Insuget™

انسوگیٹ

(HUMAN INSULIN rDNA ORIGIN)
100 IU/mL

DESCRIPTION
Human insulin, a polypeptide hormone consisting of 21 amino acid A-chain and 30 amino acid B-chain linked by two disulfide bonds, is a hormone that plays a key role in regulating carbohydrate, protein and fat metabolism. The molecular formula of human insulin is $C_{257}H_{383}N_{65}O_{77}S_6$. INSUGET is found to be chemically, physically, biologically and immunologically equivalent to pancreatic human insulin.
INSUGET-R (Regular insulin injection, soluble), human biosynthetic, is a rapid acting insulin with a relatively short duration of activity (4 to 6 hours).
INSUGET-N (NPH injection, isophane suspension), human biosynthetic, is an intermediate-acting insulin with a slower onset of action than Regular insulin and a longer duration of activity of up to 24 hours.
INSUGET 70/30 (Biphasic injection isophane suspension), is an intermediate-acting insulin with a more rapid onset of action than NPH alone and a duration of activity of up to 24 hours.

QUALITATIVE AND QUANTITATIVE COMPOSITION
INSUGET is available as:

1. INSUGET-R Regular Injection,
   Soluble 100 IU/mL
   Each mL contains:
   Human insulin E.Ph.....100 IU
   (recombinant DNA origin)
   m-Cresol E.Ph ……. 0.25% w/v
   (Used as preservative)
   Water for injection E.Ph …q.s.

2. INSUGET-N NPH Injection
   Isophane 100 IU/mL
   Each mL contains:
   Human insulin E.Ph....100 IU
   (recombinant DNA origin)
   m-Cresol E.Ph ……. 0.16% w/v and
   Phenol E.Ph ……. 0.065% w/v
   (Used as preservative)
   Water for injection E.Ph …q.s.

3. INSUGET 70/30 Biphasic Injection, Biphasic Isophane 100 IU/mL [*30% human Insulin soluble, 70% Human insulin Isophane*]
   Each mL contains:
   Human insulin E.Ph....100 IU
   (recombinant DNA origin)
   m-Cresol E.Ph ……. 0.16% w/v and
   Phenol E.Ph ……. 0.065% w/v
   (Used as preservative)
   Water for injection E.Ph …q.s.

CLINICAL PHARMACOLOGY
Mechanism of Action
The major effects of insulin on carbohydrate homoeostasis following its binding to specific cell-surface receptors on insulin-sensitive tissues, notably the liver, muscles and adipose tissue. It inhibits hepatic glucose production and enhances peripheral glucose disposal thereby reducing blood-glucose concentration. It also inhibits lipolysis thereby preventing the formation of ketone bodies.

Pharmacokinetics
Absorption
Insulin is fairly rapidly absorbed from subcutaneous tissue following injection. Insulin in the blood stream has a half-life of a few minutes. The rate of absorption from different anatomical sites may be different depending on local blood flow, with absorption from the abdomen being faster than that from the arm and that from the arm faster than from buttock or thigh. Absorption may also be increased by exercise. The absorption of insulin after intramuscular administration is more rapid than that following subcutaneous administration.

Metabolism and Excretion
Insulin is rapidly metabolised, mainly in the liver but also in the kidneys and muscle tissue. In the kidneys it is reabsorbed in the proximal tubule and either returned to venous blood or metabolised, with only a small amount excreted unchanged in the urine.

THERAPEUTIC INDICATIONS
INSUGET is indicated for the treatment of:
- Patients with Type I diabetes mellitus.
- Patients with Type II diabetes mellitus either alone or in combination with oral anti-diabetic agents.
- Patients with gestational diabetes.
- The emergency management of diabetic ketoacidosis.

DOSAGE AND ADMINISTRATION
The type of formulation, its dose and the frequency of administration should be determined by the physician, according to the needs suitable to the patient. The dose should be adjusted as necessary according to the results of regular monitoring of glucose concentrations in the blood glucose (or occasionally urine concentrations). A total dose in excess of about 80 units daily would be unusual and may indicate the presence of a form of insulin resistance.
The average daily requirement for diabetes therapy ranges between 0.5 and 0.1 IU/kg, depending on the individual needs of the patient. Optimised metabolic control, including glucose monitoring, is therefore recommended during insulin treatment.
In geriatric patients, the primary aim of treatment may be relief of symptoms and avoidance of hypoglycemic events. *INSUGET-R* may be taken 1 to 4 times daily, before meals and possibly at bed time. Regular (or rapid-acting) insulin should be administered 30 to 45 minutes before a meal. It can be mixed in the same syringe with intermediate-acting insulins, but in such situations, the regular insulin is drawn first. INSUGET–R should be given by subcutaneous injection but may, although not recommended, also be given by intramuscular injection. It may also be administered intravenously. INSUGET–R is administered subcutaneously into the thigh or abdominal wall. If convenient, the gluteal region or deltoid region may be used.
INSUGET–N (NPH) is administered subcutaneously into the thigh or abdominal wall. Preferably before meals, 1 to 2 times daily depending upon the requirement of the individual. If convenient, the gluteal region or deltoid region may be used. INSUGET–N (NPH) should be administered about 30 minutes before a meal. It can also be mixed in the same syringe with short-acting soluble insulins, and in such situations, the regular insulin is drawn first. INSUGET–N (NPH) cannot be given intravenously. *INSUGET* 70/30, a pre-mixed insulin is usually given once or twice daily, preferably just before meals when rapid initial effect together with a more prolonged effect is desired.

Ketoacidosis:
Only INSUGET-R insulin should be used. Treatment includes adequate fluid replacement, usually by infusing sodium chloride 0.9% initially and the administration of potassium salts to prevent or correct hypokalemia. Insulin should be given by continuous intravenous infusion if possible, although other routes have also been used. Insulin can also be given by intramuscular injection. In adults an initial loading dose of 20 units is followed by 6 units every hour until the blood glucose concentration falls to 10mmoL per litre, when the dose is given every 2 hours.
Since insulin normally corrects hyperglycemia before ketosis it is usually necessary to continue administration of insulin once normoglycemia has been achieved but to change the rehydration fluid to glucose-saline so that the additional glucose prevents the development of hypoglycemia.

Instructions for Use:
Care should be taken when injecting any INSUGET injection. The injection site should not be massaged. Patients must be educated to use proper injection techniques.

Before injecting the insulin:
1. Disinfect the rubber stopper.
2. Roll the vial between the palms of the hands, making sure that

there are no suspended impurities. For INSUGET-N and INSUGET 70/30 the liquid should be uniformly white and cloudy.
3. Draw into the syringe the same amount of air as the dose of insulin to be injected.
4. Inject the air into the vial.
5. Turn the vial and syringe upside down and draw the correct insulin dose into the syringe. Withdraw the needle and expel the air from the syringe and check that the dose is correct.
6. Inject immediately.

Do not use if the insulin substance (white material) remains at the bottom after mixing. Do not use if there are changes in the insulin after mixing. Do not use if solid white particles stick to the bottom or wall of the bottle, giving it a frosted appearance.

Injection sites should be rotated within an anatomic region in order to avoid lipodystrophy. An injection should be followed within 30 minutes by a meal or a snack containing carbohydrates.

Administration
1. Pinch the skin between two fingers, push the needle into the skinfold and inject the insulin under the skin.
2. Keep the needle under the skin for at least 6 seconds to make sure all the insulin has been injected.
3. If blood appears after the needle has been withdrawn, press the injection site lightly with a finger.

Do not reuse needles. Dispose of the needle in a responsible manner. Needles must not be shared.

ADVERSE REACTIONS
Hypoglycemia is the most frequently occurring undesirable effect of insulin therapy that a patient with diabetes may suffer. Symptoms of hypoglycemia usually occur suddenly. They may include cold sweat, cool pale skin, nervousness or tremor, anxious feeling, unusual tiredness or weakness, confusion, difficulty in concentration, headache, nausea and palpitation. Severe hypoglycemia may lead to unconsciousness and may result in temporary or permanent impairment of brain function or even death.
Weight gain is common when taking insulin.
Oedema and refraction anomalies may occur upon 'initiation' of insulin therapy. Local hypersensitivity reactions (redness, swelling and itching at the injection site) are those transitory reactions, which may occur during the treatment with insulin and normally disappear during continued treatment.
Lipodystrophy may occur at the injection site as a consequence of failure to rotate injection site within an area.
Generalised hypersensitivity reactions may occur occasionally and can cause generalised skin rash, itching, sweating, gastrointestinal upset, angioneurotic oedema, difficulties in breathing, palpitation and reduction in blood pressure. These are potentially life threatening.

CONTRAINDICATIONS
Insulin is contraindicated in:
- Patients with hypersensitivity to any components of this medication.
- Patients with hypoglycemia.
- Patients in coma due to hyperglycemia.

Under no circumstances should INSUGET formulation, other than INSUGET-R, be given intravenously.

PRECAUTIONS
- Insulin requirements may change significantly in diseases of the adrenal, pituitary or thyroid glands and in the presence of renal or hepatic impairment.
- Insulin requirements may be increased during illness or emotional disturbances.
- Care is also necessary during excessive exercise. Hypoglycemia caused by metabolic effects and increased insulin absorption is the usual response, but hyperglycemia may sometimes occur. Adjustment of insulin dosage may also be necessary if patients change their level of physical activity or change their usual diet.
- The use of insulin necessitates monitoring of therapy, such as the testing of blood or urine for glucose concentrations and the urine for ketones, by the patient.
- Local reactions, characterised hypersensitivity may produce urticaria, angioedema and very rarely anaphylactic reactions. If continued therapy with insulin is essential, hyposensitisation procedures may need to be performed.

Missed dose
Timing of insulin doses is extremely important. The best approach is to measure blood glucose and add a dose of regular insulin if glucose levels are too high. Otherwise, wait for the next scheduled dose.

Stopping the drug
Do not stop taking insulin injections unless ordered by your doctor. Patients with diabetes are often given general instructions for modifying their insulin doses based on home blood glucose measurements.

Drug Interactions
Beta blocking agent may mask the symptoms of hypoglycemia. *Some of the drugs leading to reduced insulin requirement:* Oral hypoglycemic agents (OHA), octreotide, monoamine oxidase inhibitor (MAOI), non selective beta blocking agents, angiotensin converting enzyme (ACE) inhibitors, salicylates, alcohol and alcohol steroids. *Some of the drugs leading to the increase insulin requirement:* Oral contraceptives, thiazides, glucocorticoids, thyroid hormones and sympathomimetics, danazol etc.

Pregnancy
It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patients throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctors if they are pregnant or are contemplating pregnancy.
Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes.

Nursing Mothers
There are no restrictions in insulin treatment while treating a diabetic nursing mother, as it involves no risk to the baby. However, the insulin dosage may need to be reduced.

INCOMPATIBILITIES
In general terms insulin should only be added to compounds with which it is known to be compatible. Insulin suspensions should not be added in infusion fluids.

STORAGE
INSUGET should be stored in a cold place ($2^{O}C$ - $8^{O}C$), Do not freez. Do not expose to excessive heat and direct sunlight. Once in use, the vial can be kept at room temperature (upto $25^{O}C$) for upto 6 weeks.
Do not use beyond this period.
Shake gently before use.

HOW SUPPLIED
INSUGET–R (Regular) 100 IU/mL is available as 10mL vial.
INSUGET–N (NPH) 100 IU/mL is available as 10mL vial.
INSUGET 70/30 100 IU/mL is available as 10mL vial.

Keep out of reach of children

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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