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34-530 Bukowina Tatrzańska
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Klient: BIOTON
Nazwa projektu: MY Diabulyn ulotka 30/70
Wymiary zewn.: 170 × 390 mm
Indeks materiałowy: Biocon: BC00573/01
Indeks materiałowy: 04-UG-MYF01-01
Nr korekty: 1
Kraj: Malezja
Data: 14.11.2024
Opracowanie: Wojciech Kubina

Kolory:
100% black 471 C
wykrojnik

Zatwierdził: Data:

Package leaflet:

Biocon Biologics™

Diabulyn™- 30/70 (Biphasic)

Insulin Injection, Biphasic Isophane

100 IU/mL

Subcutaneous use

1. NAME OF THE MEDICINAL PRODUCT

Diabulyn™ - 30/70 Insulin Injection, Biphasic Isophane 100 IU/mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Insulin Human	100 IU
(Insulin, Human of recombinant DNA origin)	
m-Cresol	1.5 mg/mL and
Phenol	0.65 mg/mL
(Used as preservatives)	
Water for Injection	q.s.

1 ml of Diabulyn™ - 30/70 suspension contains 100 IU of biphasic human insulin (*Insulinum humanum*) obtained by E. coli recombinant DNA technology process.

Each cartridge for pen contains 3 ml of suspension, corresponding to 300 IU of biphasic insulin, consisting of 30% soluble and 70% isophane insulin.

Diabulyn™- 30/70 contains human insulin only. The product is 100% consistent with the amino acid composition of the insulin produced by humans – unlike animal insulins or other insulin analogues obtained by genetic recombination whose compositions differ from human insulin to various extents.

3. PHARMACEUTICAL FORM

A white suspension which on standing deposits a white sediment and leaves a colourless or almost colourless supernatant liquid, the sediment is readily resuspended by gentle shaking. Diabulyn - 30/70 is a biosimilar medicinal product of Humulin 30/70.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of patients with diabetes mellitus for whom diet and/or oral agents are not sufficient.

4.2 Posology and Method of Administration

Posology

The dosage should be determined by the physician, according to the requirement of the patient.

Paediatric population
No data are available.

Method of Administration

Diabulyn™ - 30/70 should be given by subcutaneous injection but may, although not recommended, also be given by intramuscular injection. These formulations should not be administered intravenously.

Subcutaneous administration should be in the upper arms, thighs, buttocks or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month.

Care should be taken when injecting any Diabulyn™ - 30/70 insulin preparations to ensure that a blood vessel has not been entered. After any insulin injection, the injection site should not be massaged. Patients must be educated to use proper injection techniques.

Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis.

Diabulyn™ - 30/70 formulation is a ready-made defined mixture of soluble and isophane insulin designed to avoid the need for the patient to mix insulin preparations. A patient's treatment regimen should be based on their individual metabolic requirements.

4.3 Contraindications

Hypoglycaemia
Hypersensitivity to the active substance or to any of the excipients listed in the Section 6.1 *List of Excipients*, unless used as part of a desensitisation programme.

Under no circumstances should any Diabulyn™ formulation other than Diabulyn™ - R be given intravenously.

4.4 Special Warnings and Precautions for Use Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type, species (animal, human, human insulin analogue), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.

Some patients taking human insulin may require a change in dosage from that used with animal-source insulins. If an adjustment is needed, it may occur with the first dose or during the first several weeks or months.

A few patients who experienced hypoglycaemic reactions after transfer to human insulin have reported that the early warning symptoms were less pronounced or different from those experienced with their previous animal insulin. Patients whose blood glucose is greatly improved, e.g. by intensified insulin therapy, may lose some or all of the warning symptoms of hypoglycaemia and should be advised accordingly. Other conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, diabetic nerve disease, or medications such as beta blockers. Uncorrected hypoglycaemic and hyperglycaemic reactions can cause loss of consciousness, coma or death.

The use of dosages which are inadequate or discontinuation of treatment, especially in insulin-dependent diabetics, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Treatment with human insulin may cause formation of antibodies, but titres of antibodies are lower than those to purified animal insulin.

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.
Adjustment of insulin dosage may also be necessary if patients change their level of physical activity or change their usual diet.

Combination of Human Insulin with Thiazolidinedione
Cases of cardiac failure have been reported when thiazolidinedione was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind, if treatment with the combination of thiazolidinedione and human insulin is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Thiazolidinedione should be discontinued, if any deterioration in cardiac symptoms occurs.

Skin and Subcutaneous Tissue Disorders
Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site and dose adjustment of antidiabetic medications may be considered.

4.5 Interactions with other medicinal products and other forms of interaction

A number of medicinal products are known to interact with glucose metabolism and therefore the physician should be consulted when using other medications in addition to human insulin (see *Special Warning and Precautions for Use*). The physician must therefore take possible interactions into account and should always ask his patients about any medicinal products they take.

Insulin requirements may be increased by substances with hyperglycaemic activity, such as glucocorticoids, thyroid hormones, growth hormone, danazol, beta2-sympathomimetics (such as ritodrine, salbutamol, terbutaline), thiazides.

Insulin requirements may be reduced in the presence of substances with hypoglycaemic activity, such as oral hypoglycaemics (OHA), salicylates (for example, acetylsalicylic acid), certain antidepressants (monoamine oxidase inhibitors), certain angiotensin converting enzyme (ACE) inhibitors (captopril, enalapril), angiotensin II receptor blockers, non-selective beta-blocking agents and alcohol.

Somatostatin analogues (octreotide, lanreotide) may both decrease or increase insulin dose requirements.

4.6 Fertility, pregnancy and lactation

It is essential to maintain good control of the insulin treated (insulin-dependent or gestational diabetes) patient 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.

Patients with diabetes who are lactating may require adjustments in insulin dose and/or diet.

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Hypoglycaemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, and in extreme cases, death. No specific frequency for hypoglycaemia is presented, since hypoglycaemia is a result of both the insulin dose and other factors e.g. a patient`s level of diet and exercise.

Local allergy in patients is common (1/100 to < 1/10).

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Redness, swelling, and itching can occur at the site of insulin injection. This condition usually resolves in a few days to a few weeks. In some instances, local reactions may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique.

Systemic allergy, which is very rare (< 1/10,000) but potentially more serious, is a generalised allergy to insulin. It may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalised allergy may be life-threatening. In the rare event of a severe allergy to Diabulyn™ – 30/70, treatment is required immediately. A change of insulin or desensitisation may be required.

Lipodystrophy at the injection site is uncommon (1/1,000 to < 1/100).

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Skin and subcutaneous tissue disorders
Not known - Cutaneous amyloidosis
Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions.

4.9 Overdose
Insulin has no specific overdose definitions, because serum glucose concentrations are a result of complex interactions between insulin levels, glucose availability and other metabolic processes. Hypoglycaemia may occur as a result of an excess of insulin relative to food intake and energy expenditure.

Hypoglycaemia may be associated with listlessness, confusion, palpitations, headache, sweating and vomiting.

Mild hypoglycaemic episodes will respond to oral administration of glucose or sugar products.

Correction of moderately severe hypoglycaemia can be accomplished by intramuscular or subcutaneous administration of glucagon, followed by oral carbohydrate when the patient recovers sufficiently. Patients who fail to respond to glucagon must be given glucose solution intravenously.

If the patient is comatose, glucagon should be administered intramuscularly or subcutaneously. However, glucose solution must be given intravenously, if glucagon is not available or if the patient fails to respond to glucagon. The patient should be given a meal as soon as consciousness is recovered.

Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may occur after apparent clinical recovery.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamics Properties Pharmacotherapeutic group: Insulins and analogues for injection. intermediate acting insulin (human).

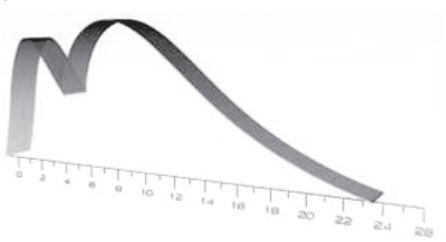
ATC Code: A10A D01

The prime activity of insulin is the regulation of glucose metabolism.

In addition, insulin has several anabolic and anti-catabolic actions on a variety of different tissues. Within muscle tissue this includes increasing glycogen, fatty acid, glycerol and protein synthesis and amino acid uptake, while decreasing glycogenolysis, gluconeogenesis, ketogenesis, lipolysis, protein catabolism and amino acid output.

The typical activity profile (glucose utilisation curve) following subcutaneous injection is illustrated below by the heavy line. Variations that a patient may experience in timing and/or intensity of insulin activity are illustrated by the shaded area. Individual variability will depend on factors such as size of dose, site of injection temperature and physical activity of the patient.

Diabulyn™ - 30/70 (Biphasic)
activity



Time (hours)

5.2 Pharmacokinetic properties
The pharmacokinetics of insulin do not reflect the metabolic action of that hormone. Therefore, it is more appropriate to examine glucose utilisation curves (as discussed above) when considering the activity of insulin.

5.3 Preclinical safety data
Diabulyn™ - 30/70 is human insulin produced by recombinant technology. No serious events have been reported in subchronic toxicology studies. Human insulin was not mutagenic in a series of in vitro and in vivo genetic toxicity assays.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
m-cresol, Phenol, Glycerol, Protamine sulphate, Zinc oxide, Hydrochloric acid, Sodium hydroxide, Disodium hydrogen phosphate dodecahydrate and Water for Injections.

The following may be used to adjust pH;
Hydrochloric acid and/or Sodium hydroxide.

6.2 Incompatibilities
Diabulyn™ - 30/70 preparations should not be mixed with insulins produced by other manufacturers or with animal insulin preparations.

6.3 Shelf life
Unopened cartridge
Please refer to carton/label

In- use
42 days.

6.4 Special precautions for storage
Unopened Cartridge
Store in a refrigerator at temperature between 2°C and 8°C.
Do not freeze.
Keep the cartridge in the outer carton in order to protect from light.
Protect from excessive heat and sunlight.
Keep out of reach of children.
Jauhi daripada kanak-kanak.
The container should be gently shaken before a dose is dialed.

In-use instruction
Do not refrigerate. Do not freeze. Diabulyn-30/70 cartridges that are in use can be kept at a temperature (not above 30°C) for up to 42 days.

6.5 Nature and content of container
3 mL colourless glass cartridges (Type 1) sealed using lined seals, plugged with plunger stoppers and glass bead.

Pack Size: Available in 5 x 3 mL pack only

6.6 Special Precautions for Disposal and Other Handling
Do not reuse needles. Dispose of the needle in a responsible manner. Needles must not be shared. Cartridges can be used until empty, then properly discard. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Instructions for use and handling
A suspension for injection in a 3mL cartridge to be used in conjunction with INSUPen Pro+ (reusable pen) only. Please refer to User Manual for more information.

a) Preparing a dose
Before using the reusable pen, the user manual must be read carefully. The reusable pen must be used as recommended in the user manual. Pens should not be used if any part looks broken or damaged.

The cartridges should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving a frosted appearance.

b) Injecting a dose
Refer to the detailed instructions for preparing the pen and injecting the dose, the following is a general description.

1. Wash your hands.
2. Choose a site for injection.
3. Clean the skin as instructed.
4. Stabilise the skin by spreading it or pinching up a large area. Insert the needle and inject as instructed.
5. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.
6. For an injection device use the outer needle cap, unscrew the needle and dispose of it safely.
7. Use of the injection sites should be rotated so that the same is not used more than approximately once a month.

7. PRODUCT REGISTRATION HOLDER, MANUFACTURER, BATCH RELEASER, IMPORTER & DISTRIBUTOR

Product Registration Holder:
Biocon Sdn. Bhd.
No. 1, Jalan Bioteknologi 1,
Kawasan Perindustrian SiLC,
79200 Iskandar Puteri, Johor, Malaysia.

Manufacturer and Batch Releaser:
Bioton S.A.
Macierzysz, ul. Poznańska 12
05-850 Ożarów Mazowiecki, Poland.

Importer and Distributor:
Duopharma Marketing Sdn. Bhd.
Lot No. 2, 4, 6, 8 & 10, Jalan P/7, Section 13,
Bangi Industrial Estate, 43650 Bandar Baru Bangi,
Selangor Darul Ehsan, Malaysia.

8. DATE OF REVISION
March 2026

04-UG-MYF01-01
BC00573/01