Duactin®

Amlodipine (Besylate)

Pharmacological properties

Duactin® is a dihydropyridine, long acting calcium channel blocker, which selectively inhibits calcium ion influx across cell membrane, with greater effect on vascular smooth muscle cells than on cardiac muscle cells.

The mechanism of antihypertensive action is due to direct relaxant effect on the vascular smooth muscle. **Duactin®** may be used as monotherapy, or in combination with other antihypertensive drugs such as thiazide diuretics, alpha blockers, beta blockers and ACE inhibitors.

The precise mechanism by which **Duactin®** relieves angina has not been fully determined. **Duactin®** may be used alone as monotherapy or in combination with other anti-anginal drugs in patients with angina that is refractory to nitrates and /or adequate dose of beta blockers.

Indications

- Treatment of hypertension.
- Preventive treatment of stable angina and spontaneous angina (including prinzmetals angina).
- Treatment of patients with severe (NYHA class III –IV) chronic heart failure without clinical signs or symptoms suggestive of underlying ischemic disease.

Dosage and administration

Usual adult dose: The initial dose is 5 mg **Duactin®** once daily which may be increased to 10mg depending on individual patients response. **Duactin®** may be taken before or after meals & no need to adjust the dose in patients with renal insufficiency. Amlodipine is not dialyzable.

Use in the elderly: Amlodipine, used at similar doses in elderly or younger patients, is equally well tolerated.
No dose adjustment of Amlodipine is required upon concomitant administration of thiazide diuretics, beta-blockers or angiotensin-converting enzyme inhibitors.

The maximum dose is 10mg.
Except in case of recent myocardial infraction, Amlodipine can be administered whatever the degree of left ventricular heart failure.

Use in children: Use is not recommended due to lack of adequate clinical experiences.

Pregnancy and lactation

Pregnancy
Animal studies did not show any teratogenic effects. Without teratogenic effect in animal, malformations in humans are not expected. To date, any substances responsible for malformations in humans have effectively been found to be teratogenic in animals in properly conducted studies on both species.
Presently, there is no relevant or enough data to assess an eventual malformation or foetotoxic effect of amlodipine when administered during pregnancy.
Consequently, as a precaution measure, it is preferable not to use amlopdipine during pregnancy.

Lactation
There is no data regarding the excretion of amlodipine in breast milk. However, as with other dihydropyridines, the quantities found in breast mild are low, and no undesirable effects were notified on the basis of isolated cases.
As a precaution measure, it is advisable to avoid if possible, the administration of this medicine to the breast-feeding woman.

Side effects

As with other calcium channel blockers, the most encountered side effects are: headache, redness or feeling of heat of the face, facial and/or ankle edema.
There have been rare reports of:
- Cardiac effects: tachycardia, palpitations, syncope.
- Cutaneomucous effects: alopecia, increased sweating, allergic reaction including pruritus, rash and angioedema. As with other dihydropyridines, slight gingival enlargement has been reported in patients with marked gingivitis/parodontitis. Such enlargement can be avoided or disappear by careful oral hygiene.
- Digestive effects: abdominal pain, dysgueusia, appetite loss, nausea, diarrhea, constipation, dry mouth.
- Neuromuscular effects: muscular cramps, myalgia, arthralgia.
- Liver effects: Hepatitis, jaundice and hepatic enzyme elevations have been reported very rarely (mostly consistent with cholestasis) with a few cases severe enough to require hospitalization. They are recovered at the treatment withdrawal.
- Lungs effects: dyspnea.
- Genito-urinary effects: pollakiuria, impotence as reported with other anti-hypertensive drugs, gynecomastia.
- Neuropsychic effects: asthenia, giddiness, sleeping disorders, paresthesia, trembling, visual disturbances, depressive disorders.
- General effect: malaise.
- Hematopoietic effect: thrombocytopenia.
- Vascular effect: vasculitis.
- As with other calcium-channel blockers, the following events have been rarely reported: anginal pain, myocardial infarction, arrhythmia. They can be linked to the pathology pre-existent to the treatment and must lead to discuss the continuation of the treatment.

Special warnings:

When clinical signs (asthenia, anorexia, persistant nausea), it is recommended to perform liver enzymes assays if increased and especially in case of jaundice, the treatment must be stopped.

Precautions

- Use in patients with impaired hepatic function:

Amlodipine half-life is prolonged in patients with impaired liver function.
Dosage recommendations have not been established, so amlodipine should be administered with caution in these patients.

Drug interactions

Unadvisable combination (care measure):

- **Dantrolene (infusion):** in animals, cases of fatal ventricular fibrillations are consistently observed when verapamil and dantrolene are administered by IV route. Thus, the combination of a calcium-channel blocker with dantrolene is potentially dangerous. However, a few patients have received the combination nifedipine and dantrolene without any trouble.

Combination needing precaution:

- **Alpha-1 blockers** (alfuzosin, prazosin): increase in the hypotensive effect. Risk of severe orthostatic hypotension. Clinical monitoring. Research of any orthostatic hypotension in the hours following the alpha-1 blocker drug administration (particularly at the beginning of the treatment).
- **Baclofene:** increase in the anti-hypertensive effect. Monitoring of the arterial pressure and posological adaptation of the anti-hypertensive drug if necessary.
- **Rifampicine:** described for verapamil, diltiazem and nifedipin. Decrease of the plasma levels of the calcium channel blocker due to an increase of its hepatic metabolism. Clinical monitoring and, eventually adjustment of the dose of the calcium channel blocker during the treatment with rifampicine and after its withdrawal.
- **Itraconazole:** extrapolated from nifedipine, felodipine and isradipine. Increased risk of oedema due to a decrease of the dihydropyridine hepatic metabolism. Clinical monitoring and, eventually adjustment of the dose of the dihydropyridine the treatment with itraconazole and after its withdrawal.

Combination to be taken into account:

- **Beta-blockers:** hypotension, heart failure in patients with latent or un-controlled heart failure (in vitro negative inotropic effect of the dihydropyridines, more or less marked depending on the products and susceptible to add to the negative inotropic effects of beta-blockers). The presence of a beta-blocker treatment can moreover minimise the reflex sympathic reaction set into action in case of excessive hemodynamic repercussion.
- **Imipramine antidepressants** (tricyclics): antihypertensive effect and risk of orthostatic hypotension increased (additive effect).
- **Corticosteroid, tetracosactid** (orally): decrease in the antihypertensive effect (hydrosodic retention of the corticosteroids).
- **Neuroleptics:** antihypertensive effect and risk of orthostatic hypotension increased (additive effect).

Furthermore, amlodipine does not modify the plasma levels or the renal clearance of digoxine in the healthy volunteers.

Effects on ability to drive and use machines:

At the beginning of the treatment, a special caution will have to be observed by drives or machines users, due to the risk of giddiness.

Contraindications

Patients with a known sensitivity to dihydropyridines.
This medicine is generally unadvised in case of combination with dantrolene.

Overdosage

Massive overdose could cause notable peripheral vasodilation leading to marked and probably prolonged systemic hypotension. Any hypotension following acute poisoning requires monitoring in a cardiology intensive unit. A vasoconstrictor could be used to restore vascular tone and blood pressure. Amlodipine is not dialyzable.

Presentation

Duactin® 5mg capsule: Amlodipine (besylate) 5mg/capsules. (available in different pack sizes).

(This is a medicament - keep medicaments out of reach of children)

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's proscription, method for use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

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