Dialon

Oral Antidiabetic Agent
Film-Coated Tablets

Composition

Each tablet contains:

Active ingredient: Metformin HCl 500mg, 850mg, or 1000mg.

Excipients:

Dialon 500mg: Microcrystalline cellulose, povidone, polysorbate 80, magnesium stearate, hypromellose, talc, titanium dioxide, and polyethylene glycol.

Dialon 850mg or 1000mg: Microcrystalline cellulose, povidone, starch, magnesium stearate, hypromellose, talc, titanium dioxide, and polyethylene glycol.

Properties

Metformin HCl, the active ingredient of **Dialon**, is a biguanide antidiabetic agent. The mode of action of metformin is not clear. It does not stimulate pancreatic beta cells to increase secretion of insulin but requires some insulin to be present in order to exert its hypoglycaemic effect. Possible mechanisms of action include delay in the absorption of glucose from the gastrointestinal tract, an increase in insulin sensitivity at receptor and postreceptor binding sites and an increase in glucose uptake into cells, and inhibition of hepatic gluconeogenesis. Insulin concentrations remain unchanged or are slightly reduced as glucose metabolism improves.

At therapeutic doses, metformin does not cause hypoglycaemia in diabetic or non-diabetic individuals. In addition, it is not associated with weight gain; therefore, it is considered useful in obese patients who gain weight on sulphonylureas despite adequate dietary modification.

Metformin HCl is slowly and incompletely absorbed from the gastrointestinal tract; the absolute bioavailability of a single 500mg dose is reported to be about 50 - 60%, although this is reduced somewhat if taken with food. Following absorption, plasma protein binding is negligible, and it is not metabolised. It is excreted unchanged in the urine. The plasma elimination half-life is reported to range from about 2 - 6 hours after oral administration.

Indications

Dialon is indicated in patients with type II diabetes mellitus. It is considered the drug of first choice in obese patients in whom strict dieting has failed to control diabetes.

Dialon is also used when type II diabetes is inadequately controlled with sulphonylurea treatment.

Dosage

Dialon tablets should be taken with or immediately after food to reduce gastrointestinal symptoms.

Patients 17 years of age and older

As monotherapy -

Initial dose: 500mg twice daily to be taken with morning and evening meals, or 850mg once daily to be taken with morning meal. The daily dosage should be increased gradually by 500mg at weekly intervals, or 850mg every 2 weeks, up to a total of 2000mg daily, given in divided doses. Patients can also be titrated from 500mg twice daily to 850mg twice daily after 2 weeks.

For those who require additional glycemic control, **Dialon** may be given to a maximum of 2550mg daily.

Maintenance dose: 500mg-850mg 2-3 times daily, to be taken with meals.

Maximum dose: **Dialon** may be given to a maximum daily dose of 2000mg-2550mg. Doses above 2000mg may be better tolerated if given 3 times daily with meals.

In combination with other antidiabetic agents -

When the combination of strict diet and **Dialon** treatment fails, a combination therapy may be considered including:

- Repaglinide or nateglinide may be given with **Dialon** if **Dialon** alone does not control the diabetes adequately.
- Combination with a sulfonylurea; if patients have not responded to 4 weeks of the maximum dose of **Dialon** monotherapy, an oral sulfonylurea should be added gradually while continuing **Dialon** at the maximum dose. The dose must be adjusted until the desired degree of glycaemic control is achieved.
- Combination with either pioglitazone or rosiglitazne, thiazolidinedione compounds, is recommended for patients who are unable to tolerate a combination of **Dialon** with a sulfonylurea, or for those who cannot achieve the desired degree of glycaemic control with such a combination. The combination of a thiazolidinedione plus **Dialon** is preferred to a thiazolidinedione plus sulfonylurea, particularly for obese patients.
- Combination with acarbose, which may have a small beneficial effect, but flatulence can be a problem.

In combination with insulin -

The current insulin dose should be continued upon initiation of **Dialon** therapy.

Initially, 500mg of **Dialon** a day. The dosage may be increased by 500mg at weekly intervals, as needed, until adequate glycaemic control is achieved. The maxmium recommended dose should not exceed 2500mg daily.

It is recommended to decrease the insulin dose by 10 - 25% when the fasting plasma glucose concentration decreases to less than 120mg/dl.

Patients 10-16 years of age

Initially, 500mg twice daily to be taken with morning and evening meals; then the daily dosage should be increased gradually by 500mg at weekly intervals, up to a maximum of 2000mg daily, given in divided doses.

If you miss a dose

- Take the missed dose as soon as possible.
- Do not take the missed dose if it is almost time for your next scheduled dose.
- Do not take two doses at the same time.

Contraindications

It should not be used in any individual having hypersensitivity reaction to metformin or to any other component in the preparation.

Metformin should be avoided in pregnant women where insulin is normally substituted (see Precautions). It is also contraindicated in lactating women, as it is found to be distributed in the breast milk.

Patients who will undergo a major surgery, that requires the use of general anaesthesia, must suspend metformin temporarily then restart it again when renal function returns to normal.

Patients suffering from congestive heart failure requiring pharmacologic treatment should not administer metformin.

Metformin is contraindicated in acute or chronic metabolic acidosis including diabetic ketoacidosis.

Metformin may provoke lactic acidosis, which is a rare but a serious metabolic complication; therefore, it should be avoided (or discontinued) in any condition that may predispose to lactic acidosis, including:

- renal impairment (even if mild or suspected)
- severe dehydration
- alcohol dependency
- tissue hypoxia which is likely to occur in patients suffering from sepsis, respiratory failure, recent myocardial infarction, or hepatic impairment. In such cases, metformin must be withdrawn.
- the use of iodine containing x-ray contrast media, as it may result in acute alteration of renal function; therefore do not restart metformin until renal function returns to normal.

Precautions

During metformin therapy, regular physical examinations are required, as often as necessary, to reassess the appropriateness of continuation of the treatment.

Blood glucose should be routinely self-monitored by the patient at home (several times a day or once to several times a week) or by the physician to confirm that blood glucose concentration is maintained.

Hypoglycaemia does not usually occur with the use of metformin unless predisposing conditions or factors are present, such as unusual fasting, concurrent use of other antidiabetic agents, or toxic doses of metformin.

Weight gain and hypoglycaemia can be a problem with the combination of metformin with insulin.

Although lactic acidosis is rarely occuring, renal function assessment is required specially in patients with higher risk of developing lactic acidosis. Therefore, serum creatinine should be measured before initiating treatment, and once or twice annually during treatment.

In any case, patients must be taught how to recognize the warning symptoms of lactic acidosis, such as diarrhoea, fast and shallow breathing, severe muscle pain or cramping, unusual sleepiness, and unusual tiredness and weakness.

Insulin therapy should be instituted temporarily during pregnancy, intercurrent illnesses (such as myocardial infarction, coma, infection, and trauma), and during surgery since the control of diabetes with oral antidiabetic agents is often inadequate in such circumstances. Insulin should also be substituted before elective surgery; omit metformin dose on the morning of surgery and give insulin if required.

Until now, safety and efficacy have not been established neither for the use of metformin in children below 10 years of age, nor for the use of it in combination with insulin or with other antidiabetic agents in children 10-16 years of age.

Generally, some elderly, debilitated, and malnourished patients may require lower initial doses, as well as, it is not advised to use the maximum doses for them.

Side Effects

Gastrointestinal adverse effects such as nausea, vomiting, transient diarrhoea, and abdominal pain are initially common with metformin, and may persist in some patients, especially when very high doses are given.

Few patients may experience anorexia and metallic taste on the start of the treatment with metformin.

Rarely, metformin may give rise to lactic acidosis which is most likely to occur in patients with renal impairment; treatment should be withdrawn (See, Contraindications).

Metformin interferes with the absorption of vitamin B_{12} absorption by competitive inhibition of calcium-dependent binding of the intrinsic factor-vitamin B_{12} complex to its receptor.

Overdosage

Hypoglycaemia has not been seen with metformin doses of up to 85g, although lactic acidosis has occurred in such circumstances.

High overdose of metformin may lead to lactic acidosis, which is a a medical emergency and must be treated in hospital. Haemodialysis is the most effective method to remove lactate and metformin.

Drug Interactions

As with other antidiabetic agents, the hypoglycaemic effect of metformin may possibly be enhanced upon concomitant administration with alcohol (risk of lactic acidosis - See, Contraindications), ACE inhibitors, MAOIs, beta-blockers (which also mask the warning signs of hypoglycaemia such as tremor), anabolic steroids, and testosterone.

On the other hand, the hypoglycaemic effect of metformin, as with other antidiabetic agents, may be antagonised by the concomitant administration with diazoxide, corticosteroids, loop and thiazide diuretics, and oral contraceptives (oestrogens and progestogens).

As with other antidiabetic agents, glucose tolerance may occasionally be impaired upon concurrent administration of metformin with nifedipine or lithium, whereas its concurrent use with fibrates may improve glucose tolerance and have an additive effect.

Concurrent administration of metformin with ketotifen has been reported to depress thrombocyte count.

Upon concurrent administration, cimetidine inhibits renal excretion of metformin resulting in an increased plasma-metformin concentrations. A reduction in metformin dosage may be required in order to reduce the risk of lactic acidosis.

Concurrent administration of oral antidiabetic agent with hormone antagonists may possibly result in:

- acceleration in metabolism of oral antidiabetic agents by aminoglutethimide.
- reduction in requirement for antidiabetic agents by octreotide.

Presentation

Dialon 500mg tablets: Pack of 48 or 480 tablets.

Dialon 850mg or 1000mg tablets: Pack of 30 tablets.

* *Store at a temperature of 15 - 25°C, in a dry place.*

THIS IS A MEDICAMENT

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicines, their 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.
- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.

***Any Information ? Call Toll Free No.* (971) 800-4994**

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