

## Products

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### Cozaar approved for stroke prevention

Merck & Co's angiotensin II receptor antagonist, losartan (Cozaar), has received US approval for use in reducing the risk of stroke in patients with hypertension and left ventricular hypertrophy (LVH).

The additional indication for the antihypertensive is based on the results of the 9,000-patient LIFE (Losartan Intervention For Endpoint Reduction in hypertension) study. It makes losartan the only product in its class approved for stroke risk reduction, although the FDA is looking at adding outcome data for other antihypertensives.

But the agency agreed with the opinion of its cardiovascular and renal advisory panel in not approving the broader indication sought by Merck of reducing the risk of cardiovascular morbidity and mortality as measured by the combined incidence of cardiovascular death, stroke and myocardial infarction in patients with LVH.

The new label also notes that there is evidence that the stroke reduction benefit does not apply to black patients.

The LIFE study, first presented at last year's American Academy of Cardiology meeting in Atlanta, showed that losartan significantly reduced the combined risk of cardiovascular death, heart attack and stroke in these patients compared with AstraZeneca's beta-blocker, atenolol (Tenormin). This included a 13% reduction in morbidity/mortality risk - the study's primary endpoint - in favour of losartan. However, the panel felt that the adjusted p value for the primary endpoint ( $p=0.021$ ), although significant, was not robust enough to meet the FDA's requirement for evidence of effectiveness from a single study (*Scrip* No 2814, p 19).

However, the study found that a regimen of losartan plus a diuretic cut the risk of stroke by 25% compared with atenolol plus a diuretic.

The new label says that the usual starting dose for hypertensives with LVH is 50mg once daily. Hydrochlorothiazide at 12.5mg daily should be added and/or the dose of losartan increased to 100mg once daily followed by an increase in HCTZ to 25mg once daily based on blood pressure response.

Around 13-18% of hypertensives aged between 40 and 74 have LVH (the most common cardiac abnormality associated with long-standing high blood pressure), and this proportion rises to 22% in those older than 75 years.

### ... product news in brief

#### ■ Interferon alpha-2a not effective in Japanese encephalitis:

Interferon alpha-2a does not appear to be an effective treatment for Japanese encephalitis, a small independent study published in *The Lancet* suggests. The trial showed no significant difference in outcome at three months in 112 Vietnamese children with suspected disease given interferon alpha-2a (Roche's Roferon, 10 million units/m<sup>2</sup> im per day for seven days) or placebo. A poor outcome (death or severe sequelae) occurred in 20 children given interferon compared with 18 in the placebo group (March 8th, p 821). Preclinical work had suggested that alpha-interferon has activity against the virus *in vitro* and the protein is produced naturally in response to viral infections. However, the researchers believe that the interferon may be effective if given at higher doses, in combination with other antivirals or by alternative routes of administration, although they add that the cost might be prohibitive in areas where the virus is endemic.

### Additional uses for Coreg in US

The US FDA has approved GlaxoSmithKline's beta-blocker, Coreg (carvedilol), to reduce the risk of death in heart attack patients with left ventricular dysfunction, an additional indication.

The expanded approval is based on data from the CAPRICORN (Carvedilol Post Infarction Survival Control in Left Ventricular Dysfunction) trial, which showed that when Coreg was initiated within 21 days of a heart attack in patients with left ventricular dysfunction, the risk of death was reduced by 23% when Coreg was maintained long term. The agency's cardiovascular and renal drugs advisory committee unanimously supported approval on January 7th (*Scrip* No 2814, p 18).

Coreg is now the only beta-blocker approved to reduce the risk of death among patients who have had a recent heart attack and have impaired cardiac function, whether or not they have symptoms of heart failure, GSK says. According to the American Heart Association, more than half a million people in the US had a heart attack in 2000 and nearly 193,000 people died as a result.

Coreg was the first agent with beta-blocking properties to be approved by the FDA for heart failure. It is already approved to reduce the risk of death in mild, moderate and severe heart failure and is also available for the treatment of essential hypertension.

### Themis to launch lipid-free propofol

The Indian company, Themis Medicare, a Gedeon Richter joint venture, has developed a lipid-free clear injection formulation of propofol. The product, to be marketed as Cleofol, has been approved by India's ministry of health and will be launched in April.

Themis says that Cleofol offers several advantages over traditional lipid-based propofol formulations, including a quick onset of action, "good quality" anaesthesia without complications such as anaphylactic shocks, apnoea or allergic reactions, and stability at room temperature. The company conducted multicentre studies involving more than 12 anaesthesiologists, in which the product was used in more than 400 surgery cases in strengths ranging from 10mg/ml to 100mg/ml (ie, 1% to 10% concentrations).

Cleofol, which is expected to be priced about 30% cheaper than international products, will be available in a multi-dose vial and a single-dose ampoule for intravenous use. Traditional lipid-based propofol formulations available in India include Diprivan, Profol, Fresofol and Propovan, and the market for such products is estimated to be worth about Rs150 million (\$3.13 million).

Separately, Themis is also developing TCL-S-FA99 for *Helicobacter pylori* infection, dyspepsia, gastritis and ulcers. The product has completed Phase III trials in India and is expected to be ready for launch in the third quarter.

### Meetings

A course on *New Methodologies in Clinical Statistical Analysis* is to be held by Vision in Business in London on June 5th-6th. *Managing Clinical research Projects* will follow on June 9th-11th. For information, telephone +44 20 7953 7450 or visit [www.visioninbusiness.com](http://www.visioninbusiness.com).