Enalaprilat

Enalaprilat is the active metabolite of enalapril. It is the first dicarboxylate-containing angiotensin-converting enzyme inhibitor and was developed partly to overcome these limitations of captopril. The sulfhydryl-moiety was replaced by a carboxylate-moiety, but additional modifications were required in its structure-based design to achieve a potency similar to captopril.

Enalaprilat, however, had a problem of its own. The consequence of the structural modifications was to give it ionisation characteristics that do not allow sufficient GI absorption for oral administration (in tablets). Thus, enalaprilat was only suitable for intravenous administration. This was overcome by the esterification of enalaprilat with ethanol to produce enalapril.

As a prodrug, enalapril is metabolized in vivo to the active form enalaprilat by various esterases.

Acts within = 15 mins of administration.

Peak plasma enalaprilat concentrations occur 2 to 4 hours after oral enalapril administration. Elimination thereafter is biphasic, with an initial phase which reflects renal filtration (elimination half-life 2 to 6 hours) and a subsequent prolonged phase (elimination half-life 36 hours), the latter representing equilibration of drug from tissue distribution sites.

The prolonged phase does not contribute to drug accumulation on repeated administration but is thought to be of pharmacological significance in mediating drug effects. Renal impairment [particularly creatinine clearance < 20 ml/min (< 1.2 L/h)] results in significant accumulation of enalaprilat and necessitates dosage reduction. Accumulation is probably the cause of reduced elimination in healthy elderly individuals and in patients with concomitant diabetes, hypertension and heart failure.

Dosage

Oral

Initial: 2.5-5 mg PO qDay

Maintenance: 10-40 mg/day PO qDay or divided q12hr IV

1.25 mg/dose IV over 5 minutes q6hr; doses up to 5 mg/dose IV q6hr have been administered.

Side effects

Hyperkalemia occurs in = 1 %. Do not use during pregnancy.