of severe haemorrhage (2). But it is not known whether this survival benefit persists over time (2).

In practice, in myocardial infarction not treated with coronary angioplasty, the addition of clopidogrel to aspirin seems to benefit some patients (about 1 in 200). This combination may therefore be used in the short term (4 weeks). However, no evidence is available beyond 4 weeks indicating a better risk-benefit balance for aspirin plus clopidogrel as compared to aspirin alone.

clopidogrel
(Plavix°)

Tablets

• **75 mg** of clopidogrel per tablet

■ **New indication:** *"ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy".*
[European marketing authorisation, centralised procedure]

antiplatelet drug

Selected references from Prescrire's literature search.

In response to our request for information, Sanofi Aventis sent us no documents whatsoever.

1- Prescrire Rédaction "clopidogrel dans l'angor instable: moins d'infarctus mais plus d'hémorragies" *Rev Prescrire* 2002; **22** (231): 617-618.
2- Prescrire Editorial Staff "Acute myocardial infarction: aspirin + clopidogrel reduce mortality by about 0.5%" *Prescrire Int* 2006; **15** (85): 194.

EDITORS' OPINION

What a shame!

45 000 patients, thousands of caregivers in 1200 participating centres, hundreds of investigators... Tens of thousands of people mobilised for a single therapeutic trial, the COMMIT study (1).

This trial was designed to compare a combination of clopidogrel and aspirin with aspirin alone in patients with ST-elevation myocardial infarction (see above).

Unfortunately, all this trial showed is that, compared with aspirin alone, the clopidogrel-aspirin combination significantly reduces overall mortality... during the next 15 days. What a shame!

What a shame that the investigators did not evaluate effects on overall mortality for at least a few months after the myocardial infarction. So much time, energy and money invested, so little information in return.

Unless, of course, the sponsors saw signs that the benefit disappeared after 15 days? That would have been a hard pill for investors to swallow.

But what about patients and caregivers? They need more information when deciding whether or not to add clopidogrel to aspirin after myocardial infarction with ST elevation.

Usually, drug companies only fund or publish trials that are likely to provide a rapid return on investment. What this means is that if patients and caregivers are to receive the information they really need, other funding sources must be found for clinical trials, independent of the private pharmaceutical industry.

Selected references from Prescrire's literature search.

1- Commit collaborative group "Addition of clopidogrel to aspirin in 45 852 patients with acute myocardial infarction: randomised placebo-controlled trial" *Lancet* 2005; **366**: 1607-1621.