

Danforge-A
(Amlodipine / Valsartan)
Tablets U.S.P.

5mg /80mg
5mg /160mg
10mg /160mg

ڈیفورج-اے
(ایملوڈیپائن/والسرتان)
5mg /80mg
5mg /160mg
10mg /160mg

QUALITATIVE AND QUANTITATIVE COMPOSITION

Danforge-A 5mg / 80mg Tablets U.S.P. :

Each film-coated tablet contains:

Amlodipine (as Besylate) U.S.P.5mg
Valsartan U.S.P.80mg

Danforge-A 5mg / 160mg Tablets U.S.P.:

Each film-coated tablet contains:

Amlodipine (as Besylate) U.S.P.5mg
Valsartan U.S.P.160mg

Danforge-A 10mg / 160mg Tablets U.S.P.:

Each film-coated tablet contains:

Amlodipine (as Besylate) U.S.P.10mg
Valsartan U.S.P.160mg

WARNING: FETAL TOXICITY

• When pregnancy is detected, discontinue Amlodipine / Valsartan Tablets U.S.P. as soon as possible. • Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

DESCRIPTION

Amlodipine / Valsartan Tablets U.S.P. is a fixed combination of amlodipine and valsartan. Amlodipine / Valsartan Tablets U.S.P. contains the Besilate salt of amlodipine, a dihydropyridine calcium-channel blocker (CCB) and Valsartan is a nonpeptide, orally active, and specific angiotensin II antagonist acting on the AT1 receptor subtype.

CLINICAL PHARMACOLOGY

Mechanism of Action: Amlodipine: Amlodipine is a dihydropyridine calcium channel blocker that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. Valsartan: Valsartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Pharmacodynamics: Amlodipine / Valsartan Tablets U.S.P. has been shown to be effective in lowering blood pressure. Both amlodipine and valsartan lower blood pressure by reducing peripheral resistance, but calcium influx blockade and reduction of angiotensin II vasoconstriction are complementary mechanisms. Pharmacokinetics: Oral administration of Amlodipine / Valsartan in normal healthy adults, peak plasma concentrations of valsartan and amlodipine are reached in 3 and 6 to 8 hours, respectively. The rate and extent of absorption of valsartan and amlodipine from Amlodipine / Valsartan Tablets U.S.P. are the same as when administered as individual tablets.

INDICATIONS AND USAGE

Amlodipine / Valsartan Tablets U.S.P. is indicated for the treatment of hypertension, to lower blood pressure:

• In patients not adequately controlled on monotherapy.

• As initial therapy in patients likely to need multiple drugs to achieve their blood pressure goals. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions.

CONTRAINDICATIONS

Hypersensitivity to the active substances, to dihydropyridine derivatives, or to any of the excipients, Concomitant use of Amlodipine / Valsartan Tablets U.S.P. with aliskiren-containing products in patients with diabetes mellitus or renal impairment (GFR <60 ml/min/1.73 m²), Severe hepatic impairment, biliary cirrhosis or cholestasis. Second and third trimesters of pregnancy, Severe hypotension, Shock (including cardiogenic shock), Obstruction of the outflow tract of the left ventricle (e.g. hypertrophic obstructive cardiomyopathy and high grade aortic stenosis), Hemodynamically unstable heart failure after acute myocardial infarction.

INTERACTIONS

Do not use with other antihypertensive agents and closely monitor when using Amlodipine / Valsartan with these; Grapefruit or grapefruit juice, CYP3A4 inhibitors, CYP3A4 inducers (anticonvulsant agents [e.g. carbamazepine, phenobarbital, phenytoin, fosphenytoin, primidone], rifampicin, Hypericum perforatum): Amlodipine should be used with caution together with CYP3A4 inducers. Simvastatin (It is recommended to limit the dose of simvastatin to 20mg daily in patients on amlodipine). Sildenafil: Monitor for hypotension when sildenafil is co-administered with amlodipine. Amlodipine may increase the systemic exposure of cyclosporine or tacrolimus when co-administered.

• Valsartan: Non-Steroidal Anti-Inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors). Monitor renal function periodically in patients receiving valsartan and NSAID therapy. Potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium and other substances that may increase potassium levels: If a medicinal product that affects potassium levels is to be prescribed in combination with valsartan, monitoring of potassium plasma levels is advised. Transporters: Co-administration of inhibitors of the uptake transporter (rifampin, cyclosporine) or efflux transporter (ritonavir) may increase the systemic exposure to valsartan. Dual blockade of the RAAS with ARBs, ACE inhibitors or aliskiren. Lithium (Monitor serum lithium levels during concomitant use).

USE IN SPECIFIC POPULATION

Pregnancy: Category D: Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death are associated with it. It is contraindicated in all trimesters of pregnancy. **Nursing mothers:** It is not known whether amlodipine or valsartan is excreted in human milk. **Pediatric Use:** Safety and effectiveness of Amlodipine / Valsartan Tablets U.S.P. in pediatric patients and children

aged below 18 years have not been established. **Geriatric Use:** Greater sensitivity of some older individuals cannot be ruled out. **Elderly (age 65 years or over):** In elderly patients, caution is required when increasing the dosage.

PRECAUTIONS

Fetal Toxicity: Pregnancy Category D: When pregnancy is detected, discontinue Amlodipine / Valsartan Tablets U.S.P. as soon as possible. Hypotension: Excessive hypotension was seen in patients with uncomplicated hypertension. Initiate therapy cautiously in patients with heart failure or recent myocardial infarction and in patients undergoing surgery or dialysis. Risk of Myocardial Infarction or Increased Angina: Worsening angina and acute myocardial infarction can develop after starting or increasing the dose of amlodipine, particularly in patients with severe obstructive coronary artery disease. Impaired Renal Function: Monitor renal function periodically in these patients. Hyperkalemia: Drugs that inhibit the renin-angiotensin system can cause hyperkalemia. Monitor serum electrolytes periodically. Dosage reduction and/or discontinuation of Amlodipine / Valsartan Tablets U.S.P. may be required. Hepatic impairment: Valsartan is mostly eliminated unchanged via the bile. The half-life of amlodipine is prolonged and AUC values are higher in patients with impaired liver function; dosage recommendations have not been established. Particular caution should be exercised when administering Amlodipine / Valsartan Tablets U.S.P. to patients with mild to moderate hepatic impairment or biliary obstructive disorders. In patients with mild to moderate hepatic impairment without cholestasis, the maximum recommended dose is 80 mg valsartan. Renal impairment: No dosage adjustment of Amlodipine / Valsartan Tablets U.S.P. is required for patients with mild to moderate renal impairment (GFR >30 ml/min/1.73 m²). Monitoring of potassium levels and creatinine is advised in moderate renal impairment. Primary hyperaldosteronism: Patients with primary hyperaldosteronism should not be treated with valsartan. Angioedema: Amlodipine / Valsartan Tablets U.S.P. A should be discontinued immediately in patients who develop angioedema and should not be re-administered. Aortic and mitral valve stenosis: As with all other vasodilators, special caution is indicated in patients suffering from mitral stenosis or significant aortic stenosis that is not high grade. Dual blockade of the renin-angiotensin-aldosterone system (RAAS): Dual blockade of RAAS through the combined use of ACE inhibitors, ARBs or aliskiren not recommended. ACE inhibitors and ARBs should not be used concomitantly in patients with diabetic nephropathy. Effects on ability to drive and use machines: If patients taking amlodipine suffer from dizziness, headache, fatigue or nausea the ability to react may be impaired so avoid to drive and use machine.

ADVERSE REACTIONS

Lymphadenopathy, tachycardia, abdominal discomfort, dry mouth, colitis, fatigue, chest pain, asthenia, pitting edema, sinusitis, bronchitis, pharyngitis, gastroenteritis, pharyngotonsillitis, bronchitis acute, epicondylitis, limb injury, gout, non-insulin-dependent diabetes mellitus, hypercholesterolemia, arthralgia, muscle spasms, myalgia, osteoarthritis, musculoskeletal chest pain, headache, sciatica, paresthesia, cervicobrachial syndrome, carpal tunnel syndrome, hematuria, nephrolithiasis, erectile dysfunction, dyspnea, epistaxis,

productive cough, pruritus, rash, hyperhidrosis, eczema, erythema flushing. Side effects: •Swelling (edema) of the hands, ankles, or feet •nasal congestion, sore throat, and discomfort when swallowing •upper respiratory tract infection (head or chest cold) •dizziness.

DOSAGE AND ADMINISTRATION

General Considerations: Dose once daily. The dosage can be increased after 1 to 2 weeks of therapy to a maximum of one 10/320 mg tablet once daily as needed to control blood pressure. The majority of the antihypertensive effect is attained within 2 weeks after initiation of therapy or a change in dose. Danforge-A may be administered with or without food. **Add-on Therapy:** A patient whose blood pressure is not adequately controlled with amlodipine (or another dihydropyridine calcium-channel blocker) alone or with valsartan (or another angiotensin II receptor blocker) alone may be switched to combination therapy with Danforge-A. A patient who experiences dose-limiting adverse reactions on either component alone may be switched to Danforge-A containing a lower dose of that component in combination with the other to achieve similar blood pressure reductions. The clinical response to Danforge-A should be subsequently evaluated and if blood pressure remains uncontrolled after 3 to 4 weeks of therapy, the dose may be titrated up to a maximum of 10/320 mg.

Replacement Therapy: For convenience, patients receiving amlodipine and valsartan from separate tablets may instead wish to receive tablets of Danforge-A containing the same component doses. Initial Therapy: A patient may be initiated on Danforge-A if it is unlikely that control of blood pressure would be achieved with a single agent. The usual starting dose is Danforge-A 5/160 mg once daily in patients who are not volume-depleted.

INSTRUCTIONS

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

PRESENTATION

Danforge[®]-A 5mg / 80mg (Amlodipine / Valsartan) tablets U.S.P. are available in Alu-Alu blister pack of 14's.
Danforge[®]-A 5mg / 160mg (Amlodipine / Valsartan) tablets U.S.P. are available in Alu-Alu blister pack of 14's.
Danforge[®]-A 10mg / 160mg (Amlodipine / Valsartan) tablets U.S.P. are available in Alu-Alu blister pack of 14's.

ہدایات:
خوراک ڈالو کی ہدایت کے مطابق استعمال کریں۔
۲۰ ڈگری سینٹی گریڈ پر رکھیں،
مختلط رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔
روشٹی گرمی اور نمی سے محفوظ رکھیں۔
تمام دوا میں پھول کی پتیختی سے دور رکھیں۔

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