Olmis™-A

(Amlodipine / Olmesartan Medoxomil)
Tablets U.S.P.

5mg/20mg 10mg/20mg
5mg/40mg 10mg/40mg

اولمِس-اے

(املوڈپائن/اولمیسارٹن میڈوکسومل) ٹیبلٹس بی۔پی۔

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QUALITATIVE AND QUANTITATIVE COMPOSITION

Olmis™-A Tablet U.S.P. 5mg/20mg: Each film-coated tablet contains:
Amlodipine as Besilate B.P. 5mg
Olmesartan Medoxomil U.S.P. 20mg
Olmis™-A Tablet U.S.P. 5mg/40mg: Each film-coated tablet contains:
Amlodipine as Besilate B.P. 5mg
Olmesartan Medoxomil U.S.P. 40mg
Olmis™-A Tablet U.S.P. 10mg/20mg: Each film-coated tablet contains:
Amlodipine as Besilate B.P. 10mg
Olmesartan Medoxomil U.S.P. 20mg
Olmis™-A Tablet U.S.P. 10mg/40mg: Each film-coated tablet contains:
Amlodipine as Besilate B.P. 10mg
Olmesartan Medoxomil U.S.P. 40mg

USE IN PREGNANCY *See full prescribing information for complete boxed warning. When pregnancy is detected,* discontinue Olmis-A Tablet as soon as possible. When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.

DESCRIPTION

The Amlodipine Besilate and Olmesartan Medoxomil are components of Olmis-A.

CLINICAL PHARMACOLOGY

Mechanism of Action: Olmis-A Tablet is a combination of an angiotensin II receptor antagonist, olmesartan medoxomil, and a calcium channel blocker, amlodipine besilate. The combination of these active ingredients has an additive antihypertensive effect, reducing blood pressure to a greater degree than either component alone.
Pharmacodynamics:
Pharmacotherapeutic group: Angiotensin II antagonists and calcium channel blockers.
Pharmacokinetics: The pharmacokinetics of amlodipine and olmesartan medoxomil from Olmis-A are equivalent to the pharmacokinetics of amlodipine and olmesartan medoxomil when administered separately.
Absorption: Amlodipine. After oral administration of therapeutic doses of amlodipine, absorption produces peak plasma concentrations between 6 and 12 hours. Absolute bioavailability is estimated as between 64% and 90%. Olmesartan medoxomil. Olmesartan medoxomil is rapidly and completely bioactivated by ester hydrolysis to olmesartan during absorption from the gastrointestinal tract. The absolute bioavailability of olmesartan medoxomil is approximately 26%. After oral administration, the peak plasma concentration (Cmax) of olmesartan is reached after 1 to 2 hours. Food does not affect the bioavailability of olmesartan medoxomil.
Distribution: Amlodipine. Ex vivo studies have shown that approximately 93% of the circulating drug is bound to plasma proteins in hypertensive patients. Steady-state plasma levels of amlodipine are reached after 7 to 8 days of consecutive daily dosing. **Olmesartan medoxomil:** The volume of distribution of olmesar-tan is approximately 17 L. Olmesartan is highly bound to

plasma proteins (99%) and does not penetrate red blood cells. The protein binding is constant at plasma olmesartan concentrations well above the range achieved with recommended doses.
Metabolism & Excretion: Amlodipine. Amlodipine is extensively (about 90%) converted to inactive metabolites via hepatic metabolism. Elimination from the plasma is biphasic with a terminal elimination half-life of about 30 to 50 hours. Ten percent of the parent compound and 60% of the metabolites are excreted in the urine.
Olmesartan Medoxomil: Following the rapid and complete conversion of olmesartan medoxomil to olmesartan during absorption, there is virtually no further metabolism of olmesartan. Total plasma clearance of olmesartan is 1.3 L/h, with a renal clearance of 0.6 L/h. Approximately 35% to 50% of the absorbed dose is recovered in urine while the remainder is eliminated in feces via the bile.
Geriatric: The pharmacokinetic properties of Olmis-A in the elderly are similar to those of the individual components.
Amlodipine: Elderly patients have decreased clearance of amlodipine with a resulting increase in AUC of approximately 40% to 60%, and a lower initial dose may be required. Olmesartan medoxomil. The pharmacokinetics of olmesartan medoxomil were studied in the elderly (≥65 years). Overall, maximum plasma concentrations of olmesartan were similar in young adults and the elderly. Modest accumulation of olmesartan was observed in the elderly with repeated dosing; AUCss, τ was 33% higher in elderly patients, corresponding to an approximate 30% reduction in CLR.
Pediatric: Amlodipine. Sixtytwo hypertensive patients aged 6 to 17 years received doses of amlodipine between 1.25 mg and 20 mg. Weightadjusted clearance and volume of distribution were similar to values in adults.
Olmesartan medoxomil: The pharmacokinetics of olmesartan medoxomil have not been investigated in patients <18 years of age.
Gender: Population pharmacokinetic analysis indicated that female patients had approximately 15% smaller clearances of olmesartan than male patients. Gender had no effect on the clearance of amlodipine.
Olmesartan medoxomil: Minor differences were observed in the pharmacokinetics of olmesartan medoxomil in women compared to men. AUC and Cmax were 10% to 15% higher in women than in men.
Renal Insufficiency:
Amlodipine: The pharmacokinetics of amlodipine are not significantly influenced by renal impairment. Patients with renal failure may therefore receive the usual initial dose.
Olmesartan medoxomil: In patients with renal insufficiency, serum concentrations of olmesartan were elevated compared to subjects with normal renal function. After repeated dosing, the AUC was approximately tripled in patients with severe renal impairment (creatinine clearance <20 mL/min). The pharmacokinetics of olmesartan medoxomil in patients undergoing hemodialysis has not been studied. No initial dosage adjustment is recommended for patients with moderate to marked renal impairment (creatinine clearance <40 mL/min).
Hepatic Insufficiency: Amlodipine. Patients with hepatic insufficiency have decreased clearance of amlodipine with a resulting increase in AUC of approximately 40% to 60%.
Olmesartan medoxomil: Increases in AUC0-∞ and Cmax were observed in patients with moderate hepatic impairment compared to those in matched controls, with an increase in AUC of about 60%.
Heart Failure: Amlodipine. Patients with heart failure have decreased clearance of amlodipine with a resulting increase in AUC of approximately 40% to 60%.

INDICATION:

Olmis-A is a dihydropyridine calcium channel blocker and angiotensin II receptor blocker combination product indicated for the treatment of hypertension, alone or with other antihypertensive agents, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Olmis-A is indicated as initial therapy in patients likely to need multip le antihypertensive agents to achieve their blood pressure goals.

CONTRAINDICATIONS:

None.

INTERACTIONS:

Drug Interactions with Amlodipine: In vitro data indicate that amlodipine has no effect on the human plasma protein binding of digoxin, phenytoin, warfarin, and indomethacin. **Effect of Other Agents on Amlodipine Cimetidine:** Co-administration of amlodipine with cimetidine did not alter the pharmacokinetics of amlodipine. Grapefruit juice: Co-administration of 240 mL of grapefruit juice with a single oral dose of amlodipine 10 mg in 20 healthy volunteers had no significant effect on the pharmacokinetics of amlodipine **(antacid):** Co-administration of the antacid with a single dose of amlodipine had no significant effect on the pharmacokinetics of amlodipine. **Sildenafil:** A single 100 mg dose of sildenafil in subjects with essential hypertension had no effect on the pharmacokinetic parameters of amlodipine. When amlodipine and sildenafil were used in combination, each agent independently exerted its own blood pressure lowering effect. **Effect of Amlodipine on Other Agents Atorvastatin:** Co-administration of multiple 10 mg doses of amlodipine with 80 mg of atorvastatin resulted in no significant change in the steady state pharmacokinetic parameters of atorvastatin. Digoxin: Co-administration of amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers. Ethanol (alcohol): Single and multiple 10 mg doses of amlodipine had no significant effect on the pharmacokinetics of ethanol. Warfarin: Co-administration of amlodipine with warfarin did not change the warfarin prothrombin response time. No significant drug interactions were reported in studies in which olmesartan medoxomil was co-administered with digoxin or warfarin in healthy volunteers. The bioavailability of olmesartan medoxomil was not significantly altered by the coadministration of antacids [Al(OH)3/Mg(OH)2]. Olmesartan medoxomil is not metabolized by the cytochrome P450 system and has no effects on P450 enzymes; thus, interac-tions with drugs that inhibit, induce, or are metabolized by those enzymes are not expected. Non-Steroidal Anti-Inflammatory Agents including Selective Cy-clooxygenase-2 Inhibitors (COX-2 Inhibitors) In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors, with angiotensin II receptor antagonists, including olmesartan medoxomil, may result in dete-rioration of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function peri-odically in patients receiving olmesartan medoxomil and NSAID therapy. The antihypertensive effect of angiotensin II receptor antagonists, including olmesartan medoxomil may be attenuated by NSAIDs including selective COX-2 inhibitors.

USE IN SPECIFIC POPULATION

- In patients with an activated renin-angiotensin system, such as volumeor salt-depletion, renin-angiotensin-aldosterone system (RAAS) blockers such as olmesartan medoxomil can cause ex-cessive hypotension. In susceptible patients, e.g., with renal ar-tery stenosis, RAAS blockers can cause renal failure.
- Start amlodipine alone or add amlodipine at 2.5 mg in patients ≥75 years old or in hepatically impaired patients. Elderly and patients with hepatic impairment have decreased clearance of amlodipine. Initial therapy with Olmis-A is not recommended in patients ≥75 years old or hepatically impaired patients.

WARNINGS AND PRECAUTIONS

- Hypotension in volume- or salt-depleted patients with treatment initiation may be anticipated. Start treatment under close supervision.
- Increased angina or myocardial infarction with calcium channel blockers may occur upon dosage initiation or increase.
- Impaired renal function: changes in renal function may be anticipated in susceptible individual.

ADVERSE REACTIONS

Most common adverse reaction (incidence ≥3%) is edema other adverse reactions included are hypotension othostatio hypotension rasb, pruritus, palpitation, and nocturia.

DOSAGE AND ADMINISTRATION

General Considerations: The side effects of olmesartan medoxomil are generally rare & apparently independent of dose. Those of amlodipine are generally dose-dependent (mostly edema).

Maximum antihypertensive effects are attained within 2 weeks after a change in dose. Olmis-A may be taken with or without food. Olmis-A may be administered with other antihypertensive agents. Dosage may be increased after 2 weeks. The maximum recommended dose of Olmis-A is 10/40 mg.

Replacement Therapy: Olmis-A may be substituted for its individually titrated components. When substituting for individual components, the dose of one or both of the components can be increased if blood pressure control has not been satisfactory.

Add-on Therapy: Olmis-A may be used to provide additional blood pressure lowering for patients not adequately controlled with amlodipine (or another dihydropyridine calcium channel blocker) alone or with olmesartan medoxomil (or another angiotensin receptor blocker) alone.

Initial Therapy: The usual starting dose of Olmis-A is 5/20 mg once daily. The dosage can be increased after 1 to 2 weeks of therapy to a maximum dose of one 10/40 mg tablet once daily as needed to control blood pressure. Initial therapy with Olmis-A is not recommended in patients ≥75 years old or with hepatic impairment

Overdose: There is no information on overdosage with Olmis-A in humans.

INSTRUCTIONS

Dosage as directed by the physician.
Store at 20°C - 25°C, excursions permitted to 15°C - 30°C.
Protect from sunlight and moisture.
Keep all medicines out of the reach of children.

PRESENTATION

Olmis-A Tablet 5mg/20mg: Available in 2 x 10's Alu-Alu blister pack of tablets.
Olmis-A Tablet 5mg/40mg: Available in 2 x 10's Alu-Alu blister pack of tablets.
Olmis-A Tablet 10mg/20mg: Available in 2 x 10's Alu-Alu blister pack of tablets.
Olmis-A Tablet 10mg/40mg: Available in 2 x 10's Alu-Alu blister pack of tablets.

علامات: ہائی بلڈ پریشر کے مریضوں میں استعمال کے لئے۔

مضر اثرات: ایڈیما، بلڈ پریشر میں کمی، الرجی اور پرورائٹس۔

احتیاطی تدابیر: بلڈ پریشر میں کمی ہوسکتی ہے لہذا احتیاط سے استعمال کریں۔

دوا شروع کرنے یا مقدار بڑھانے سے اینجائنا یا مایوکارڈیل انفارکشن کا خطرہ ہوسکتا ہے۔

گردے کی مریضوں میں گردے کی کارکردگی متاثر ہوسکتی ہے۔

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر رکھیں،

محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔

سورج کی روشنی اور نمی سے محفوظ رکھیں۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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ISO 9001:2015 ISO 14001:2015 ISO 45001:2018