SciLin® M30 – 100 IU

Recombinant Human Insulin
Suspension for Injection S.C.

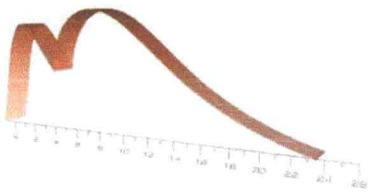
COMPOSITION
Each ml contains:
Recombinant Human Insulin 100 IU
(as inactive m-cresol and phenol stabilised insulin suspension)

PRODUCT DESCRIPTION
SciLin® M30 is a sterile suspension of human insulin obtained by *E. coli* DNA recombination.
The pen cartridge contains 3 ml of suspension, corresponding to 300 IU of biphasic insulin, consisting of 30% soluble and 70% isophane insulin.

A typical activity profile (glucose consumption curve) on subcutaneous insulin administration is shown below. During therapy, deviations from the mean value in time and depending on insulin action intensity are recorded. Individual deviations may be associated with such factors as: dose size, injection site, body temperature and physical activity.

SciLin® M30

Insulin activity



Time (hours)

PHARMACOLOGY
Insulin is a hormone produced in the specialized pancreas cells. It participated in carbohydrate, fat, and protein metabolism, causing, among others, glucose lowering in blood serum. Insulin deficiency in organism causes diabetes. The injected Insulin acts identically as the organism produced hormone. The administered orally Insulin is totally resolved in the digestive tract and therefore the Insulin preparation are administered in injections. Human Insulin preparation comes in the following form : Biphasic isophane suspension that therapeutic action starts within 30 minutes after administration, maximum effect between 2nd and 8th hours and the hypoglycaemic effect continues up to 24 hours and depends on the administered dose. In healthy humans about 5% of Insulin is bound with blood proteins. Insulin was also detected in cerebrospinal fluid where its concentration constituted around 25% of total Insulin concentration in blood serum. Insulin is metabolized in liver and kidneys. Some quantities of Insulin are metabolized in muscles and fat tissue. Insulin is identically metabolized in healthy and diabetic humans. It is eliminated through kidneys. The half-life of Insulin is circa 4 minutes. Liver and kidneys sickness may delay Insulin elimination. In elderly patients, Insulin elimination is slower and its hypoglycaemic effect is prolonged.

INDICATIONS
Diabetes mellitus treatment in patients who require Insulin.

CONTRA-INDICATIONS
Hypoglycaemia.
Hypersensitivity to insulin or to any of the excipients, unless it is a part of a desensitisation programme.

ADVERSE REACTIONS
In insulin therapy, the most frequent undesirable effect is hypoglycaemia. Severe hypoglycaemia may lead to loss of consciousness and even death. The frequency of hypoglycaemia is not determined since hypoglycaemia can be a consequence of insulin administration as well as other factors, e.g. diet or physical activity.
A topical allergic reaction is a frequent (1/100 to <1/10) undesirable effect. At insulin injection site erythema, oedema and itching may occur. The symptoms usually disappear in a couple of days or weeks. In some cases topical reactions can be caused by factors other than insulin, e.g. irritating substances included in skin disinfectants or a wrong injection technique.
Systemic allergic reactions indicative of generalised hypersensitivity to insulin are very rare (<1/10000) but are potentially more dangerous. The symptoms include: eruption all over body, dyspnoea, wheezing breath, lowered arterial pressure, accelerated pulse and sweating. In serious cases, generalised allergy symptoms can be life threatening. Rare cases of severe allergy to **SciLin® M30** require immediate treatment. Insulin change or desensitisation can be necessary.
Infrequently (1/1000 to < 1/100) lipodystrophy at injection site occurs.

Following adverse reactions have been reported during post-marketing experience:
- Cases of oedema, particularly if previous poor metabolic control is improved by intensified insulin therapy;
- Cases of weight gain;
- Injection site reaction: injection site discoloration, injection site bleeding, injection site induration, injection site mass, injection site nodule, injection site pain, injection site rash, injection site urticaria, injection site pustule;
- Cases of pruritus and generalized pruritus:
- Cases of dizziness.

Reporting of suspected adverse reactions

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Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

PRECAUTIONS

A change of the type or brand of insulin used requires doctor's supervision. A change of insulin strength, brand (manufacturer), type (soluble, isophane, biphasic), origin (animal, human, human insulin analogue) and/or production method (DNA recombination or animal origin) may require dose modification.

In some patients, a change from animal insulin to human insulin may require dose modification. If dose modification is required, it should be done at the administration of the first dose of the new insulin or during the first weeks or months following the change.

In some patients changing from animal insulin to human insulin, early warning symptoms of hypoglycaemia can be less distinctive or totally different from those developed during application of animal insulin. With better glycaemia control (e.g. with intensive insulin therapy), the warning symptoms of hypoglycaemia can be less distinctive or may not develop at all. Patients should be informed about the risk. Other factors changing or weakening early warning symptoms of hypoglycaemia are: long-lasting diabetes, diabetic neuropathy, some medications, e.g. β-adrenolytics. Uncontrolled hypoglycaemia or hyperglycaemia may lead to loss of consciousness, coma or death.

Inappropriate dosing or therapy discontinuation, especially in insulin-dependent diabetes, may cause hyperglycaemia and ketoacidosis – life threatening conditions.

Human insulin administration can lead to production of antibodies, however their titre is lower than in the case of purified animal insulin.

Insulin requirement can change significantly with adrenal, pituitary and thyroid disease, renal or hepatic dysfunction.

Insulin requirement can increase during illness or emotional disturbances.

Dose modification can also be required when the patient changes their physical activity or diet.

Concomitant administration of **SciLin® M30** with pioglitazone:

Cardiac insufficiency cases have been reported with concomitant administration of insulin with pioglitazone, especially in patients with cardiac insufficiency risk factors. This should be considered before using any combination treatment with **SciLin® M30** and pioglitazone. When combination treatment is administered, patients should be monitored for signs and symptoms of cardiac insufficiency, increased body weight and oedema. If cardiovascular symptoms occur, pioglitazone should be discontinued.

ADMINISTRATION DURING PREGNANCY AND BREAST-FEEDING

Pregnancy

Pregnancy in diabetic women requires Insulin application. The accurate glucose level maintenance in pregnancy is extremely important as hyperglycemia in pregnant woman may badly harm the fetus. In the first trimester of pregnancy the Insulin requirement rapidly falls and it is necessary to reduce the Insulin dose which further on gradually growth in the second and third trimester, generally by 75% of before pregnancy dose. Just after delivery, the Insulin requirement rapidly falls again.

Breastfeeding

It is acceptable to breast-feed during the Insulin treatment, considering this hormone is resolve in the digestive tract. During lactation period, the need of Insulin is lower than before pregnant and it gets equalized to the original level after 6 – 9 months.

EFFECTS ON THE ABILITY OF DRIVING AND OPERATING MACHINERY

The influence of Insulin doses administration on the ability of driving vehicles has not been examined. It may be handicapped by hyperglycaemia that causes disturbances of the central nervous system with the following symptoms : Headache, anxiety, double seeing, disorders of association and distance evaluation. At the commencement of Insulin treatment, change of Insulin preparation during the stress or excessive physical effort, when considerable differences of glucose concentration in blood occur, disorders in ability of driving and operating machinery may happen. It is recommended to control the glucose concentration in blood during long journey.

DRUG INTERACTIONS

Some medicinal products can change glucose metabolism. The doctor should take the potential interaction into account and ask the patient about other medicaments used by them.

Insulin requirement can be increased by substances showing hyperglycaemic action, such as glucocorticosteroids, thyroid hormone, growth hormone, danazol, β_2-sympathicomimetics (ritodrine, salbutamol, terbutaline), diuretic thiazides and niacin.

Insulin requirement may decrease when hypoglycaemic agents are used, e.g. oral hypoglycaemic medications, salicylates (e.g. acetylsalicylic acid), some antidepressants (monoamine oxidase inhibitors), some angiotensin convertase inhibitors (captopril, enalapril), non-selective beta-adrenolytic drugs and alcohol.

Insulin requirement may be changed by somatostatin analogues (octreotide, lanreotide).

DOSAGES

There are many known and practiced schemes of human Insulin treatment. A doctor must choose and individually adjust a treatment to a patient, according to these requirements. Based on the Insulin concentration in a patient's blood a doctor adjusts a proper Insulin dose and an Insulin concentration in patient's blood. You must not apply any other Insulin preparation except the one recommended by your doctor. Before use, you should always check on the label, name and a code of the Insulin and make sure it is identical with the prescribed one. You should check the expiry date on the container. Do not use after the expiry date.

Mode of Use

SciLin® M30 preparations are for subcutaneous injection. A few minutes before use, **SciLin® M30** should be taken out of the fridge in order to reach a room temperature. During the preparation administration, general hygiene rules should be observed : Hands must be washed before the procedure and the injection site disinfected. Before administration, the **SciLin® M30** Cartridge must be carefully watched. **SciLin® M30** Suspension should be homogenously opaque (uniformly cloudy or milky). The vial or cartridge should not be used if after mixing contain of both remains clear or there is a film of white substance on the bottom, there are white clusters floating, or solid, white particles remain stick to the walls making the preparation look frozen. You must be especially careful not to introduce **SciLin® M30** into a blood vessel during the injection. In order to operate the injector (load the cartridge,

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insert the needle, carry out the injection) you must strictly observe the manufacturer's instructions. **SciLin® M30** should be mixed before every injection by mean of rotation up and down 10 times or rotation on palm until homogenous suspension appears. Rotation should be continued until homogenous cloudy or milky suspension appears. Content of cartridge can be mixed fixed into pen. In emergencies you may use the cartridge in a normal Insulin syringe and proceed as described above (in accordance with the Insulin concentration and dose).

OVERDOSAGE
When overdosage happen, hypoglycaemia symptoms will occur included : Intense hunger, anxiety, apathy, trembling, sweating, vomiting. In mild hypoglycaemia it is enough to have sweet beverages or carbohydrate – reach food. It is advisable to rest. The patients should carry with them sugar cubes, glucose or sweets. It is not advisable to have chocolate that contains fat, which delay glucose absorption. Severe hypoglycaemia may lead to convulsion and loss of consciousness or death. When overdosage of Insulin occurs, hypoglycaemia may develop becoming hypokalemia (potassium concentration in blood is dropping). In acute hypoglycaemia, when patients are not able to take food they should be administered 1 mg of glycogen into the muscle and/or glucose intravenously.

SHELF LIFE
The shelf life is 3 years.

PRESENTATION
Box of 5 cartridges @ 3 mL
Reg. No. DKI1908100843A1

HARUS DENGAN RESEP DOKTER

STORAGE
Store between 2°C - 8°C. Do not freeze. Protect from light, keep out of reach of children. **SciLin® M30** which has been frozen must not be used. Insulin suspensions should not be used if they not appear uniformly white and cloudy after suspension.
The storage life of **SciLin® M30** after the first opening of the cartridge last maximally 28 days in room temperature (15°C to 25°C).

Manufactured by:
BIOTON S.A.,
Poland.

Imported by:
PT. Darya-Varia Laboratoria, Tbk.
Citeureup, Bogor - Indonesia

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