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atorvastatin + amlodipine

New Drug

Just a commercial ploy

atorvastatin + amlodipine
(Caduet°)

Tablets

- **10 mg** of atorvastatin + **5 mg** of amlodipine per tablet
- **10 mg** of atorvastatin + **10 mg** of amlodipine per tablet

■ **Indication:** *"(…) prevention of cardiovascular events in hypertensive patients with 3 associated cardiovascular risk factors (…)".*
[French marketing authorisation folllowing EU mutual recognition]

lipid-lowering drug
(statin) + antihypertensive agent
(calcium channel blocker)

● **No assessment of morbidity or mortality; second-choice component drugs.**

NOTHING NEW

Pfizer now markets a fixed-dose combination of atorvastatin + amlodipine (Caduet°) for cardiovascular prevention.

Atorvastatin is not a first-choice statin: pravastatin and simvastatin have better-documented risk-benefit balances (1). Amlodipine is a first-choice calcium channel blocker but not a first-line antihypertensive drug: a thiazide diuretic such as chlortalidone, or hydrochlorothiazide, remains the standard first-line treatment (2).

This new fixed-dose combination has not been evaluated for its effect on morbidity or mortality. All we have are the results of two dose-finding studies, neither of which challenged the currently recommended initial doses (3,4). The French committee assessing the therapeutic value of new drugs correctly concluded that this product does not represent a therapeutic advance for patients (3).

In short, the apparent convenience of this fixed-dose combination of atorvastatin and amlodipine might lead prescribers to overlook the fact that other statins and antihypertensive drugs have better risk-benefit balances. Additionally, the choice of brand name, Caduet°, is unfortunate, as it bears so little resemblance to the international non proprietary names (INN) of the two components of this product.

EDITORS' OPINION

Fixed-dose combinations: two wrongs fail to make a right

Doses of drug treatments for hypertension are adjusted on the basis of a patient's blood pressure levels. Doses of treatments for hypercholesterolaemia are based on cholesterol levels. A fixed-dose combination product is hardly ideal when the dose of the antihypertensive drug has to be adjusted in a patient whose cholesterol level is properly controlled, or when the dose of the lipid-lowering drug has to be adjusted in a patient whose blood pressure is under control. When the dose of one component is adjusted, there is a risk that the patient will receive the wrong dose of the other drug. Even if all conceivable dose ratios were commercially available (which is not the case for the fixed-dose combination of atorvastatin + amlodipine (see above)), it would increase the risk of confusion for prescribers, pharmacists and patients alike.

What hard evidence is there that a small reduction in the daily number of medications actually improves adherence to treatment? In practice, adverse effects are an important cause of poor adherence. If separate drugs are prescribed instead of a fixed-dose combination, a patient with muscle disorders, for example, will be able to stop taking the cholesterol-lowering drug but not necessarily the antihypertensive drug.

With a fixed-dose combination, however, both drugs are likely to be withdrawn.

And when a combination product is withdrawn, some patients may be surprised to discover that they were actually taking two treatments for which the aims of therapy differed, especially when their treatment was presented as generally beneficial to health.

Finally, when neither component of a fixed-dose combination is a first-choice drug for its indication, then introducing this type of product to the market is a step backwards, not forwards, in overall healthcare quality. But for Pfizer, the name of the game seems to be Profit.

Selected references from Prescrire's literature search.

Pfizer failed to respond to our requests for information.

1- Prescrire Rédaction "Choix d'une statine" *Rev Prescrire* 2006; **26** (276): 692-695.
2- Prescrire Editorial Staff "Adult hypertension: reducing cardiovascular morbidity and mortality" *Prescrire Int* 2005; **14** (75): 25-33.
3- Haute autorité de santé - Commission de la transparence "Avis de la Commission-Caduet" 14 December 2005: 8 pages.
4- U.S. Food and Drug Administration - Center for Drug Evaluation and Research "Application number 21-540 - Statistical review and evaluation" 19 December 2003: 63 pages.