PACKAGE LEAFLET: INFORMATION FOR THE USER

Siofor® 500

500 mg, film-coated tablet
Active substance: metformin hydrochloride

For use in children above 10 years and adults

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

1. WHAT SIOFOR® 500 IS AND WHAT IS IT USED FOR

Siofor® 500 belongs to a group of medicines for treating non-insulin-dependent diabetes (type 2 diabetes mellitus) in adults and in children above 10 years of age.

Siofor® 500 is a medicine for lowering too-high blood glucose levels in patients with diabetes (diabetes mellitus type 2); particularly in overweight patients in whom adequate adjustment of blood glucose levels has not been achieved through diet and exercise alone.

Adults

The doctor can prescribe you Siofor® 500 alone (monotherapy) or in combination with other oral blood glucose-lowering medicines or insulin.

Children and adolescents

In children above 10 years and adolescents, the doctor can prescribe Siofor® 500 as monotherapy or in combination with insulin.

After the failure of dietary measures in overweight adult patients with diabetes (diabetes mellitus type 2), it has been possible to demonstrate a lowering of the frequency of diabetes-related complications under treatment with metformin as the therapy of first choice.

2. BEFORE YOU TAKE SIOFOR® 500

Do not take Siofor® 500 if you:
- are allergic (hypersensitive) to metformin hydrochloride or any of the other ingredients of Siofor® 500;
- suffer from over-acidification of the blood in diabetes (diabetic ketoacidosis) or threateningly high blood glucose values as the pre-stage of a diabetic coma;
- suffer from kidney failure or have impaired kidney function;
- currently (acutely) suffer from states that can lead to an impairment to kidney function, for example
  - fluid loss due to persistent vomiting or severe diarrhoea,
  - severe infections,
  - circulatory failure (shock);
- are due to have examinations conducted on you with the administration of iodine-containing contrast media into the blood vessels. Siofor® 500 is to be withdrawn 48 hours before, during and up to 48 hours after the examination;
- suffer from acute or chronic diseases that can lead to oxygen deficiency in the body tissues (tissue hypoxia), such as
  - heart failure or lung function disturbances,
  - recent heart attack,
  - circulatory failure (shock);
- have impaired liver function or acute alcohol poisoning or suffer from alcoholism;
- are breast-feeding.

Take special care with Siofor® 500:
- if you suffer from disturbances to liver function;
- inform your doctor if you contract a bacterial or viral infection (for example influenza, respiratory tract infection, urinary tract infection);
- in situations where there may be impairment to kidney function (e.g. at the beginning of a therapy with certain medicines for treating high blood pressure or a rheumatic disease).

The risk of an undesirable accumulation, and thus the risk of an over-acidification of the blood with lactic acid (lactic acidosis), are determined mainly by the kidney function, which is why verified normal kidney function is a precondition for a therapy with Siofor® 500.

The assessment of your kidney function, on the basis of determination of your serum creatinine levels, must therefore be repeated at intervals of at least once a year, possibly even earlier. If your serum creatinine value is on the upper limit of the norm range, have the check conducted at least two to four times a year. It must be noted that, particularly in elderly patients, the serum creatinine value alone is not always meaningful; it may then be necessary for another value to be determined for assessment of the kidney function, the creatinine clearance, before the beginning of therapy.

In examinations with administration of iodine-containing contrast media into the vessels, the risk of acute kidney failure exists. Your therapy with

Siofor® 500 must therefore be withdrawn two days before the examination is conducted, and may only be recommenced two days after the examination if a new examination has previously determined that kidney function is normal.

If you are scheduled to have an operation under general anaesthetic or spinal anaesthesia, treatment with Siofor® 500 must be interrupted two days beforehand and may also only be continued two days after the procedure if normal kidney function is present.

Children and adolescents:
The diagnosis of type 2 diabetes must be verified by the doctor before a treatment with Siofor® 500 is begun in children and adolescents.

During one-year controlled clinical trials, no influence on growth and puberty through metformin was observed, but there are no long-term results to date.

As only a few children of the age-group between 10 and 12 years were included in the clinical studies, particular caution should be exercised when children of this age-group are treated with Siofor® 500.

Elderly people
Due to the impaired kidney function common in elderly patients, the dosage of Siofor® 500 should be in line with the kidney function. For this reason, have measurements of kidney function values regularly conducted at the doctor's.

Special warnings
In the case of an undesirable accumulation, metformin can trigger or facilitate the occurrence of an over-acidification of the blood (lactic acidosis), a complication that – if not treated promptly – can assume life-threatening proportions (e.g. coma). Besides overdose, causes of an over-acidification with lactic acid can be ignoring the presence or occurrence of contra-indications. The contra-indications must therefore be strictly observed (see "Do not take Siofor® 500 if you:").
Signs of commencing over-acidification of the blood with lactic acid (lactic acidosis) can resemble the side effects of metformin on the gastro-intestinal tract: nausea, vomiting, diarrhoea and abdominal pains. The fully-blown picture with muscular pains and cramps, excessive increase in the breathing and clouding of consciousness with coma can develop within hours and requires immediate emergency treatment in a hospital.

Taking/using other medicines
Please inform your doctor or pharmacist if you are additionally taking/using other medicines or have taken/used them recently, even if they are non-prescription medicines. During a long-term medicinal therapy with Siofor® 500, both the commencement and the withdrawal of an additional medicinal therapy can interfere with the blood glucose adjustment.

Siofor® 500 is influenced as follows:

Increase in the effect up to increased side-effect risk

Certain medicines for treating high blood pressure (ACE inhibitors), as well as iodine-containing X-ray contrast media or alcohol-containing medicines.

Weakening of the effect

Cortisone-containing medicines (corticosteroids), certain medicines for treating bronchial asthma (ß-sympathomimetics), urine output-increasing medicines (diuretics).

Taking Siofor® 500 with food and drink

Continue your diet during therapy with Siofor® 500 and pay particular attention to an even distribution of carbohydrate intake over the day. If you are overweight, you should continue your reduction diet under the supervision of a doctor.

You should abstain from alcoholic drinks or foods during therapy with Siofor® 500, as the administration of large quantities of alcohol represents a risk for low blood glucose (hypoglycaemia) and a severe side effect of Siofor® 500 (lactic acidosis) occurring.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy

Patients with diabetes who are, or wish to become, pregnant, should not be treated with Siofor® 500. In these cases, blood glucose levels should be adjusted to normal values with insulin. Inform your doctor accordingly, so that they can transfer treatment to insulin.

Breast-feeding

You must not take this medicine during the breast-feeding period.

Driving and using machines

A therapy with Siofor® 500 alone does not lead to low blood glucose (hypoglycaemia) and therefore has no effects on the ability to drive or the ability to operate machines.

On combination treatment with other medicines with a blood glucose-lowering effect (e. g. sulphonylureas, insulin) your ability to drive and the operation of machines or working without a secure foothold may be impaired by possible low blood glucose.

3. HOW TO TAKE SIOFOR® 500

Always take Siofor® 500 exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The dosage of Siofor® 500 must be established by the doctor specially for each patient on the basis of the blood glucose values and be monitored by regular checks by the doctor.

Film-coated tablets with an active-substance content of 850 mg and divisible film-coated tablets with an active-substance content of 1000 mg metformin hydrochloride are also available for individual adjustment to the required maintenance dose.

The usual dose is:

Adults

Age	Single dose	Total daily dose
Adults	1 film-coated tablet (equivalent to 500 mg metformin hydrochloride)	2 - 3 film-coated tablets (equivalent to 1000 - 1500 mg metformin hydrochloride); maximum of 6 film-coated tablets (equivalent to 3000 mg metformin hydrochloride)

Children above 10 years and adolescents

Single (monotherapy) or combination therapy with insulin

Age	Single dose	Total daily dose
Children above 10 years and adolescents	1 film-coated tablet (equivalent to 500 mg metformin hydrochloride)	Initially one film-coated tablet; the dose can be increased to a maximum of 4 film-coated tablets (equivalent to 2000 mg metformin hydrochloride)

Swallow the film-coated tablets whole with or after meals with sufficient liquid (preferably with a glass of drinking water [200 ml]).

When taking two or more film-coated tablets, they must be taken distributed over the day, for example one film-coated tablet each after breakfast and dinner.

Please speak to your doctor if you have the impression that the effect of Siofor® 500 is too strong or too weak.

If you take more Siofor® 500 than you should
Notify your doctor at once if you have taken a greater quantity of Siofor® 500 than you should have.

An overdose with Siofor® 500 does not lead to low blood glucose (hypoglycaemia) but entails the risk of over-acidification of the blood with lactic acid (lactic acidosis).

Signs of commencing over-acidification of the blood with lactic acid can resemble the direct side effects of metformin on the gastro-intestinal tract: nausea, vomiting, diarrhoea and abdominal pains. The fully-blown picture with muscular pains and cramps, deep, fast breathing, as well as clouding of consciousness and coma, can develop within hours and requires immediate emergency admission to a hospital.

If you forget to take Siofor® 500:
If you have forgotten to take Siofor® 500, take the prescribed quantity of Siofor® 500 at the next administration time and try to keep to the instructions in future. Do not under any circumstances attempt to make up for a missed administration by taking a correspondingly higher number of film-coated tablets in one go.

If you stop taking Siofor® 500
If you discontinue the treatment with Siofor® 500 without being instructed to do so by a doctor, you must anticipate that blood glucose levels will rise uncontrollably, and that the delayed complications of diabetes, such as eye, kidney and vessel damage, will occur in the long term.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Siofor® 500 can cause side effects, although not everybody gets them.

The following frequencies are taken as a basis for evaluation of side effects:

Very common:	*More than 1 in 10 treated patients*
Common:	*Fewer than 1 in 10 but more than 1 in 100 treated patients*
Uncommon:	*Fewer than 1 in 100 but more than 1 in 1000 treated patients*
Rare:	*Fewer than 1 in 1,000 but more than 1 in 10,000 treated patients*
Very rare:	*Fewer than 1 in 10,000 treated patients, not known (cannot be estimated from the available data)*

Important side effects or signs that you should pay attention to, and measures if you are affected:
If you are affected by one of the side effects stated below, do not take Siofor® 500 any longer and go to your doctor at once if possible.

- Very rare
  Metabolism and nutritional disorders
  Severe metabolic derangement in the sense of an over-acidification of the blood with lactic acid (lactic acidosis). Vomiting and abdominal pains that may be accompanied by muscular pains and cramps or severe general fatigue may be signs of this (see "Special warnings").

  Skin and subcutaneous tissue disorders
  Skin reactions such as erythema, pruritus and urticaria.

Hepatobiliary disorders
Liver function test abnormal or liver inflammation (hepatitis) that are reversible after withdrawal of Siofor® 500.

Other possible side effects

- Very common

Gastrointestinal disorders
Nausea, vomiting and diarrhoea, abdominal pains, loss of appetite. These usually occur at the beginning of therapy and disappear spontaneously in the majority of cases. In order to prevent these complaints, it is recommended that Siofor® 500 be taken with or after meals in the form of two or three single doses. If these complaints persist for a long period, withdraw Siofor® 500 and speak to your doctor.

- Common

Nervous system disorders

Taste changed.

- Very rare

Metabolism and nutrition disorders

A decrease of vitamin B12 absorption with decrease of serum levels has been observed in patients treated long-term with metformin. This should be considered as a possible cause in patients with megaloblastic anaemia.

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

5. HOW TO STORE SIOFOR® 500

Keep out of the reach and sight of children.

Do not use Siofor® 500 after the expiry date which is stated on the folding box and the blister after EXP.: The expiry date refers to the last day of that month.

6. FURTHER INFORMATION

What Siofor® 500 contains

Film-coated tablets

The active substance is metformin hydrochloride.

1 film-coated tablet contains 500 mg metformin hydrochloride.

The other ingredients are hypromellose, povidone K 25, magnesium stearate (Ph. Eur.), macrogol 6000, titanium dioxide (E 171).

What Siofor® 500 looks like and contents of the pack

White, round, biconvex film-coated tablet, packaged in PVC/aluminium or PVC/PVDC/aluminium blister.

Packages with 10 film-coated tablets,
Packages with 30 film-coated tablets,
Packages with 60 film-coated tablets,
Packages with 90 film-coated tablets,
Packages with 120 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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