Hydrochlorothiazide Tablets

2.1 General Considerations

DOSAGE AND ADMINISTRATION (2)

See published guidelines, such as those of the National High Blood Pressure Education Program's Joint National Committee 10/320/25

Tablets: (amlodipine/valsartan/hydrochlorothiazide mg)

* Sections or subsections omitted from the full prescribing information are not listed.

Do not coadminister aliskiren with amlodipine/valsartan/hydrochlorothiazide in patients with diabetes.

These highlights do not include all the information needed to use AMLODIPINE/VALSARTAN/HCTZ Tablets safely and effectively. See full prescribing information for details.

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Studies with valsartan

Amlodipine maleate has been shown to prolong both the gestation period and the duration of labor in rats at this dose. The number of intrauterine deaths was significantly increased (about 5-fold) for rats receiving doses of 600 mg/kg/day during organogenesis or late gestation and lactation. In rabbits, fetotoxicity (i.e., resorptions, litter loss, decreases in litter weight and size) was observed at doses of 4 and 16 mg/kg/day amlodipine. In a study in which rabbits were administered amlodipine at 2, 4, and 16 mg/kg/day for 10 days, decreases in body weight gain of dams and fetuses were noted at the 16 mg/kg/day dose, without any evidence of maternal toxicity. In most studies, amlodipine-induced decreases in body weight gain were accompanied by a decrease in food consumption in pregnant females, which was not seen at lower doses. In a study in which rabbits were administered amlodipine at doses of 2, 4, and 16 mg/kg/day to pregnant females from gestation days 15 through 20, a low incidence of skeletal abnormalities (single, unossified vertebrae) was seen at the high dose. Inhibition of organogenesis was not seen when amlodipine was administered at doses up to 16 mg/kg/day to pregnant females from gestation days 6 through 15 or 15 through 20. However, when amlodipine was administered at doses up to 40 mg/kg/day to pregnant females from gestation days 15 through 20, a low incidence of skeletal abnormalities (single, unossified vertebrae) was seen at the high dose. Inhibition of organogenesis was not seen when amlodipine was administered at doses up to 16 mg/kg/day to pregnant females from gestation days 6 through 15 or 15 through 20.

Studies with amlodipine

Amlodipine maleate has been shown to prolong both the gestation period and the duration of labor in rats at this dose. The number of intrauterine deaths was significantly increased (about 5-fold) for rats receiving doses of 600 mg/kg/day during organogenesis or late gestation and lactation. In rabbits, fetotoxicity (i.e., resorptions, litter loss, decreases in litter weight and size) was observed at doses of 4 and 16 mg/kg/day amlodipine. In a study in which rabbits were administered amlodipine at 2, 4, and 16 mg/kg/day for 10 days, decreases in body weight gain of dams and fetuses were noted at the 16 mg/kg/day dose, without any evidence of maternal toxicity. In most studies, amlodipine-induced decreases in body weight gain were accompanied by a decrease in food consumption in pregnant females, which was not seen at lower doses. In a study in which rabbits were administered amlodipine at doses of 2, 4, and 16 mg/kg/day to pregnant females from gestation days 15 through 20, a low incidence of skeletal abnormalities (single, unossified vertebrae) was seen at the high dose. Inhibition of organogenesis was not seen when amlodipine was administered at doses up to 16 mg/kg/day to pregnant females from gestation days 6 through 15 or 15 through 20. However, when amlodipine was administered at doses up to 40 mg/kg/day to pregnant females from gestation days 15 through 20, a low incidence of skeletal abnormalities (single, unossified vertebrae) was seen at the high dose. Inhibition of organogenesis was not seen when amlodipine was administered at doses up to 16 mg/kg/day to pregnant females from gestation days 6 through 15 or 15 through 20.

Mutagenicity assays did not reveal any valsartan-related effects at either the gene or chromosome level. These assays included in vitro assays with bacterial (Salmonella typhimurium and Escherichia coli) and mammalian cells (Chinese hamster ovary cells) and in vivo assays with Syrian hamster bone marrow cells and Chinese hamster ovary cells. Valsartan was negative in assays with rat and human lymphocytes. Valsartan was not mutagenic in the mouse lymphoma assay. Valsartan was not clastogenic in the mammalian cell chromosome aberration assay. Valsartan was not genotoxic in the mouse micronucleus test. Valsartan was negative in the Ames mutagenicity assay of Salmonella typhimurium using the forward mutation and reverse mutation assays and in the in vitro cytogenetic test with Chinese hamster ovary cells, and a rat micronucleus test.

About 70% of an orally administered dose of hydrochlorothiazide is eliminated in the urine as unchanged drug. The plasma elimination half-life of hydrochlorothiazide is about 6 hours in patients with normal renal function. The plasma elimination half-life of hydrochlorothiazide increases in a linear fashion with the reduction of creatinine clearance down to about 4 hours in patients with severe renal impairment (creatinine clearance less than or equal to 10 mL/min).

In a dedicated drug interaction study, administration of cholestyramine 2 hours before hydrochlorothiazide did not affect the plasma concentrations of hydrochlorothiazide. However, the plasma concentrations of hydrochlorothiazide were decreased after administration of cholestyramine 2 hours after hydrochlorothiazide. Therefore, it is recommended to administer hydrochlorothiazide at least 4 hours after cholestyramine.

Skeletal muscle relaxants:

Thiazide-induced hypokalemia or hypomagnesemia may predispose the patient to digoxin toxicity.

Cholestyramine:

The most common side effects of amlodipine/valsartan/hydrochlorothiazide include:

- edema (swelling of the hands, ankles, or feet)
- headache
- constipation
- diarrhea
- flatulence
- muscle cramps
- rash

Tell your doctor if you have any side effect that bothers you or if it does not go away.

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