Instruction of  
Recombinant Human Insulin Isophane Injection

Name:

Generic Name: Recombinant Human Insulin Isophane Injection
Commercial Name: Gansulin N (Dongbao Cartridge)
English Name: Recombinant Human Insulin Isophane Injection
Chinese Spelling: Dijingdanbai Chongzu Renyidaosu Zhusheye

Major Ingredients:
Active Ingredients: recombinant human insulin
Inactive Ingredients: glycerin, disodium hydrogen phosphate, phenol, m-cresol, protamin

Molecular Structure:

\[
\begin{align*}
&\text{Glu-Val-Ile-Gly-H} \\
&\text{Gln-Cys-Cys-Thr-Ser-Ile-Cys-Ser-Leu-Tyr-Gln-Leu-Glu-Asn-Tyr-Cys-Asn-OH} \\
&\text{Gln-His-Leu-Cys-Gly-Ser-His-Leu-Val-Glu-Ala-Leu-Tyr-Leu-Val-Cys-Gly-Glu} \\
&\text{Asn-Val-Phe-H} \quad \text{HO-Thr-Lys-Pro-Thr-Tyr-Phe-Phe-Gly-Arg}
\end{align*}
\]

Formula: \( C_{257}H_{338}N_{65}O_{77}S_6 \)
Molecular Weight: 5807.69

Properties:
This drug is white or white-like aseptic suspension, which will be uniformly suspended after shaking.
The pH ranges from 7.0 to 7.8.

Pharmacology and Toxicology:
The product is human insulin made by DNA recombinant technology so it has the same structures and functions as natural insulin. The product can regulate the glucose metabolism and stimulate the ingestion and utilization of glucose by livers, bones, and fat tissue. It can accelerate the transformation from glucose to glycogen stored in muscles and livers and inhibit the
gluconeogenesis, thus, to lower the blood glucose.

**Pharmacokinetics:**

The starting time and duration of the effect can vary considerably after subcutaneous injection of insulin due to the individual differences. Normally, it comes into effect slowly after injection, reaches its peak within 6-9 hours and lasts about 24 hours.

**Indications:**

Type I or Type II Diabetes.

**Usage & Dosage:**

**Usage**

1. The product is a white or white-like suspension. It should be injected subcutaneously 1 hour before breakfast and dinner. The exact time for administration is suggested by doctors with regard to each individual’s case.

2. Prepare before use
   According to the instruction of Dongbao Pen, insert the Dongbao cartridge into the pen correctly and equip the Dongbao Penfine needle. Gently turn the pen upside down for 8-10 times until the insulin in the cartridge becomes uniformly mixed suspension. Adjust the dosage button to get a correct dose. After remove the needle cap and discharge air bubbles in the cartridge, it is ready to be injected. In order to avoid cross contamination, do not let the needle touch anything during the process of preparation.

3. Injection Site
   Choose the area where skin is less tight, such as the upper arm, thigh, buttock and abdomen, etc. The site for injection should be rotated, that is, one site should not be injected twice in consecutive two weeks. The site should have at least 1 cm from the previous one.

4. Injection Method
   After you have chosen the injection site, you should sanitize the skin by alcohol tampon. After 1-2 minutes of volatilization, stabilize the skin by pinching up or spread it by hand. Put the needle in such a position as to form a 45° angle with the skin. Puncture the needle into skin and then inject the insulin. Then pull the needle out and apply gentle pressure over the injected site for several seconds by alcohol tampon. Do not rub the
injection site for fear that the subcutaneous tissue is damaged and insulin effuses.

Dosage
The dosage form, the dosage and the administration time of the insulin are different due to the individual differences of each patient. In addition, the dosage is also affected by food, working style and exercising intensity. Therefore, patients should use the insulin under doctor’s instructions. Consult your doctor for necessary adjustment in your insulin use in case of illness such as nausea or vomit, significant increase of exercising intensity, or before traveling.

Adverse effect:
Hypoglycemosis is the most common adverse effect during Insulin treatment and the symptoms of hypoglycemosis may occur suddenly. Few cases of the allergic reaction such as local red and swollen, itching, or lipid atrophy and hyperplasia are reported. The systemic allergic reaction (whole body tetter, shortage of breath, asthma, blood pressure drop, pulse acceleration, excessive perspiration, and the severe cases endangering the life) is seldom reported.

1. Lipodystrophy
Subcutaneous injection of insulin rarely causes the lipid atrophy or hyperplasia. If so happens, the doctor should be informed. The situation may be improved by changing the injection method.

2. Insulin Allergy:
   - Local Allergy: The patients occasionally experience the allergic reaction such as red and swollen or itching. These symptoms are called local allergy. It usually disappears in a few days or a few weeks. In some instances, the allergy may be caused by other reasons rather than insulin, such as skin disinfectant and poor injection techniques. If local allergy happens, please contact the doctor immediately.
   - Systemic Allergy: In a case when the whole body is allergic to insulin, it is called systemic allergy. It seldom happens, but it is very serious if it occurs. The symptoms include: whole body tetter, shortage of breath, asthma, blood pressure drop, pulse acceleration, excessive perspiration, and the severe cases endangering the life. If systemic allergy happens, please contact the doctor immediately.

Contraindication:
Hypoglycemosis
This drug is strictly prohibited to the patients who have allergic reaction when using insulin.

Cautions:

1. Diabetic patients should examine regularly the blood glucose or urine glucose. If the examination consistently shows that the blood glucose is above or below normal level or the urine glucose is positive, it means that the diabetes is not properly controlled. You should contact the doctor and keep an extra supply of insulin as well as a spare syringe and needle on hand. The diabetic identification should always be worn so that appropriate treatment can be given if complications occur away from home.

2. Any change of insulin application should be made cautiously and only under instructions of the doctors. Before using the insulin each time, you should carefully examine whether the purity, valence, registered trademark, type, species (cattle, pig or human), method of manufacture (recombinant human insulin, insulin extracted from animals) are suggested by the doctor. Any of the above changes will lead to the adjustment of dosage.

3. Patients, who were on treatment with animal insulin, should adjust dosage under doctor’s instruction when changing to human insulin.

4. Before using, check whether the caps of vial is well-sealed and examine the brand name, letter designation on the label so as to assure that the drug is in accordance with the doctor’s prescription.

5. Before withdrawing the drug, check the appearance of the solution in the bottle first. Recombinant Human Insulin Isophane Injection should be a white or white-like suspension. If there are sediments or groups of floaters still remain in the bottle after shaking, do not use it. In case of anything unusual or need to change the dosage, it should be reported to doctors immediately for advice.

6. Insulin should be stored in the refrigerator under 2-8°C. Be sure not to freeze it or place it near the freezing compartment. Do not use the Insulin that has been frozen. Never use the Insulin that has passed the expiration date. In case the protective cap is not properly sealed, then it should be returned to the pharmacy.

Pregnancy and nursing:
It is more difficult to treat diabetes during pregnancy. Female patients, who plan to be pregnant or are pregnant or during the nursing period, should follow doctor’s instructions.

**Children:**

Special attention should be paid to children’s exercise intensity and diet in order to control blood glucose level when using insulin. Administration should be given by parents or doctors according to prescribed dosage.

**Elderly patients:**

With the change of structures and functions of tissues and organs, the decline of physiological and biochemical strength, and the decline of regulatory function and adaptability, the old people should pay more attention to the use of insulin.

1. Pathological change of adrenal gland, pituitary and hypothyroid or deterioration of liver or kidney disease easily leads to hypoglycemia.
2. Escape or delay of meal dinner will result in hypoglycemia.
3. Designated people should take care of the dosage and injection if necessary.

**Interactive with other drugs:**

When using oral contraceptive drug, adrenal cortical hormone, hypothyroid hormone, etc., the drugs that can result in the rise of blood glucose, you might need to increase the amount of Insulin.

When using drugs with hypoglycemic activities, salicylate, sulfanilamide and other anti-depressants, which will result in the decrease of blood glucose, the dosage of insulin should be reduced.

Pay attention to your diet and avoid alcoholic drinks.

In case you use other drugs at the same time, please ask for the doctor’s advice.

**Excessive dosage of insulin:**

Excessive use of insulin may lead to hypoglycemia during the treatment.

Slight or moderate hypoglycemia may suddenly occur with the following symptoms:

- Sweating
- Dizziness
- Drowsiness
- Insomnia
Palpitation                                Anxiety
Tremor                                     Blurred vision
Hunger                                     Slurred speech
Restlessness                                Depressed mood
Tingling in the hands, feet, tongue and lips     Irritability
Lightheadedness                             Abnormal behavior
Inability to concentrate                   Unsteady movement
Headache                                   Personality changes

The symptoms of the severe hypoglycemia can include follows:
Disorientation                             Seizures
Unconsciousness                             Death

It is important to get immediate treatment when hypoglycemia occurs.
Early warning symptoms of hypoglycemia may be difficult to observe under certain conditions, such as long duration of diabetes, diabetic nerve disease, administration of \( \beta \)-receptor inhibitors, change in insulin preparations or intensified control (3 or more insulin injections per day) of diabetes.
A few patients who have experienced hypoglycemic reactions after change from animal insulin to human insulin have reported the early warning symptoms of hypoglycemia were less pronounced or different from those experienced with their previous insulin.
Without recognition of early warning symptoms, it may be then difficult to avoid more serious hypoglycemia. Therefore it is necessary to monitor blood glucose frequently in order to avoid the occurrence of hypoglycemia.
Slight to moderate hypoglycemia can be adjusted by eating and drinking beverage with sugar. Patients should always carry candy or other glucose tablets. Patients with serious hypoglycemia need other’s assistance. Patients who lose their consciousness and cannot take sugar by themselves require an injection of glucagons or should be treated with intravenous administration of glucose at a medical faculty.
Patients must learn to recognize their own symptoms of hypoglycemia. If you are not sure about these symptoms, you should monitor your blood glucose frequently to help you learn to recognize the symptoms that you experience with hypoglycemia.
If you have frequent hypoglycemia or experience difficulty in recognizing the symptoms, you should consult your doctors to discuss possible changes in therapy, diet plans, and/or exercise programs to help you avoid hypoglycemia.

**Specification**

3 ml / 300 units / pen cartridge
**Storage**

Store under the temperature of 2-8°C. It is better to keep the drug in the refrigerator and do not store it in or close to the freezing box. In case the insulin for recent use cannot be refrigerated, try to keep it in a cool place and keep away from heat and light. The insulin in use can be kept under the room temperature for a month.

**Package**

One cartridge per box
Packing materials: Tube cartridge for antibiotic use, Butyl Bromide Rubber Closure

**Expiry date**

2 years

**Approval Number**

State Drug Approval No. S20020091

**Manufacturer**

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