For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Biphasic Isophane Insulin Injection BP
(Recombinant DNA origin)

WOSULIN™- 30/70

WOCKHARDT

30/70
Monocomponent
Insulin
(HUMAN)

For SC use only

COMPOSITION

Each ml contains:		
Insulin Human (30% Regular Insulin Human neutral & 70% isophane Insulin)	USP	100 IU
M-Cresol as preservative	USP	0.16% w/v
Phenol as preservative	USP	0.065% w/v
Water for Injection	USP	q.s.

DIABETES

Insulin is a hormone produced by the pancreas, a large gland that lies near the stomach. This hormone is necessary for the body's correct use of food, especially sugar. Diabetes occurs when the pancreas does not make enough insulin to meet your body's needs.

To control your diabetes, your doctor has prescribed injections of insulin products to keep your blood glucose at a nearnormal level. You have been instructed to test your blood and/or your urine regularly for glucose. Studies have shown that some chronic complications of diabetes such as eye disease, kidney disease, and nerve disease can be significantly reduced if the blood sugar is maintained as close to normal as possible. Proper control of your diabetes requires close and constant cooperation with your doctor. Despite diabetes, you can lead an active and healthy life if you eat a balanced diet, exercise regularly, and take your insulin injections as prescribed. Always keep an extra supply of insulin as well as a spare syringe and needle handy.

DESCRIPTION

Recombinant WOSULIN-30/70 is a recombinant human insulin, synthesized in a laboratory strain of Hansenula polymorpha (a yeast), in which the gene for human insulin has been inserted by the recombinant DNA technique. It is a mixture of insulin human regular injection 30% with isophane insulin human suspension 70% providing an intermediate - acting insulin with an onset of action similar to regular insulin (0.5 hours). The onset of action of WOSULIN-30/70 is dependent on dose, site of injection, blood supply, temperature and physical activity.

The duration of effect is about 18-24 hours. The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual.

It is a sterile solution and is for subcutaneous injection only. It should not be used intravenously or intramuscularly.

MECHANISM OF ACTION

Like all other insulins, the glucose lowering effect of WOSULIN-30/70 is due to the facilitated uptake of glucose in body tissues. This uptake occurs following the binding of insulin to its receptors present in the muscle and adipose tissue. The blood glucose lowering effect of insulin also occurs due to the simultaneous inhibition of glucose output from the liver.

PHARMACOKINETICS

Insulin has a half-life of a few minutes in the blood stream. Consequently, the time course of action of any insulin may vary considerably in different individuals or at different times in the same individual. As with all insulin preparations, the intensity and duration of action of WOSULIN-30/70 is dependent on the dose, site of injection, blood supply, temperature, and physical activity.

An average action profile after subcutaneous injection indicates:

● Onset within 0.5 hours ● Peak levels attained between 2-12 hours ● Duration of action approximately 18-24 hours.

INDICATIONS

WOSULIN-30/70 is indicated for the following:

- Treatment of all patients with type 1 diabetes
- Treatment of patients with type 2 diabetes who are not adequately controlled by diet and / or oral hypoglycemic agents.
- For the initial stabilization of diabetes in patients with diabetic ketoacidosis, hyperosmolar non-ketotic syndrome and during periods of stress such as severe infections and major surgery in diabetic patients.
- Treatment of gestational diabetes

DOSAGE AND ADMINISTRATION

The dosage of WOSULIN-30/70 is determined by the physician, as per the needs of the patient. With WOSULIN-30/70, it is important to use a syringe that is marked for the desired strength, for e.g. U-40 or U-100 insulin preparations. Failure to use the proper syringe can lead to a mistake in dosage, causing serious problems such as severe hypoglycemia or hyperglycemia. The average range of total daily insulin requirement for maintenance in type 1 diabetic patients ranges between 0.5 and 1.0 IU / kg. Further, in insulin resistance, the daily requirement of insulin may be substantially higher. In patients with type 2 diabetes, the requirements of insulin are lower i.e. approximately 0.3-0.6 IU / kg / day.

WOSULIN-30/70 is administered subcutaneously in the abdominal wall, the thigh, gluteal region or the deltoid region.

● Toavoid lipodystrophy, the site of injection should be frequently changed. Any injection of insulin should be followed by a meal or snack contalning carbohydrates within 30 minutes.

Adjustment of dosage may be necessary if you undertake increased physical activity or change your usual diet.

USE ALONG WITH OTHER INSULINS

WOSULIN-30/70 injection can be used in combination with human insulin regular.

CONTRAINDICATIONS

WOSULIN-30/70 is contraindicated in the following conditions.

- Hypoglycemia
- Hypersensitivity to insulin or any other component of the formulation

PRECAUTIONS

Pregnancy: There are no restrictions on the use of insulin during pregnancy since insulin does not cross the placental barrier. Published studies with human insulins suggest that optimizing overall glycemic control, including postprandial control, before conception and during pregnancy improves fetal outcome. Although the fetal complications of maternal hyperglycemia have been well documented, fetal toxicity also has been reported with maternal hypoglycemia. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. During the perinatal period, careful monitoring of infants born to mothers with diabetes is warranted.

Nursing Mothers: There are no restrictions on the use of insulin in lactating mothers as insulin treatment of nursing mothers does not involve any risk to the baby. However, caution should be exercised when administered to nursing mothers and the dosage of insulin may be reduced.

Effects on the ability to drive and use machines: The patient's ability to concentrate and react may be impaired as a result of hypoglycemia. This may constitute a risk in situations where these abilities are of special importance (e.g. Driving a car or operating machinery).

You are therefore advised to avoid hypoglycemia during driving. This is particularly significant in patients who have reduced awareness of the warning signs of hypoglycemia or have frequent episodes of hypoglycemia.

SWITCHING TO DIFFERENT TYPE OF INSULIN

If you are switching to another type of insulin, it should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (rapid acting insulin, intermediate acting insulin, long acting insulin etc), species (animal, Insulin human analog) and/or method of manufacturer (recombinant versus animal source insulin) may result in the need for a change in dose.

Patients switching to WOSULIN-30/70 may require a change in dosage from that used with their usual insulin.

LABORATORY TESTS

As with all insulins, the therapeutic response to human insulin should be monitored by periodic blood glucose tests.

Periodic measurement of glycosylated hemoglobin is recommended for the monitoring of long term glycemic control.

DRUG INTERACTIONS

Insulin requirements may be increased by medications with hyperglycemic activity such as corticosteroids, isoniazid, certain lipid-lowering drugs (e.g. niacin), estrogens, oral contraceptives, phenothiazines, and thyroid replacement therapy. Insulin requirements may be decreased in the presence of drugs with hypoglycemic activity, such as oral hypoglycemic agents, salicylates, sulfa antibiotics, certain antidepressants (monoamine oxidase inhibitors), certain angiotensin converting enzyme inhibitors, beta adrenergic blockers, inhibitors of pancreatic function (e.g. Octreotide), and alcohol. Beta adrenergic blockers may mask the symptoms of hypoglycemia in some patients.

Renal Impairment : The requirements for insulin may be reduced in patients with renal impairment.

Hepatic Impairment : Although impaired hepatic function does not affect the absorption or disposition of WOSULIN-30/70, careful glucose monitoring and dose adjustments of insulin may be necessary.

ADVERSE EFFECTS

The most commonly seen adverse reaction with WOSULIN-30/70 are:

1. **Hypoglycemia :**

Hypoglycemia is one of the most common adverse effect seen with the use of any type of insulin including human insulin.

This can occur because of the following:

- Use of too much insulin
- Missed meal / delayed meal
- Intercurrent infection or illness
- Strenuous exercise.

Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver disease may also lead to hypoglycemia.

Concomitant administration with other drugs that lower blood glucose such as oral hypoglycemics, salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants may lead to hypoglycemia.

Concomitant consumption of alcohnlic beverages may also lead to hypoglycemia. Symptoms of mild to moderate hypoglycemia may occur suddenly and can include: Sweating; dizziness; palpitation; tremor; hunger; restlessness; tingling in the hands, feet, lips, or tongue; lightheadedness; inability to concentrate; headache; drowsiness; sleep disturbances; anxiety; blurred vision; slurred speech; depressive mood; irritability; abnormal behavior; unsteady movement; personality changes. Signs of severe hypoglycemia can include: Disorientation; unconsciousness; seizures; death. Therefore, it is important that assistance be obtained immediately. Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as long duration of diabetes, diabetic nerve disease, coadministration of medications such as beta blockers, change in insulin preparations, or intensified control (3 or more insulin injections per day) of diabetes.

The use of preparations of WOSULIN-30/70 should minimize the incidence of adverse effects associated with the use of animal insulins.

2. **Oedema**

Oedema and refraction anomalies may occur upon initiation of insulin therapy. These symptoms are usually of a transitory nature.

3. **Allergy to Insulin :**

3. a: Systemic Allergy: Less common, but potentially more serious, is generalized allergy to insulin, which may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalized allergy may be life threatening.

3. b: Local Allergy: Patients occasionally experience redness, swelling, and itching at the site of injection of insulin. This condition called local allergy, usually clears up in a few days to a few weeks. In some instances, this condition may be related to factors other than insulin, such as irritants in the skin cleansing agent.

4. **Lipoatrophy and lipodystrophy**

Lipodystrophy occurs at the site of injection after long usage. However, this is less common with the newer preparations of insulin.

5. **Insulin resistance**

When insulin requirement is increased (> 200 IU / day), insulin resistance is said to have developed. Thefollowing are the different grades of insulin resistance:

Acute: Acute insulin resistance develops rapidly and is usually a short term problem. It usually occurs due to an underlying infection, trauma, surgery and emotional stress. Treatment is to overcome the precipitating factor and to give high doses of regular insulin.

Chronic: This type of insulin resistance is generally seen in patients treated for years with conventional preparations of beef or pork insulins and it is more common in patients with Type 2 diabetes. Development of such a type of insulin resistance is an indication for switching patients to the newer preparations of insulin. After instituting the newer preparations, insulin requirement gradually declines over weeks and months and majority of patients stabilize at approximately 60 IU / day.

OVERDOSAGE

Hypoglycemia may occur as a result of an excess of insulin relative to food intake, energy expenditure, or both. Mild episodes of hypoglycemia usually can be treated with oral glucose. It is therefore recommended that the diabetic patient constantly carry some sugar lumps, sweets, biscuits, or sugary fruit juice. Adjustments in drug dosage, meal patterns, or exercise, may be needed. More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with intramuscular / subcutaneous glucagon or concentrated intravenous glucose. Glucose must also be given intravenously, if the patient does not respond to glucagon within 10 to 15 minutes. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery.

STORAGE

WOSULIN-30/70 should be stored in a refrigerator (2°C to 8°C) but not allowed to freeze. When in use, vial may be kept at room temperature (15°C to 25°C) for up to six weeks. Do not expose to excessive heat or direct sunlight.

WOSULIN- 30/70 must be kept out of reach of children.

Insulin preparations, which have been frozen, must not be used. Once opened (when the stopper or seal has been punctured with a needle), insulin is kept at room temperature. Cold insulin can be irritating to inject. Thus, patients should be asked to roll the vial in their hands 10 times prior to drawing it up in the syringe (after allowing the vial to sit for 30 minutes at room temperature if the vial is stored in the refrigerator).

PACK : WOSULIN-30/70 100 IU/ml - 10ml vial

Manufactured by :
WOCKHARDT LTD.
Aurangabad, India
TM Trademark of Wockhardt

L. I. B0096

PROCEDURE FOR INSULIN ADMINISTRATION

1. Wash your hands carefully. Shake or roll Wosulin-30/70 insulin vial 10 times to completely mix the insulin

2. Inspect the vial. Wosulin-30/70 should appear uniformly cloudy or milky. The Insulin injection should not be used if there is anything unusual in appearance.

3. When using a new vial, flip off the plastic protective cap, but do not remove the stopper. The tip of the vial should be wiped with an alcohol swab

4. Draw air into the syringe equal to your insulin dose

5. Insert needle into vial through rubber top and push plunger to empty the air into the vial

6. Turn the bottle and syringe upside down. Hold the bottle and syringe firmly in one hand and shake gently. Making sure that the tip of the needle is in the liquid, withdraw the correct dose of insulin into the syringe.

7. Before removing the needle from the vial, check the insulin syringe for air bubbles, which reduces the amount of insulin in it. If bubbles are present, hold the insulin straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose again.

8. Lightly pinch up the skin, holding the syringe like a pencil.

9. Insert the needle into the skin and push the plunger slowly. Make sure that the needle is all the way in.

10. Wait for 5 seconds and pull out the syringe. Do not rub the area.

PATIENT'S INFORMATION AND RECORD

Points you should know:

- Remember the brand name and type of insulin prescribed.
- Never expose insulin to extreme temperatures
- Use only the right concentration of the insulin prescribed (40 IU or 100 IU) with the right syringe.
- The insulin vials have a protective colour-coded cap which must be removed before use. If the plastic cap is loose or missing, return the vial to the pharmacy.
- WOSULIN is free from, Insulin derived from Animals.

Your Daily Insulin Intake Calendar

DATE	INSULIN DOSE	TIME	BRAND	DATE	INSULIN DOSE	TIME	BRAND