Olam-H®
(Olmesartan medoxomil, Amlodipine and Hydrochlorothiazide Tablet)

Quantitative composition.
Each film coated tablet contains: **Olmesartan medoxomil 20mg, Amlodipine (as besylate) 5.0mg and Hydrochlorothiazide 12.5mg**
Pharmaceutical form: Tablet
Pharmacology:
Olmesartan medoxomil is a potent, orally active, selective angiotensin II receptor (type AT_1) antagonist. It is expected to block all actions of angiotensin II mediated by the AT_1 receptor, regardless of the source or route of synthesis of angiotensin II. The selective antagonism of the angiotensin II (AT_1) receptors results in increases in plasma renin levels and angiotensin I and II concentrations, and some decrease in plasma aldosterone concentrations. The mechanisms of the antihypertensive action of Amlodipine tablets are due to a direct relaxant effect on vascular smooth muscle. The precise mechanism by which Amlodipine tablets relieves angina has not been fully determined but Amlodipine tablets reduces total ischaemic burden by the following two actions. Amlodipine dilates peripheral arterioles and thus, reduces the total peripheral resistance (afterload) against which the heart works. Since the heart rate remains stable, this unloading of the heart reduces myocardial energy consumption and oxygen requirements. The mechanism of action of Amlodipine also probably involves dilatation of the main coronary arteries and coronary arterioles, both in normal and ischaemic regions. This dilatation increases myocardial oxygen delivery in patients with coronary artery spasm. Hydrochlorothiazide, a thiazide diuretic, inhibits water reabsorption in the nephron by inhibiting the sodium-chloride symporter (SLC12A3) in the distal c onvoluted tubule, which is responsible for 5% of total sodium reabsorption. Normally, the sodium-chloride symporter transports sodium and chloride from the lumen into the epithelial cell lining the distal convoluted tubule. The energy for this is provided by a sodium gradient established by sodium-potassium ATPases on the basolateral membrane. Once sodium has entered the cell, it is transported out into the basolateral interstitium via the sodium-potassium ATPase, causing an increase in the osmolarity of the interstitium, thereby establishing an osmotic gradient for water reabsorption. By blocking the sodium-chloride symporter, hydrochlorothiazide effectively reduces the osmotic gradient and water reabsorption throughout the nephron.
Pharmacokinetics:
Olmesartan medoxomil is a pro-drug. It is rapidly converted to the pharmacologically active metabolite, olmesartan, by esterases in the gut mucosa and in portal blood during absorption from the gastrointestinal tract. No intact olmesartan medoxomil or intact side chain medoxomil moiety have been detected in plasma or excreta. The mean absolute bioavailability of olmesartan from a tablet formulation was 25.6%.The mean peak plasma concentration (C_{max}) of olmesartan is reached within about 2 hours after oral dosing with olmesartan medoxomil, and olmesartan plasma concentrations increase approximately linearly with increasing single oral doses up to about 80 mg. Food had minimal effect on the bioavailability of olmesartan and therefore olmesartan medoxomil may be administered with or without food. The terminal elimination half- life of olmesartan varied between 10 and 15 hours after multiple oral dosing. Steady state was reached after the first few doses and no further accumulation was evident after 14 days of repeated dosing. Renal clearance was approximately 0.5 – 0.7 L/h and was independent of dose. After oral administration of therapeutic doses, amlodipine is well absorbed with peak blood levels between 6-12 hours post dose. Absolute bioavailability has been estimated to be between 64 and 80%. The volume of distribution is approximately 21 l/kg. The terminal plasma elimination half-life is about 35-50 hours and is consistent with once daily dosing. Amlodipine is extensively metabolised by the liver to inactive metabolites with 10% of the parent compound and 60% of metabolites excreted in the urine.The onset of the diuretic action of hydrochlorothiazide occurs in 2 hours and the peak action in about 4 hours.
Diuretic activity lasts about 6 to 12 hours. Hydrochlorothiazide is eliminated rapidly by the kidney. The mechanism of the antihypertensive effect of thiazides may be related to the excretion and redistribution of body sodium.
Indications:
Hypertension, Prophylaxis of chronic stable angina pectoris, Prinzmetal's (variant) angina when diagnosed by a cardiologist and potassium-conserving diuretic and anti-hypertensive for the treatment of patients with congestive heart failure or hepatic cirrhosis with ascites and oedema.
Administration and Dosage:
To be taken orally.
Hypertension, Prophylaxis of chronic stable angina pectoris, Prinzmetal's (variant) angina when diagnosed by a cardiologist and potassium-conserving diuretic and anti-hypertensive for the treatment of patients with congestive heart failure or hepatic cirrhosis with ascites and oedema: One tablets daily and can be increase to two tablets given in divided doses.
Contraindications:
Olam –H is contraindicated in second and third trimesters of pregnancy, Biliary obstruction , concomitant use with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 mL/min/1.73 m^2) and Hyperkalaemia (plasma potassium over 5.5 mmol/l).
Hypersensitivity to the amiloride hydrochloride, hydrochlorothiazide, acetazolamide or other thiazide or sulfonamide-derived drugs.
Warning and Precautions:
Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting. Such conditions should be corrected before administration. In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with other drugs that affect this system has been associated with acute hypotension, azotaemia, oliguria or, rarely, acute renal failure. Increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that affect the renin-angiotensin-aldosterone system. Concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure).
Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended.
Drug interaction:
Dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting agent. Concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other drugs that may increase serum potassium levels (e.g. heparin) may lead to increases in serum potassium. The risk of the concomitant use of NSAIDs and angiotensin II antagonists in the occurrence of acute renal failure should be monitoring of renal function at the beginning of treatment should be recommended as well as regular hydration of the patients.
Pregnancy and Lactation:
The use of angiotensin II antagonists is contra-indicated during the 2nd and 3rd trimester of pregnancy. Olmesartan is excreted in the milk of lactating rats but it is not known whether olmesartan is excreted in human milk. Hydrochlorothiazide is excreted in human milk in small amounts. Thiazides in high doses causing intense diuresis can inhibit the milk production.
Effects on ability to drive and use machines: Olam- H tablets has minor or moderate influence on the ability to drive and use machines.
Dizziness or fatigue may occasionally occur in patients taking antihypertensive therapy, which may impair the ability to react.
Adverse reactions:
Olmesartan common side effects includes: Dizziness, Back pain, Sinus inflammation and increased potassium level in blood., Fatigue, Ankle swelling, Sleepiness, Flushing (sense of warmth in the face, ears, neck and trunk), Headache, Nausea, Dizziness, Palpitations, Edema and Abdominal pain, Increased blood uric acid, decreased potassium level in blood, glucose intolerance and altered blood lipids.
Overdosage and treatment:
The most likely effect of overdosage is hypotension. In the event of overdosage, the patient should be carefully monitored and treatment should be symptomatic and supportive. No information is available regarding the dialysability of olmesartan.
Presentation:
Tablet: Blister packs of 3 x 10`s in a unit box.
Shelf life: 3 years from the date of manufacture.
Storage: Store in a dry place, below 30^0C. Protect from light. Keep all medicines out of reach of children.
Distribution category: Prescription only medicine (POM).
Manufactured by:

DAWA Limited, Plot No. 7879/8, Baba Dogo Road, Ruaraka
P. O. Box 16633 – 00620, Nairobi, Kenya.

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