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 following
EU mutual recognition]

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

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

Pfizer now markets a
fixed-dose combination
of atorvastatin + am-
lodipine (Caduet®) for
cardiovascular prevent-
ion.

Atorvastatin is not a first-choice statin: pravastatin and simvastatin have bet-
ter-documented risk-benefit bal-
ances (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 stan-
dard first-line treatment (2).

This new fixed-dose combination has
not been evaluated for its effect on mor-
bidity or mortality. All we have are the
results of two dose-finding studies, nei-
ther of which challenged the currently
recommended initial doses (3, 4). The
French committee assessing the therape-
utic value of new drugs correctly con-
cluded that this product does not repre-
sent a therapeutic advance for
patients (3).

In short, the apparent convenience of
this fixed-dose combination of atorvas-
tatin and amlodipine might lead pre-
scribers to overlook the fact that other
statins and antihypertensive drugs have
better risk-benefit balances. Addi-
tionally, 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.

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

Doses of drug treatments for hyper-
tension 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 ide-
al when the dose of the antihypertensive
drug has to be adjusted in a patient
whose cholesterol level is properly con-
trolled, 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 compo-
nent 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 + amlodip-
ine (see above)), it would increase the
risk of confusion for prescribers, phar-
macists and patients alike.

What hard evidence is there that a
small reduction in the daily number of
medications actually improves adher-
ence to treatment? In practice, adverse
effects are an important cause of poor
adherence. If separate drugs are pre-
scribed instead of a fixed-dose combi-
nation, 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, how-
ever, both drugs are likely to be with-
drawn.

And when a combination product is
withdrawn, some patients may be sur-
prised to discover that they were actual-
ly 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.

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