

WOSULIN R

Insulin Human Injection USP 100 IU/ml
Human Recombinant (r - DNA)

Read all of this leaflet carefully before you start taking WOSULIN R

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, health care provider 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, health care provider or pharmacist.

In this leaflet:

- a) What is WOSULIN R and what it is used for?
- b) Before you take or use WOSULIN R
- c) How to take or use WOSULIN R.
- d) Possible side effects
- e) How to store WOSULIN R
- f) Further information

a) What Is Wosulin R And What It Is Used For

WOSULIN-R Cartridge contains Insulin human Regular (recombinant DNA origin). It is a clear, colorless solution which has a short duration of action. Insulin human regular 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 Insulin human production.

It is a sterile solution for parenteral use. It can be used subcutaneously or intravenously.

The onset of action of Insulin human regular is rapid (approx. within 30 mins) and it has a relatively short duration of action (4-6 hours) as compared with other longer-acting formulations of Insulin.

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 millilitre.

Insulin Human Regular is indicated for the following:

1. Treatment of patients with type I diabetes.
2. Treatment of patients with type II diabetes who are not adequately controlled by diet and /or oral hypoglycaemic agents.
3. 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.
4. Treatment of gestational diabetes. WOSULIN-R may be administered intravenously under proper medical supervision in a clinical setting for glycemic control.

WOSULIN R

Insulin Human Injection USP 100 IU/ml
Human Recombinant (r - DNA)

b) Before you take or use WOSULIN R.

WOSULIN Insulin human Regular is contraindicated in the following conditions:

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

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 patient 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 hypoglycaemia

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

WOSULIN R

Insulin Human Injection USP 100 IU/ml
Human Recombinant (r - DNA)

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 Insulin human regular, careful glucose monitoring and dose adjustments of insulin may be necessary.

c) How to take or use WOSULIN R.

The dosage of Insulin human Regular 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 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.

Insulin human regular Is usually administered subcutaneously in the abdominal wall, the thigh, the gluteal region or the deltoid region. 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 (Cartridge)

- a. Disinfect 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-R after removing from the sealed pack for any crystallization, clumping or discolouration. If present, discard and use a new Cartridge.
- b. After you attach the needle, dial 2 units on the dose selector to remove any air that may be inside the needle.
- c. Wash your hands and clean the skin with alcohol where the injection is to be made.
- d. 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.
- e. Dispose off the needle in the recommended way.
- f. For additional Information, read the Instruction manual of Wosulin Pen and also log on to www.wockhardt diabetes.com.

WOSULIN R

Insulin Human Injection USP 100 IU/ml

Human Recombinant (r - DNA)

DOSAGE AND ADMINISTRATION (For vial)

Subcutaneous (SC)

WOSULIN-R is usually given SC three or more times daily before meals. The dosage and timing of WOSULIN-R should be individualized and determined in accordance with the needs of the patient. WOSULIN-R may also be used in combination with oral anti hyperglycemic agents or longer acting insulin products to suit the needs of the individual patients with diabetes. The injection of WOSULIN-R should be followed by a meal within approximately 30 minutes of administration. The average range of total daily insulin requirement for maintenance therapy in insulin-treated patients without severe insulin resistance lies between 0.5 and 1 unit/kg/day.

However, in pre-pubertal children it usually varies from 0.7 to 1 unit/kg/day, but can be much lower during the period of partial remission. In situations of insulin resistance, e.g. during puberty or due to obesity, the daily insulin requirement may be substantially higher.

WOSULIN-R may be administered by SC injection in the abdominal wall, the thigh, the gluteal region or in the upper arm. SC injection into the abdominal wall ensures a faster absorption than from other injection sites. Injection into a lifted skin fold minimizes the risk of intramuscular injection. Injection sites should be rotated within the same region. As with all insulin, the duration of action will vary according to the dose, injection site, blood flow, temperature, and level of physical activity.

Intravenous (IV)

IV administration of WOSULIN-R is possible under medical supervision with close monitoring of blood glucose and potassium levels to avoid hypoglycemia and hypokalemia. For IV use, WOSULIN-R should be used at concentrations from 0.1 unit/mL to 1 unit/mL in infusion systems with the infusion fluids 0.9% sodium chloride using polyvinyl chloride infusion bags. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Never use WOSULIN-R if it has become viscous (thickened) or cloudy; use it only if it is clear and colorless. WOSULIN-R should not be used after the printed expiration date.

Mixing of Insulins

- WOSULIN-R is short-acting and is often used in combination with intermediate- or long-acting insulins.
- The order of mixing and brand or model of syringe should be specified by the physician.

A U-100 insulin syringe should always be used. Failure to use the correct syringe can lead to dosage errors. In general, when an intermediate-acting insulin (e.g., NPH insulin isophane suspension) is mixed with short-acting soluble insulin (e.g., regular), the short-acting insulin should be drawn into the syringe first.

WOSULIN R

Insulin Human Injection USP 100 IU/ml
Human Recombinant (r - DNA)

d) Possible side effects

The most commonly seen adverse reaction with Insulin human Regular are:

1. Hypoglycaemia: Hypoglycaemia 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 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; light headedness; 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, co-administration 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 Insulin human Regular 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. Hyperglycemia and ketoacidosis

WOSULIN R

Insulin Human Injection USP 100 IU/ml
Human Recombinant (r - DNA)

In patients with insulin-dependent diabetes, prolonged hyperglycemia can result in diabetic ketoacidosis. The first symptoms of diabetic ketoacidosis usually come on gradually, over a period of hours or days, and include a drowsy feeling, flushed face, thirst, loss of appetite, and fruity odor on the breath. With ketoacidosis, urine tests show large amounts of glucose and acetone. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected, prolonged hyperglycemia or diabetic ketoacidosis 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. Lipoatrophy and lipodystrophy

Lipoatrophy / 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 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.

WOSULIN R

Insulin Human Injection USP 100 IU/ml
Human Recombinant (r - DNA)

e) How to store WOSULIN R.

For Cartridge

Insulin human Regular 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 or may be carried at room temperature (up to 25°C) for up to 4 weeks. Do not expose to excessive heat or direct sunlight. Insulin human Regular Cartridge must be kept out of reach of children.

Insulin preparations, which have been frozen, must not be used. Insulin human Regular solutions should not be used if they do not appear water- clear and colourless.

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.

Insulin human Regular Cartridge should never be used after the expiry date.

For vial

WOSULIN-R should be stored in a refrigerator (+2° C to +8° C) but not allowed to freeze. Once opened, Wosulin R vial should be stored at temperature not above 30°C for upto 6 weeks. Do not expose to excessive heat or direct sunlight. WOSULIN-R must be kept out of reach of children.

Insulin preparations, which have been frozen, must not be used. WOSULIN-R solutions should not be used if they do not appear water-clear and colourless.

Once opened (when the stopper or seal has been punctured with a needle), WOSULIN-R 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).

Do not use WOSULIN-R after the expiration date stamped on the label or if it has been frozen.

f) Further information

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

WOSULIN R

Insulin Human Injection USP 100 IU/ml
Human Recombinant (r - DNA)

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.

Presentation:

WOSULIN R- Cartridge of 3 ml

WOSULIN-R 100 IU/ml - 10ml vial

M. L. No. AD/004

Manufactured in India by WOCKHARDT LIMITED

Biotech Park, H-14/2 MIDC, Waluj, Aurangabad 431 136

® Regd. Trademark of Wockhardt