

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

3 ml
100 IU/ml

30/70 Monocomponent Insulin
For  use only

WOCKHARDT

COMPOSITION
Each ml contains:
Insulin Human USP 100 IU
(50% Insulin Human neutral and 50% Isophane Insulin)
in Citrate USP 0.16% w/v as preservative
Phenol USP 0.085% w/v as preservative
Water for Injection USP q.s.

DESCRIPTION
WOSULIN-30/70 Cartridge is a mixture of insulin human regular 30% with isophane insulin human suspension - NPH 70% (recombinant DNA origin). It is synthesized in a special non-disease producing laboratory strain of the yeast *Hansenula polymorpha*. This special host cell line has been genetically altered by the addition of the gene for human insulin production.
It provides an intermediate-acting insulin (with a longer duration of activity than regular insulin) and an onset of action similar to regular insulin (0.5 hours).
The onset of action of Wosulin 30/70 is rapid and the duration of effect is about 18-24 hours. The time course of action of any insulin may vary considerably in different individuals and 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.

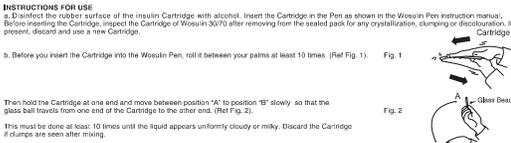
This human insulin (recombinant DNA origin) is structurally identical to the insulin produced by the human pancreas. The concentration of this product is 100 units of insulin per milliliter.
MECHANISM OF ACTION
Like all other insulins, the glucose lowering effect of Wosulin 30/70 is due to the facilitated 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 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 8-10 minutes in the blood stream. Consequently, the time course of action of any insulin may vary considerably in different individuals and 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.
• Treatment of Gestational diabetes

DOSE AND ADMINISTRATION
The dosage of Wosulin 30/70 is determined by the physician, as per the needs of the patient. The average range of total daily insulin requirement for maintenance in type 1 diabetes patients ranged between 0.5 and 1.0 IU / kg / day. 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. Lo. approximately 0.3 - 0.6 IU / kg / day.
Wosulin 30/70 is administered subcutaneously in the abdominal wall, the thigh, the gluteal region or the deltoid region. Insulin suspensions must never be administered intravenously.

To avoid lipodystrophy, the site of injection should be frequently changed and any injection of insulin should be followed by a meal or snack containing carbohydrates within 30 minutes. Adjustment of dosage may be necessary if patients undertake increased physical activity or change their usual diet.
INSTRUCTIONS FOR USE
a. To inspect the rubber surface of the insulin Cartridge with alcohol. Insert the Cartridge in the Pen as shown in the Wosulin Pen instruction manual. Before inserting the Cartridge, inspect the Cartridge of Wosulin 30/70 after removing from the sealed pack for any crystallization, clumping or discoloration, if present, discard and use a new Cartridge.



c. If the Cartridge is already inside the Wosulin Pen, turn the Pen up and down gently at least 10 times until the liquid appears uniformly cloudy or milky. This has to be done before each injection. (Ref Fig. 3).

d. After you attach the needle, dial 2 units on the dose selector to remove any air that may be inside the needle.
i. Wash your hands and clean the skin with alcohol where the injection is to be made.
1. With one hand, lightly pinch up the skin. Insert the needle as advised by your doctor or educator. Push and hold the release button of the Pen. Count to 10 and pull out the needle. Do not massage the area as this may cause back leakage of insulin.
g. Dispose off the needle in the recommended way.
h. For additional information, read the instruction manual of Wosulin Pen and also log on to www.wockhardtindia.com.

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 glycaemic 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. Careful monitoring of the pregnancy is required throughout pregnancy. 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). Patients should therefore be 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 PATIENTS TO DIFFERENT TYPE OF INSULIN
Transferring a patient to another type of insulin 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 manufacture (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 glycaemic control.
DRUG INTERACTIONS
Insulin requirements may be increased by medications with hyperglycaemic activity such as corticosteroids, isoniazid, certain lipid-lowering drugs (e.g. niacin), serotonins, oral contraceptives, phenothiazines, and thyroid replacement therapy.
Insulin requirements may be decreased in the presence of drugs with hypoglycaemic activity, such as oral hypoglycaemic 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 hypoglycaemics, salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants may lead to hypoglycemia.
Concomitant consumption of alcoholic 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; blurred speech; depressive mood; irritability; abnormal behavior; uneasy 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, co-administration of medications such as beta-blockers, change in insulin preparations, or interrelated 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. Hypoglycemia and ketoadiposis
In patients with insulin-dependent diabetes, prolonged hyperglycemia can result in diabetic acidosis. The first symptoms of diabetic acidosis usually come on gradually, over a period of hours or days, and include a dryness feeling, flushed face, thirst, loss of appetite, and fruity odor on the breath. With acidosis, urine tests show large amounts of glucose and acetone. Heavy breathing and a rapid pulse are more severe symptoms. If untreated, prolonged hypoglycemia or diabetic acidosis can result in loss of consciousness or death. Therefore, it is important that one should obtain medical assistance immediately.

4. Allergy
Allergy to Insulin
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.
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.

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

6. Insulin resistance
When insulin requirement is increased (> 200 IU / day), insulin resistance is said to have developed. The following 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 insulin 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 initiating the newer preparations, insulin requirement gradually declines over weeks and months and majority of patients stabilize at approximately 60 IU / day.

OVERDOSE
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, seizures, or neurologic impairment may be treated with intramuscular / subcutaneous glucose or concentrated intravenous glucose. Glucose must also be given intravenously, if the patient does not respond to glucose within 10 to 15 minutes. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery.

STORAGE AND CAUTION
Wosulin 30/70 Cartridge which is not in use should be stored in a refrigerator (2° to 8°C) but not allowed to freeze. When in use, Cartridge may be used in Wosulin Pen may be stored at room temperature (15° to 25°C) for up to 4 weeks. Do not expose to excessive heat or direct sunlight. Wosulin 30/70 Cartridge must be kept out of reach of children.
Insulin preparations, which have been frozen, must not be used.
Wosulin 30/70 should not be used if it does not appear uniformly cloudy or milky after shaking.
Remove the needle after each injection, otherwise temperature changes may cause liquid to leak out of the needle and the insulin concentration may increase.
Do not refill the Cartridge.

Wosulin 30/70 Cartridge should never be used after the expiry date.
PRESENTATION
WOSULIN 30/70 - Cartridge of 3 ml. M. L. No. ADJ04

Manufactured in India by **WOCKHARDT LIMITED**
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