United Pharmaceuticals

DIAPHAGE®

Metformin Hydrochloride

Description:

DIAPHAGE® (Metformin Hydrochloride) is an oral biguanide anti-hyperglycemic agent. It improves glucose tolerance without producing hypoglycemia by decreasing hepatic glucose production and intestinal absorption as well as increasing peripheral glucose uptake.

Properties:

Metformin is absorbed from the gastrointestinal tract. The absolute bioavailability of 500 mg Metformin given under fasting conditions ranges between 50% to 60%. The maximum plasma concentration is attained at about 2-3 hours, and the average steady state concentration ranges from 1 to 2 mcg/ml at the usual dosing rate. The apparent volume of distribution following oral administration averaged 654±358L. Metformin is negligibly bound to plasma proteins. It is excreted unchanged in the urine and does not undergo hepatic metabolism nor biliary excretion. Following oral administration of Metformin, about 90% of the absorbed drug is eliminated via the renal route within the first 24 hours, with a plasma elimination half-life of about 6.2 hours.

Indications:

As an adjunct to adequate diet and exercise, **DIAPHAGE®** is intended for the treatment of type 2 diabetes.

In adults, **DIAPHAGE®** may be given alone or with oral anti-diabetic agents, or with Insulin. In children from 10 years old and adolescents, **DIAPHAGE®** may be given alone or with Insulin.

A reduction of diabetic complications has been shown in overweight type 2 diabetic adult patients treated with Metformin as first-line therapy after diet therapy.

Dosage and administration:

- The dosage of **DIAPHAGE®** is determined by the doctor on an individual basis according to the results of laboratory blood glucose measurement.
- Swallow **DIAPHAGE®** tablets without chewing during or at the end of meals. For example, for a dosage of two tablets daily, take one tablet with breakfast and one tablet with the evening meal.
- In all cases, patient should strictly comply with the doctor's prescription.
- In case of decreased renal function, the dosage should be adjusted based on renal function.

The initial dosage is usually one tablet of **DIAPHAGE®** 500 mg or one tablet of **DIAPHAGE®** 850 mg once daily in children from 10 years old and adolescents and one tablet of **DIAPHAGE®** 500 mg or one tablet of **DIAPHAGE®** 850 mg; 2 or 3 times daily in adults. The maximum recommended dose is 2 g daily in children and 3 g daily in adults (taken as 2 or 3 divided doses).

It is possible to replace two **DIAPHAGE®** 500 mg tablets with one **DIAPHAGE®** 1 gm tablet.

Duration of treatment: **DIAPHAGE®** must be taken daily without interruption. In case you stop the treatment, consult your doctor.

If you have forgotten to take a **DIAPHAGE®** tablet, take the next dose at the usual time. Do not double the dose of **DIAPHAGE®** tablets.

Contraindications:

- Known hypersensitivity to Metformin Hydrochloride or any of the product ingredients.
- Severe destabilization of diabetes (ketoacidosis or pre-coma).
- Renal insufficiency, even if moderate (impairment of kidney function with increased blood creatinine levels or decreased creatinine clearance < 60 ml/min).
- Infectious diseases (for example respiratory tract infection, urinary tract infection).
- Following an X-ray examination involving the use of Iodinated contrast media (for example intravenous urography, angiography).
- Disease that may cause tissue hypoxia (heart failure, recent myocardial infarction, respiratory insufficiency, shock).
- Hepatic insufficiency (impaired liver function).
- Persistent or severe diarrhea, recurrent vomiting.
- Excessive consumption of Alcoholic beverages.
- During breast-feeding.

Precautions:

- Vomiting, abdominal pain with muscle cramps and/or a general feeling of malaise with severe fatigue occurring during therapy may be signs of serious destabilization of the diabetes (diabetic ketoacidosis or lactic acidosis) requiring specific treatment. If this occurs, patient should stop taking Metformin immediately and consult the doctor promptly. Lactic acidosis is a medical emergency and must be treated in a hospital. The most effective way to remove lactate and Metformin from the blood is hemodialysis.
- The doctor will prescribe periodic laboratory tests to determine the blood glucose and will check the kidney function (creatinine levels or creatinine clearance) before treatment initiation and regularly thereafter since Metformin is excreted mainly by the kidneys. Special caution should be exercised in situations where kidney function may become impaired, for example in the elderly or when initiating antihypertensive treatment or diuretic treatment and when starting treatment with a non-steroid anti-inflammatory.
- Certain illnesses or medications such as corticosteroids, diuretics, β2 agonists (e.g. Salbutamol, Terbutaline) and angiotensin-converting enzyme inhibitors may cause more or less severe destabilization of diabetes. The patient should inform the doctor of any other treatment you are receiving and of any infectious illnesses such as influenza, respiratory tract infection or urinary tract infection.
- If patients are scheduled to undergo X-ray examinations involving the use of Iodinated contrast media, such as intravenous urography or angiography, the doctor will ask patient to discontinue treatment with Metformin prior to or at the time of the test and will not resume treatment until 48 hours after the test and after ensuring that the kidneys are functioning normally. If patients are hospitalized for tests, a surgical procedure, or for any other reason, inform the doctor that about taking Metformin. Avoid consumption of alcoholic beverages.
- In children, a follow-up of the Metformin effect on growth and puberty especially in pre-pubescent children is recommended.
- Effect on ability to drive and use machines: When used alone, Metformin does not cause hypoglycemia. Consequently, there is no particular risk when driving or using machines. However, in association with other anti-diabetic agents (Sulphonylurea, Insulin, Glinides or other hypoglycemic agents), it is important to be aware of the onset of hypoglycemia, and of its effects on concentration.

Use during pregnancy and lactation:

Pregnancy: During pregnancy, treatment of diabetes is based on Insulin therapy. If you discover that you are pregnant while taking Metformin, the treatment will be replaced by Insulin. Inform the doctor so that she/he may make the necessary changes to the treatment and inform the doctor if you wish to become pregnant.

Lactation: Metformin is contraindicated during breast-feeding. As a general rule, if you are pregnant or breast-feeding you should always ask your doctor for advice before taking a medication.

Drug interactions:

Inform the doctor or the pharmacist if you are taking or have recently taken another drug, e.g. corticosteroids, non-steroid anti-inflammatories, antihypertensive agents of the angiotensin-converting enzyme inhibitors, class1 diuretics, β2 agonists (e.g. Salbutamol, Terbutaline), Iodinated contrast media or medications containing Alcohol, even if an over-the-counter medication is involved.

Side effects:

As with all medications, Metformin can cause side effects.

The following side effects were observed in clinical studies or in routine patient management.

Very common: Gastrointestinal discomfort such as nausea, vomiting, diarrhea, abdominal pain and loss of appetite may occur especially at the beginning of treatment. These symptoms are generally transient and can be reduced by taking the tablets with meals. If symptoms persist, stop taking the treatment and consult the doctor.

Common: Taste disturbance.

Very rare:

- Lactic acidosis is a very serious complication, which results in vomiting, abdominal pain with muscle cramps and /or a general feeling of malaise with severe fatigue and which requires specific treatment. If this occurs patient should stop taking Metformin immediately and consult the doctor promptly. Lactic acidosis is a medical emergency and must be treated in a hospital.
- Skin reactions such as erythema, itching or urticaria (eruption with itching).
- Decreased Vitamin B12 levels (to take into consideration if you are suffering from megaloblastic anemia).

Isolated cases: Liver function tests abnormalities or hepatitis resolving upon Metformin discontinuation.

Overdosage:

If you have taken more **DIAPHAGE®** tablets than indicated, consult your doctor or pharmacist immediately.

Storage conditions:

DIAPHAGE® 500: Store between 15 - 30ºC.
DIAPHAGE® 850: Store up to 30ºC.
DIAPHAGE® 1gm: Store up to 30ºC.

Presentation:

DIAPHAGE® 500: Each film coated tablet contains Metformin Hydrochloride 500 mg in packs of 50 tablets.
DIAPHAGE® 850: Each film coated tablet contains Metformin Hydrochloride 850 mg in packs of 30 tablets.
DIAPHAGE® 1gm: Each film coated tablet contains Metformin Hydrochloride 1g in packs of 30 tablets.
Hospital packs are also available.

Excipients:-

Diaphage® 500mg & 850mg Tablets: Microcrystalline Cellulose, Povidone, Croscarmellose sodium, Stearic Acid & Opadry Coat.
Diaphage® 1gm Tablets: Povidone 30, Magnesium Stearate & Opadry Coat.

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 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.
· Keep medicament out of the reach of children.

COUNCIL OF ARAB HEALTH MINISTERS
UNION OF ARAB PHARMACISTS

The United Pharmaceutical Manufacturing Co. Ltd.
P.O. Box 69 Amman 11591, Jordan

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