

Duotrol 500mg/5mg (Metformin Hydrochloride and Glibenclamide Film Coated Tablets)

Metformin hydrochloride/Glibenclamide (500 mg/5mg)

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What Duotrol is used for

Duotrol is made up of two antidiabetic medicines, which belong to the groups of medicines called biguanide (metformin hydrochloride) and sulphonylurea (glibenclamide).

Duotrol is taken orally for the treatment of type 2 diabetes mellitus in adult patients. It is used to replace the combination of the two active substances, metformin hydrochloride and glibenclamide given separately in patients previously treated with this combination.

How Duotrol works

Insulin is a hormone that enables body tissues to take up glucose (sugar) from the blood and to use it for producing energy or to store it for future use. Patients with type 2 diabetes mellitus (i.e., non-insulin dependent diabetes) do not produce enough insulin in their pancreas or their body does not respond properly to the insulin it produces. This causes an increased level of glucose in the blood. Duotrol helps to reduce their blood sugar towards a normal level.

Before you use Duotrol

- When you must not use it

Do not take Duotrol

- If you are allergic (hypersensitive) to metformin hydrochloride, glibenclamide or other sulphonamides or any of the other ingredients of Duotrol

- if you have severely reduced kidney function.
- if you have lactic acidosis [too much lactic acid in the blood (see "Risk of lactic acidosis" below)] or ketoacidosis. Ketoacidosis is a condition in which substances called 'ketone bodies' accumulate in the blood and which can lead to diabetic pre-coma. Symptoms of acidosis may include stomach pain, abnormal breathing and drowsiness (if severe).
- if you have liver function problems
- if you have a severe infection (for example an infection of the air passages or an urinary tract infection)
- if you suffer from type 1 diabetes mellitus (i.e. insulin-dependent) or if you have severe loss of diabetes control with either pre-coma or ketosis (a condition caused by substances called 'ketone bodies' accumulating in the blood; you may notice that your breath has an unusual, fruity odour)
- if you are dehydrated (for example due to persistent or severe diarrhoea, recurrent vomiting)
- if you are treated for heart problems, have recently had a heart attack, have severe circulatory problems or breathing difficulties
- if you suffer from porphyria (a rare, hereditary disease due to an enzyme deficiency causing the body to produce and excrete too much porphyrin, a component used to make the part of blood pigment that carries oxygen)
- if you use miconazole (a medicine to treat certain yeast infections) even for local use
- if you drink alcohol excessively (either every day or only from time to time)
- if you are breast-feeding.

- Before you start to use it

Make sure you ask your doctor for advice,

- if you need to have an examination such as X-ray or scan involving the injection of contrast medicines that contain iodine into your bloodstream
- if you need to have a surgery under general, spinal or peridural anaesthesia
- if you must stop taking Duotrol for a certain period of time before and after the examination or the surgery. Your doctor will decide whether you need any other treatment for this time. It is important that you follow your doctor's instructions precisely.
- if you experience symptoms of low blood sugar (hypoglycaemia). The warning signs may occur suddenly and can include cold sweat, cold and pale skin, dizziness, headache, rapid heartbeat, feeling sick, feeling very hungry, temporary changes in vision, drowsiness, unusual tiredness and weakness, nervousness or tremor, feeling anxious, feeling confused, difficulty in concentrating. If you notice any of these signs:
 - first eat glucose tablets or a high sugar snack (honey, sweets, biscuits, fruit juice),
 - Stop taking this medicine immediately and tell your doctor straight away as you may need to be hospitalised to bring your blood glucose back under control,
 - then rest.

Take special care with Duotrol

Risk of lactic acidosis

Duotrol may cause a very rare, but very serious side effect called lactic acidosis, particularly if your kidneys are not working properly. The risk of developing lactic acidosis is also increased with uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration, liver problems and any medical conditions in which a part of the body has a reduced

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supply of oxygen (such as acute severe heart disease). If any of the above apply to you, talk to your doctor for further instructions.

Stop taking Duotrol for a short time if you have a condition that may be associated with dehydration (significant loss of body fluids) such as severe vomiting, diarrhoea, fever, exposure to heat or if you drink less fluid than normal. Talk to your doctor for further instructions.

Stop taking Duotrol and contact a doctor or the nearest hospital immediately if you experience some of the symptoms of lactic acidosis, as this condition may lead to coma.

Symptoms of lactic acidosis include:

- vomiting
- stomach ache (abdominal pain)
- muscle cramps
- a general feeling of not being well with severe tiredness
- difficulty in breathing

Lactic acidosis is a medical emergency and must be treated in a hospital.

During treatment with Duotrol, your doctor will check your kidney function at least once a year or more frequently if you are elderly and/or if you have worsening kidney function.

General advice: Inform your family, friends and colleagues to turn you on your side and get medical aid straight away if you become unconscious. They should not give you any food or drink when you are unconscious. It could choke you.

A low blood sugar level might occur if:

- you eat too little or miss a meal
- your diet contains insufficient or unbalanced levels of sugar
- you drink alcohol
- you exercise more than usual

- you have liver, kidney or certain hormone problems
- the dosage of your medicine is too high
- you are an elderly person
- you are taking certain medicines and Duotrol at the same time (see 'Taking other medicine').
- if you suffer from any infectious illnesses such as flu, infection of the air passages or urinary tract infection.
- if you have an inherited condition where your red blood cells don't produce enough of the enzyme G6PD (G6PD deficiency), taking Duotrol may cause your red blood cells to be destroyed too quickly (haemolytic anaemia).

- Taking other medicines

While taking Duotrol, you must not use any of the following medicines:

- miconazole even for local use (see 'When you must not take it')
- iodinated contrast agents (see 'When you must not take it')

Special precautions may be required if you take Duotrol and any of the following medicines at the same time:

- angiotensin-converting enzyme inhibitors (used to treat a variety of cardiovascular conditions, such as high blood pressure, and some other diseases)
- diuretics (used to remove water from the body by increasing urine production)
- beta-blockers (used to treat a variety of cardiovascular conditions, such as high blood pressure, and some other diseases)
- beta-2 agonists (used to treat asthma, such as ritodrine, salbutamol or terbutaline)
- bosentan (used to high blood pressure in the lungs)
- corticosteroids and tetracosactide (a class of hormones used to treat a variety of conditions, e.g. severe inflammation of the skin or in asthma)

- certain painkillers (i.e. nonsteroidal anti-inflammatory drugs, such as phenylbutazone)
- fluconazole (used to treat certain yeast infections)
- chlorpromazine (a neuroleptic medicine, which affects how your brain works)
- desmopressin (generally used to reduce urine production)
- danazol (used to treat endometriosis, a condition where the tissue lining of the uterus is found outside the uterus)

Special precautions may include self-monitoring of blood glucose, blood tests and modification of dosage.

Avoid medicines containing alcohol.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

How to use Duotrol

- How much to use

Always take Duotrol exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Only adults may take this medicine. Your doctor will adapt the dosage of your treatment depending on its effect on your blood tests. Continue to follow any dietary advice your doctor has given you. Duotrol cannot replace the benefits of a healthy lifestyle.

Have a regular meal schedule with a sufficient and balanced sugar intake.

This will decrease the risk of low blood sugar. The usual starting dose is equivalent to the individual doses of metformin hydrochloride and glibenclamide you received before being treated with Duotrol.

Maximum daily dose:
2000 mg metformin/20 mg
glibenclamide

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Dosage adjustment in elderly patients: Take special care if you are an elderly person. The dose of Duotrol will be carefully increased depending on your blood sugar levels and your kidney function. Make sure that you consult your doctor regularly.

- When to use it

Take the tablets with a meal. Swallow each tablet whole with a glass of water. Do not crush or chew them before swallowing.

Take the tablets

- once a day, in the morning (breakfast) if you take 1 tablet per day
- twice a day, in the morning (breakfast) and evening (dinner) if you take 2 per day
- three times a day, in the morning (breakfast), noon (lunch) and evening (dinner), if you take 3 tablets per day.

- How long to use it

Continue taking your medicine for as long as your doctor or pharmacist tells you. It does not cure your condition. Therefore you must continue to take it as directed by your doctor if you expect to keep your glucose levels controlled.

- If you forget to use it

Do not take a double dose to make up for a forgotten dose. Take the next dose at the usual time.

- If you use too much (overdose)

If you have taken more Duotrol tablets than you should have, you may experience lactic acidosis or low blood sugar. Inform your doctor immediately

While you are using Duotrol

- Things you must do

Tell your doctor if you are, you think you might be or are planning to become pregnant. During pregnancy, diabetes should be treated with insulin. If you find out that you are pregnant while taking Duotrol, consult your doctor so that he/she may change your treatment.

- Things you must not do

Avoid alcohol when you take this medicine as alcohol can increase certain side-effects such as lactic acidosis and a low blood sugar level (see 'side-effects'). This also applies to medicines containing alcohol.

Breast-feeding:

You must not take Duotrol, if you are breast-feeding or if you are planning to breast-feed your baby.

- Things to be careful of

Do not drive or use machines:

- if your vision is blurred. This may happen at the beginning of the treatment because of a lower level of sugar in your blood.
- if you feel that symptoms of low blood sugar begin to appear.

Side effects

Like all medicines, *Duotrol* can cause side effects, although not everybody gets them.

Visit your doctor or pharmacist immediately if you experience any side effects after taking this medicine.

Vision disorders: When you start taking this medicine, it may disturb your vision due to a lower level of sugar in your blood. However, this reaction usually disappears after a while.

Low blood sugar: For symptoms of low blood sugar, see 'Take special care with Duotrol'.

Very common side effects (in more than 1 in 10 patients)

- gastrointestinal disorders such as nausea, vomiting, diarrhoea, bellyache and loss of appetite.
- Decreased or low vitamin B12 levels in the blood (symptoms may include extreme tiredness (fatigue), a sore and red tongue (glossitis),

pins and needles (paraesthesia) or pale or yellow skin). Your doctor may arrange some tests to find out the cause of your symptoms because some of these may also be caused by diabetes or due to other unrelated health problems.

These side effects occur most frequently after starting therapy. It helps if you spread the doses over the day and if you take the tablets with a meal. Should these symptoms continue, stop taking this medicine and consult your doctor.

Common side effects (in less than 1 in 10, but more than 1 in 100 patients)

- taste disturbance

Uncommon side effects (in less than 1 in 100, but more than 1 in 1,000 patients)

- abnormal urea and creatinine levels in the blood, which show changes in the way the kidneys are working.
- a crisis of certain forms of porphyria (porphyria hepatica or porphyria cutanea) may occur in patients with certain enzyme deficiency.

Rare side effects (in less than 1 in 1,000, but more than 1 in 10,000 patients)

- reduction in the number of white blood cells, which makes infections more likely
- reduction in blood platelets which increases risk of bleeding or bruising
- skin reactions including itching, skin rash

Very rare side effects (in less than 1 in 10,000 patients)

- lactic acidosis: "see 'Take special care with Duotrol'"
- severe reduction in the number of white blood cells (agranulocytosis), anaemia due to a too extensive breakdown of the red blood cells (haemolytic anaemia), lack or insufficient number of new bloods

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cells produced by the bone marrow (bone marrow aplasia) and very severe reduction in the number of blood cells (pancytopenia; this can make the skin look pale, can cause weakness or breathlessness, can increase the risk of bleeding or bruising or make infections more likely)

- abnormalities in liver function tests or inflammation of the liver (hepatitis; this can cause tiredness, loss of appetite, weight loss, with or without yellowing of the skin or whites of the eyes). If this happens to you, stop taking Duotrol and talk to your doctor.
- excessive skin sensitivity to sun, serious allergic reactions of the skin or blood vessels
- intolerance to alcohol (with symptoms such as general feeling of discomfort, redness of face, rapid heartbeat)
- low level of sodium, which can cause tiredness and confusion, muscle twitching, fits or coma

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npa.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)]

Storage and Disposal of Duotrol

- Storage

Store below 30°C. Protect from light and moisture.

Keep all medicines out of reach of children.

- Disposal

Medicines should not be disposed of via wastewater or household waste. Ask

your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product Description

- What it looks like

Yellow, capsule shaped, biconvex, film coated tablets with 'U 24' debossed on one side and plain on the other side.

- Ingredients

- Active ingredient(s)
Metformin hydrochloride
Glibenclamide

- Inactive ingredients
Sodium Starch Glycolate (Type A), Povidone (Kollidon 30), Silica, Colloidal Anhydrous, Magnesium Stearate, Purified Water, Opadry 04G520007 yellow

Composition of Opadry 04G520007 yellow:

- HPMC 2910/Hypromellose (46.23%w/w)
- Talc (27.740%w/w)
- Titanium Dioxide (13.350%w/w)
- Propylene Glycol (3.59%w/w)
- Macrogol/PEG (3.590%w/w)
- Quinoline Yellow Aluminum Lake (2.800%w/w)
- Iron Oxide Yellow (2.700%w/w)

- MAL number:

MAL*****

Manufacturer

USV Private Limited
H-13,16,16A,17,18,19,20,21,E-22,
OIDC, Mahatma Gandhi Udyog Nagar,
Dabhel, Daman – 396210, India.

Product Registration Holder

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