Myazil *Plus*

(Azilsartan/Amlodipine)

مائی ایزل پلَس

(ایزل سارٹن/ ایملو ڈیپین)

20mg/2.5mg & 20mg/5mg Tablets

۲۰ ملی گرام/ ۲.۵ ملی گرام
۲۰ ملی گرام/ ۵ ملی گرام
گولیاں

COMPOSITION
Myazil Plus 20mg/2.5mg Tablet
Each film coated tablet contains:
Azilsartan..... 20mg
Amlodipine as Besylate 2.5mg

Myazil Plus 20mg/5mg Tablet
Each film coated tablet contains:
Azilsartan..... 20mg
Amlodipine as Besylate 5mg

Pharmaceutical form: Tablet

QUALITATIVE AND QUANTITATIVE COMPOSITIONS:
Qualitative declaration:
Azilsartan/Amlodipine as Besylate
Quantitative declaration:
Azilsartan/Amlodipine as Besylate 20/2.5mg
Azilsartan/Amlodipine as Besylate 20/5mg

PHARMACEUTICAL FORM:
Myazil Plus 20mg/2.5mg Tablet
Peach colored round film coated tablet plain on both sides.
Myazil Plus 20mg/5mg Tablet
Yellow colored round film coated tablet plain on both sides.

CLINICAL PARTICULARS:
Therapeutic indications:
It is effective for the treatment of the hypertension by reducing resistance of peripheral blood vessels.

Posology and method of administration:
Take 1 tablet 1 time a day. If you missed a dose, do not take the double dose and do not take additional dose if the next regular intake time is in less than 8 hours.

CONTRAINDICATIONS:
- Before taking Amlodipine Besylate tell your doctor if you have congestive heart failure or liver disease.
- Drinking alcohol can further lower your blood pressure and may increase certain side effects of Amlodipine Besylate.
- If you are being treated for high blood pressure, keep using this medication even if you feel well. High blood pressure often has no symptoms. You may need to use blood pressure medication for the rest of your life.
- Amlodipine Besylate is only part of a complete program of treatment that may also include diet, exercise, weight control, and other medications. Follow your diet, medication, and exercise routines very closely.
- Your chest pain may become worse when you first start taking Amlodipine Besylate or when your dose is increased.

SPECIAL WARNING AND PRECAUTIONS FOR USE:
- Patients with renal or liver disorders,
- Patients with cerebrovascular disorder or hyperkalemia,
- Patients receiving hemodialysis,
- Patients under low-salt diet treatment,
- Preoperative patients, children,
- Pregnant, possibly pregnant or breastfeeding women.

FERTILITY, PREGNANCY AND LACTATION:
Pregnancy
Do not administer to pregnant women or women who may be pregnant. If pregnancy is found during administration, administration should be discontinued immediately.
Lactation
It is advisable not to breast-feed. When azilsartan was administered perinatally and during lactation to rats by gavage, renal pelvis dilatation was observed in offspring at 0.3 mg/kg/day or higher, and body weight gain was suppressed at 10 mg/kg/day or higher. It has also been reported that amlodipine besilate is excreted in human breast milk.

UNDESIRABLE EFFECTS:
- Facial/tongue/throat swelling, breathlessness[angioedema]
- Feeling cold, vomiting, falling unconscious[shock, syncope, loss of consciousness]
- Decreased urination output, swelling of face and hands/feet, fever[acute renal disorder]
- Numbness of hands/feet and lips, muscle weakness[hyperkalemia]
- Yellowing of the skin/white of the eyes, general malaise, loss of appetite[hepatitis, liver disorder, jaundice]
- Muscle pain lassitude, reddish brown urine[rhabdomyolysis]

OVERDOSE
Symptoms: Excessive peripheral vasodilation can cause marked hypotension and reflex tachycardia, including shock.
Action: There is no specific antidote. Since azilsartan and amlodipine besilate, which are ingredients of this drug, have a high protein binding rate, removal by dialysis is not effective.

PHARMACOLOGICAL PROPERTIES:
Pharmacodynamic properties

Mechanism of action
Azilsartan: Azilsartan binds to the angiotensin II type 1 (AT 1) receptor and antagonizes angiotensin II, and exhibits antihypertensive action mainly by reducing peripheral vascular resistance caused by inhibiting its potent vasoconstrictive action.
Amlodipine as Besylate: It selectively binds to voltage-gated calcium channels in cell membranes, reduces Ca 2+ influx into cells, and relaxes coronary and peripheral smooth muscle. It has been recognized that its calcium antagonistic action develops slowly and exhibits longevity, and its cardiodepressive action is weak and exhibits vascular selectivity.

Pharmacodynamic effects
The medication works by blocking angiotensin II receptor and affecting calcilum channel of smooth muscle of blood vessels. By this, Myazil plus tablets reduce resistance of peripheral blood vessel.

Pharmacokinetic properties
A single oral dose of 20 mg/5 mg combination tablet of azilsartan/amlodipine as Besylate or 20 mg of azilsartan and 5 mg of amlodipine as Besylate (combination of amlodipine as Besylate) was orally administered to healthy adults (n = 26) under fasting conditions. Concentration trends and pharmacokinetic parameters are shown below, and bioequivalence was confirmed .Plasma concentration change.

Absorption: When a single 20mg/5mg combination tablet of azilsartan/amlodipine as Besylate was orally administered to healthy adults (12 subjects) under fasting conditions or after breakfast, there was no food effect on the Cmax and AUC of azilsartan and amlodipine as Besylate 6).

Metabolism: Azilsartan is metabolized to metabolite MI by decarboxylation and to metabolite M-II by CYP2C9. The AT1 receptor inhibitory activity of MI and M-II was about 1/1,000 of that of the unchanged drug (in vitro) 7) 8) . Azilsartan did not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4, and did not induce CYP3A (in vitro) 7). Amlodipine as Besylate, a calcium channel blocker, is mainly metabolized by CYP3A4.

Excretion: When a single 20mg/5mg combination tablet of azilsartan/amlodipine Besylate was orally administered to healthy adults (12 subjects) under fasting conditions, the cumulative urinary excretion rate up to 120 hours after administration was 16.6% for azilsartan and 6.6% for amlodipine as Besylate) .

Incompatibilities: Not applicable
Shelf life: 2 years
- Store away from direct sunlight, heat and moisture.
- Discard the remainder

Nature and contents of container and special equipment for use/administration or Implantation:
The container closure system Alu-Alu blisters of pack sizes 10's, 20's, 30's and 100's in a secondary unit carton.

Special precautions for disposal:
No special requirements

Registration/marketing authorization holder:
Kaizen Pharmaceuticals (Pvt) Ltd.,
Date from which marketing is authorized:
N/A
Date of revision of the text:
Not applicable.

STORAGE CONDITIONS AND INSTRUCTIONS
- Store below 30˚C in a dry place, protect from light.
- To be dispensed on the prescription of a registered medical practitioner only.
- Keep out of the reach of children.

ہدایات:
- خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
- دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
- صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کریں۔
- بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.
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