Onato® Tablets

(Amlodipine Besylate)

DESCRIPTION:
Onato® (Amlodipine Besylate) is a calcium ion influx inhibitor (calcium entry blocker or calcium ion antagonist). Amlodipine is a member of the dihydropyridine class of calcium antagonists **Chemical Name:** 3-ethyl-5-methyl-2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate benzenesulphonate. Its empirical formula is $C_{20}H_{25}ClN_2O_5C_6H_6O_3S$

COMPOSITION:
Each tablet contains : Amlodipine Besylate EP equivalent to Amlodipine 5mg
Each tablet contains : Amlodipine Besylate EP equivalent to Amlodipine 10mg

MECHANISM OF ACTION:
The therapeutic effect of this group of drugs is believed to be related to their specific cellular action of selectively inhibiting transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle

A. Hypertension Amlodipine reduces arterial blood pressure by direct peripheral arterial vasodilation and reduction in peripheral vascular resistance

B. Angina The precise mechanism by which Amlodipine relieves angina has not been fully delineated. Amlodipine is a dilator of peripheral arteries and arterioles which reduces the total peripheral resistance and, therefore, reduces the workload of the heart (afterload). The unloading of the heart is thought to decrease ischemia and relieve effort angina by reducing myocardial energy oxygen consumption and oxygen requirements

PHARMACOKINETICS:
Absorption:
After oral administration of therapeutic doses of Amlodipine, absorption occurs gradually with peak plasma concentration reached between 6 and 12hours. Absolute bioavailability has been estimated to be between 64 and 90%. The bioavailability of Amlodipine is not altered by the presence of food

Metabolism:
Amlodipine is metabolized through the cytochrome P450 system, mainly via CYP 3A4 isoenzyme

Excretion:
Amlodipine is extensively (about 90%) converted to inactive metabolites (via hepatic metabolism) with about 10% of the parent compound and 60% of the metabolites excreted in the urine

INDICATIONS:
Hypertension:
Onato® (Amlodipine Besylate) is indicated for the treatment of mild to moderate essential hypertension combination of **Onato®** with a diuretic, a beta-blocking agent, or an angiotensin converting enzyme inhibitor has been found to be compatible and showed additive antihypertensive effect

Chronic Stable Angina:
Onato® is indicated for the management of chronic stable angina (effort-associated angina) in patients who remain symptomatic despite adequate doses of beta-blockers and/or organic nitrates or who cannot tolerate those agents

CONTRA-INDICATIONS:
Onato® (Amlodipine Besylate) is contra-indicated in patients with hypersensitivity to the drug or other dihydropyridines and in patients with severe hypotension (less than 90mmHg systolic)

WARNINGS:
Use in Patients with Impaired Hepatic Function:
There are no adequate studies in patients with liver dysfunction and dosage recommendations have not been established. In a small number of patients with mild to moderate hepatic impairment given single dose of 5mg, Amlodipine half-life has been prolonged (see Metabolism). **Onato®** should, therefore, be administered with caution in these patients and careful monitoring should be performed. A lower starting dose may be required (see dosage and administration)

PRECAUTIONS:
Hypotension:
Onato® (Amlodipine Besylate) may occasionally precipitate symptomatic hypotension. Careful monitoring of blood pressure is recommended, especially in patients with a history of cerebrovascular insufficiency, and those taking medications known to lower blood pressure

Peripheral Edema:
Mild to moderate peripheral edema was the most common adverse events observed with its use

Use in Pregnancy:
Amlodipine is in the FDA pregnancy category C. **Onato®** should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus

Nursing Mothers:
It is not known whether Amlodipine is excreted in human milk. Since Amlodipine safety in newborns has not been established, **Onato®** should not be given to nursing mothers

Use in Children:
The use of **Onato®** is not recommended in patients less than 6years of age since safety and efficacy have not been established in that population. The effect of **Onato®** on blood pressure in patients less than 6years of age is not known. For peadiatric administration the risk/benefit assessment should be conducted by a qualified physician

Use in Elderly:
In elderly patients (>65years) clearance of Amlodipine is decreased with a resulting increase in AUC. **Onato®** should be used cautiously in elderly patients. Dosage adjustment is advisable (see dosage and administration)

DRUG INTERACTIONS:
Amlodipine undergo biotransformation by the cytochrome P450 system, mainly via CYP 3A4 isoenzyme. Coadministration of Amlodipine with other drugs which follow the same route of biotransformation may result in altered bioavailability of Amlodipine or these drugs. Drugs known to be inhibitors of the cytochrome P450 system include: azole antifungals, cimetidine, cyclosporine, erythromycin, quinidine, terfenadine, warfarin
Drugs known to be inducers of the cytochrome P450 system include: phenobarbital, phenytoin, rifampin. Drugs known to be biotransformed via P450 include: benzodiazepines, imipramine, theophylline

SIDE EFFECTS:
Amlodipine Besylate may cause the following side effects. Most side effects are mild or moderate that includes headache, swelling of legs or ankles , tiredness, extreme sleepiness, stomach pain, nausea , dizziness, flushing (hot or warm feeling in face), arrhythmia (irregular heartbeat) and heart palpitations (very fast heartbeat)

DOSAGE AND ADMINISTRATION:
Dosage should be individualized depending on patient's tolerance and responsiveness For both hypertension and angina, the recommended initial dose of **Onato®** (Amlodipine Besylate) is 5mg once daily. If necessary, dose can be increased after 1-2 weeks to a maximum dose of 10mg once daily

Use in the Elderly or in Patients with Impaired Renal Function:
The recommended initial dose in patients over 65years of age or patients with impaired renal function is 5mg once daily. If required, increasing in the dose should be done gradually and with caution (see precautions)

Use in Patients with Impaired Hepatic Function:
Dosage requirements have not been established in patients with impaired hepatic function When **Amlodipine** is used in these patients, the dosage should be carefully and gradually adjusted depending on patients tolerance and response. A lower starting dose of 2.5mg once daily should be considered (see warnings)

Use in Children:
The effective antihypertensive oral dose in peadiatric patients ages 6-17years is 2.5mg to 5mg once daily. Doses should be determined based upon the medical need of the patients Or as directed by the physician

PRESENTATION:
Onato® 5mg tablet in blister pack of 20's
Onato® 10mg tablet in blister pack of 20's

STABILITY:
See expiry on the pack

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity
Store at 25ºC or below
Improper storage may deteriorate the medicine

اُناٹو ٹیبلٹ

(ایملوڈیپین بیسیلیٹ)

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ہدایات: بچوں کی پہنچ سے دور رکھیں

دوا کو دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ

یا اس سے کم درجہ حرارت پر رکھیں ورنہ دوا خراب ہو جائے گی

Manufactured by:
SAMI PHARMACEUTICALS (PVT) LTD.
F-95, S.I.T.E., Karachi-Pakistan

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