

# Bleeding Precaution Added to Clopidogrel Label

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A precaution has been added to the clopidogrel label regarding the increased risk of major bleeding when this platelet aggregation inhibitor is used with aspirin in a certain high-risk patients.

Clopidogrel, an antiplatelet drug marketed as Plavix by Sanofi-Synthelabo Inc., is approved by the Food and Drug Ad-

ministration for reduction of atherothrombotic events in patients with a recent myocardial infarction, recent stroke, or peripheral arterial disease; and in patients with acute coronary syndrome.

Specifically, the addition to the clopidogrel label reads, "In patients with recent TIA [transient ischemic attack] or stroke who are at high risk for recurrent ischemic events, the combination of aspirin and Plavix has not been shown to be more effective than Plavix alone, but the combi-

nation has been shown to increase major bleeding."

In the Clopidogrel in Unstable Angina to Prevent Recurrent Ischemic Events (CURE) study and in the Clopidogrel Versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) study, there was an increased risk of bleeding and a decreased benefit with concomitant use of clopidogrel with aspirin compared with aspirin alone in patients aged 75 years and older, according to an FDA spokesperson.

The results of another study support these findings regarding the risk of bleeding with aspirin and clopidogrel, the spokesperson said. That study, the Management of Atherothrombosis With Clopidogrel in High-Risk Patients With Recent Transient Ischemic Attack or Ischemic Stroke (MATCH) trial, compared clopidogrel plus aspirin with clopidogrel alone in patients with recent ischemic stroke or TIA. Clopidogrel was approved in 1997. ■

## New Indication in Heart Failure

NYHA Class II-IV and LVEF  $\leq$ 40%

## In HF, ATACAND is the only ARB proven to

- Reduce both CV death and HF hospitalizations
- Provide these benefits with or without an ACEI
- Provide these benefits when used with both an ACEI and  $\beta$ -blocker
- Provide the convenience of once-daily dosing in HF



Safety and effectiveness in pediatric patients have not been established. Greater sensitivity of some older individuals (eg,  $\geq$ 75 years) with heart failure must be considered.

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In heart failure patients receiving ATACAND, hypotension, increases in serum creatinine, and hyperkalemia have occurred. Caution should be observed for hypotension when initiating therapy. Evaluation of patients with heart failure should always include assessment of renal function and volume status. Monitoring of blood pressure, serum creatinine, and serum potassium is recommended during dose escalation and periodically thereafter.

During concomitant use of ATACAND and lithium, careful monitoring of serum lithium levels is recommended.

The adverse event profile of ATACAND in heart failure patients was consistent with the pharmacology of the drug and the health status of the patients. In the CHARM program, comparing ATACAND in total daily doses up to 32 mg once daily (n=3803) with placebo (n=3796), 21.0% of patients discontinued ATACAND for adverse events vs 16.1% of placebo patients.

Please see adjacent brief summary of full Prescribing Information, including boxed WARNING regarding use in pregnancy.

Reference: 1. McMurray JJV, Östergren J, Swedberg K, et al, for the CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet*. 2003;362:767-771.

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