Controlled-Onset

DESCRIPTION

Covera-HS (verapamil hydrochloride) Extended-Release Tablets are a calcium ion channel blocking agent that has been specifically developed to maintain a consistent plasma level of drug over 24 hours (Rate Control) and to maintain a consistent plasma level of drug through a specific portion of the cardiac cycle (Potentiation of Beta-Blocker Action).

Mechanism of action
In vitro, verapamil binding is voltage-dependent with affinity increasing as the cardiac cell membrane depolarizes.

CLINICAL PHARMACOLOGY

PHARMACOKINETICS

Verapamil is almost completely absorbed following oral administration. The mean absolute bioavailability of Oral Covera-HS tablets administered on an empty stomach is approximately 65%. The absolute bioavailability of Oral Covera-HS tablets is greater than 80% after multiple doses. The extent of absorption is proportional to the dose. Absorption is not significantly affected by food intake. Verapamil undergoes extensive first-pass metabolism, with approximately 75% metabolism occurring in the liver and about 25% metabolism occurring in the gastro-intestinal tract. At usual clinical doses, the extent of oral absorption is greater than 90%.

The systemic availability of verapamil hydrochloride from Covera-HS 818 tablets is approximately 87%. After oral administration, the systemic availability of single Covera-HS tablets in elderly subjects is 10% lower than in younger subjects. The pharmacokinetic characteristics of Covera-HS tablets are not significantly affected by renal impairment. The mean absolute bioavailability of oral Covera-HS tablets in patients with mild hepatic impairment was approximately 70% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters. The mean absolute bioavailability of oral Covera-HS tablets in patients with moderate hepatic impairment was approximately 75% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters. The mean absolute bioavailability of oral Covera-HS tablets in patients with severe hepatic impairment was approximately 65% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters. The mean absolute bioavailability of oral Covera-HS tablets in patients with severe renal impairment was approximately 95% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters.

The mean absolute bioavailability of oral Covera-HS tablets in patients with moderate hepatic impairment was approximately 75% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters. The mean absolute bioavailability of oral Covera-HS tablets in patients with severe hepatic impairment was approximately 65% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters. The mean absolute bioavailability of oral Covera-HS tablets in patients with severe renal impairment was approximately 95% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters.

The mean absolute bioavailability of oral Covera-HS tablets in patients with moderate hepatic impairment was approximately 75% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters. The mean absolute bioavailability of oral Covera-HS tablets in patients with severe hepatic impairment was approximately 65% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters. The mean absolute bioavailability of oral Covera-HS tablets in patients with severe renal impairment was approximately 95% of that in healthy volunteers, with no significant differences in pharmacokinetic parameters.

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Use in patients with impaired renal function: About 78% of an administered dose of verapamil is excreted as metabolites in the urine. Verapamil is not removed by hemodialysis. Until further data are available, verapamil should be administered with caution to patients with impaired renal function. If renal function is severely impaired, it may be necessary to decrease the dosage of verapamil when it is administered to patients with attenuated neuromuscular transmission.

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