Biphasic Isophane Insulin Injection IP

INSUGEN[®] - ⁵⁰/₅₀ (Biphasic) इन्सुजेन -५%

INSUGEN®-50/50 (Biphasic) (Biphasic Isophane Insulin Injection IP)

COMPOSITION

Each mL contains Human Insulin IP 40 IU (50% as soluble insulin injection and 50% as isophane insulin injection) (Human Insulin of recombinant DNA origin) m-Cresol USP 0 16% w/v Phenol IPO 065% w/v Water for injection IP q.s. One IU (International Unit) of insulin is equivalent to 0.035 mg of human insulin For a full list of excipients, see List of excipients section.

PHARMACEUTICAL FORM

Suspension for injection in a vial. Cloudy white aqueous suspension

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties Pharmacotherapeutic group: Insulins and analogues for injection, intermediate-acting combined with fast-acting, insulin (human). ATC Code: A10AD01

Mechanism of Action

The blood glucose lowering effect of insulin is due to the facilitated uptake of glucose following binding of insulin to receptors on muscle and fat cells and to the simultaneous inhibition of glucose output from the liver

INSUGEN®-50/50 is dual-acting insulin. Onset of action is within ½ hour, reaches a maximum peak effect within 2 to 8 hours and the entire duration of action is up to 24 hours.

Pharmacokinetic Properties

Insulin in the blood stream has a half-life of a few minutes. Consequently, the time-action profile of an insulin preparation is determined solely by its absorption characteristics. This process is influenced by several factors (e.g. insulin dosage, injection route and site, thickness of subcutaneous fat, type of diabetes). The pharmacokinetics of insulir products are therefore affected by significant intra- and inter-individual variation. Absorption

The absorption profile is due to the product being a mixture of insulin products with fast and protracted absorption respectively. The maximum plasma concentration of the fast-acting insulin is reached within 1.5 to 2.5 hours after subcutaneous administration. Distribution

No profound binding to plasma proteins, except circulating insulin antibodies (if present) has been observed Metabolism

Human insulin is reported to be degraded by insulin protease or insulin-degrading enzymes and possibly protein disulfide isomerase. A number of cleavage (hydrolysis) sites on the human insulin molecule have been proposed; none of the metabolites formed ving the cleavage are active Elimination The terminal half-life is determined by the rate of absorption from the subcutaneous

The contribution of the decomposition of the contribution of the absorbing and the decomposition of the decomposition rather than of the elimination per set of insulin from plasma (insulin in the blood stream has a t_n of a few minutes). Trials have indicated a t_n of about 5 to 10 hours.

Preclinical Safety Data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction

CLINICAL PARTICULARS Therapeutic Indication

INSUGEN[®]-50/50 for the treatment of diabetes mellitus in patients who requires injectable insulin

logy and Method of Administration

INSUGEN*50/50 is dual-acting insulin. It is biphasic formulation containing both fast-acting and intermediate-acting insulin. Premixed insulin products are usually given once or twice daily when a rapid initial effect together with a more prolonged effect is desired

Dosage

Dosing is individual and determined in accordance with the needs of the patient. The individual insulin requirement is usually between 0.3 and 1.0 IU/kg per day. The daily insulin requirement may be higher in patients with insulin resistance (e.g. during puberty or due to obesity) and lower in patients with residual, endogenous insulin production. In patients with diabetes mellitus optimised glycaemic control delays the onset of late diabetic complications. Close blood glucose monitoring is therefore recommended. An injection should be followed within 30 minutes by a meal or snack containing

Dosage adjustment in special populations

Renal and Hepatic Impairment Renal or hepatic impairment may reduce insulin requirement. As with all insulin medicinal products, in patients with renal or hepatic impairment, glucose monitoring should be intensified and the human insulin dose should be adjusted on an individual basis

Paediatrics In general, paediatric patients with type 1 diabetes are more susceptible to hypoplycaemia than adult patients with type 1 diabetes. As in adults, the dosage of insulin must be individualized in paediatric patients based on metabolic needs and frequent monitoring of blood glucose

Geriatrics

Use caution in patients with advanced age, due to the potential for decreased renal function in this population. <u>Transfer from other insulin medicinal products</u> Adjustment of dosage may also be necessary if patients change physical activity or their

usual diet. Dosage adjustment may be necessary when transferring patients from one insulin preparation to another. Close glucose monitoring is recommended during the transfer and in the initial weeks thereafter (see Special Warnings and Precautions for Use section)

Others Concomitant illness, especially infections and feverish conditions, usually increases the

atient's insulin requirement Administration



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40 IU/mL

10 mL

absorption than from other injection sites Injection into a lifted skin fold minimises the risk of unintended

INSUGEN[®]-50/50 should be administered 30 minutes before a meal. The needle should be kept under the skin for at least 6 seconds to make sure the entire dose is injected. If blood appears after the needle has been withdrawn, press the injection site lightly with a

finger Injection sites should be rotated within an anatomic region in order to avoid lipodystrophy. The vials are for use with insulin syringes with a corresponding unit scale

Instructions to be given to the patient

efore injecting this insulin, Wash hands with soap and water

Disinfect the rubber stopper with an alcohol swab

- Roll the vial between the palms of the hands until the liquid is uniformly white and cloudy. Resuspending is easier if the insulin has reached room temperature.
- Draw air into the syringe, in the same amount as the volume of insulin to be injected Inject the air into the vial: push the needle through the rubber stopper and press the
- plunger. Turn the vial and syringe upside down
- Draw the correct dose of insulin into the syringe.

Pull the needle out of the vial. Make sure that there is no air left in the syringe: point the needle upwards and push the air out.

10. Check you have the right dose 11. Inject the insulin into the subcutaneous tissue

Contraindications INSUGEN[®]-50/50 is contraindicated in the patients with:

Hypersensitivity to the active substance or to any of the excipients (see List of Excipients section).

Hypoglycaemia.

Special Warnings and Precautions for Use Before travelling between different time zones, the patient should be advised to consult the physician, since the patient may have to take insulin and meals at different times. Always use a new needle and syringe each time you take INSUGEN®-50/50 injection to

Missed dose/change of insulin

In case of missed dose, measure the blood glucose and add a dose of regular insulin if glucose levels are too high. Otherwise, it is recommended to wait for the next scheduled dose. Any change of dose or transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand anoand oe ooke made ander ander ander ander ander ander et al. (in ander ande when switching the patients to INSUGEN®-50/50, it may occur with the first dose o during the first several weeks or months.

A few patients who have experienced hypoplycaemic reactions after transfer from animal source insulin have reported that early warning symptoms of hypoglycaemia were less pronounced or different from those experienced with their previous insulin.

Hyperglycaemia

ate dosage or discontinuation of treatment especially in type 1 diabetes may Inadequate Gospital or Galocality and the sentence of the sent acetone odour of breath. In type 1 diabetes, untreated hyperglycaemic events eventually lead to diabetic ketoacidosis, which is potentially lethal. Hypoglycaemia

Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requiriment (see Undericable Effective Constraints)

ripodyczemia may occur in reie maun obce s too ringri in reason to me insuan Omision of a meal or unplanned, strenuus physical sercices may lead to hypodycaemia. Patients whose blood glucose control is greatly improved e.g. by interstieli misuih treagy, may experience a change in their usual varming symptoms of hypodycaemia and should be advised accordingly. Intravenously administered insulin, resulting a more rapid orasi of action than subcultaneously administered insulin, resulting misuing more and on a mean subcultaneously administered insulin, resulting more may do may to action than subcultaneously administered insulin, resulting more may do may to action than subcultaneously administered insulin, resulting more means that the subcultaneously administered insulin, resulting more means that the subcultaneously administered insulin, resulting more means that the subcultaneously administered multin, resulting more means that the subcultaneously administered multin, resulting more means that the subcultaneously administered multin, resulting more means that the subcultaneously administered multin means that the subcultaneously administered multing more means that the subcultaneously administered multing means that the subcultaneously administered multing more means that the subcultaneously administered multing more means that the subcultaneously administered multing means the subcultaneously administered multing means the subcultaneously administered multing more means the subcultaneously administered multing means the subcultaneou

close monitoring for hypoglycaemia. As with all insulins, use caution in patients with hypoglycaemia unawareness and in patients who may be predisposed to hypoglycaemia (e.g. patients who are fasting or have erratic food intake, paediatric patients, and the elderly). The patient's ability to reare estudie rode instance; plocamoic plasme, while the tead rymmic plasme, and tead rymmic plasme, and tead rymmic plasme, and the tead rymmic plasme, and te

section) Usual warning symptoms may disappear in patients with long-standing diabetes

Hypokalaemia

All insulins, including INSUGEN[®]-50/50, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalaemia that, if left untreated, may cause respiratory paralysis, ventricular arrhythmia, and death. Use caution in patients who may be at risk for hypokalaemia (e.g., patients using potassium-lowering medications and patients taking medications sensitive to serum potassium concentrations). Hypersensitivity reactions

Local reactions

As with any insulin therapy, injection site reactions may occur and include pain, itching As wird any insum therapy, injection site reactions induced and include pain, include pain, hives, swelling and inflammation. Continuous rotation of the injection site within a given area may help to reduce or prevent these reactions. Reactions usually resolve in a few days to a few weeks. Or rare occasions, injection site reactions may require discontinuation of INSUGEN%50/50

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Severe, life-threatening, generalized allergy, including anaphylaxis may occur with any insulin, including INSUGEN[®]-50/50. Generalized allergy to insulin may manifest as a

For the use of only a registered medical practitioner or hospital or laboratory

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generalised skin rash, itching, sweating, gastrointestinal upset, and angioneurotic oedema, difficulties in breathing, palpitation, reduction in blood pressure and fainting /loss of consciousness. Generalised hypersensitivity reactions are potentially

A specific overdose of insulin cannot be defined. However, hypoglycaemia may develop over sequential stages:

Mild hypoglycaemic episodes can be treated by oral administration of glucose or sugary products. It is therefore recommended that the diabetic patients carry some sugar lumps, sweets, biscuits or sugary fruit juice.

Severe hypoplycaemic episodes, where the patient has become unconscious, can be

treated by glucago (0.5 to 1 mg) given intramuscularly or subcutaneously by a person who has received appropriate instruction, or by glucose given intravenously

by a medical professional. Glucose must also be given intravenously, if the patient

does not respond to glucagon within 10 to 15 minutes. Upon regaining consciousness, administration of oral carbohydrate is recommended for the patient in order to prevent relapse.

List of Excipients Glycerol, Metacresol, Hydrochloric acid, Sodium hydroxide, Protamine Sulphate, Zinc

Insulin products should only be added to compounds with which it is known to be compatible.

Unopened vials: Store in a refrigerator at temperature between 2°C and 8°C. Donot freeze.

Vals during use vials that are in use can be kept at a temperature not above 25°C up to 6 weeks. It should not be allowed to freeze.

Special Precautions for Disposal and Other Handling Insulin preparations which have been frozen must not be used. After removing INSUGEW-50/50 vial if from the refrigerator it is recommended to allow

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Any unused product or waste material should be disposed of in accordance with local

INSUGEN⁶:50/50 is available as 10 mL glass vials (USP Type I) closed with bromobutyl rubber stopper and sealed with aluminium flip-off seal. These vials are packed in a carton

In case of any product related complaints or adverse events related to Biocon products,

Call Toll Free No.: 1800-102-9465 OR visit our website www.biocon.com and fill voluntary reporting form available under 'Report Adverse EventSide Effects and Product Complaints' and send the duly filled form to us at drugssfeyt@biocon.com. For general

queries regarding diabetes and its management. Call Toll Free No.: 1800-425-7667

Overdose

PHARMACEUTICAL PARTICULARS

Incompatibilities

Please refer to carton/labe

Storage and Precautions

Keep out of reach of children.

after resuspension.

Pack sizes: 1v10 ml

Markotod by

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Protect from excessive heat and sunlight

Nature and Contents of Container

Biocon Biologics India Limited

Leaflet Revised: December 2019

Biocon House, Semicon Park, Electronics City, Phase - II,

Bengaluru - 560 100 India

- Registered trademark

ong with prescribing information sheet

Shelf Life

Oxide, Phenol, Dibasic sodium phosphate, Water for Injection

Insulin suspensions should not be added to infusion fluids.

Do not store in or too near the freezer section or cooling elemen

Keep the vial in the outer carton in order to protect from light.

40 IU/mL

10 mL

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whole body rash (including pruritus), dyspnea, wheezing, hypotension, tachycardia, or diaphoresis. INSUGEN®50/50 contains metacresol, which may cause allergic reactions. Due to the risk of precipitation in pump catheters, **INSUGEN®-50/50** should not be used in insulin pumps for continuous subcutaneous insulin

Fluid retention and heart failure with concomitant use of PPAR-

gamma agonists Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists including pioglitazone, can cause dose related fluid retention, particularly when used in combination with

insulin. Fluid retention may lead to or exacerbate heart failure. Patients treated with insulin, including INSUGEN[®] 50/50, and a PPAR-gamma agonist should be observed for signs and symptoms of heart failure. If heart failure develops, it should be managed according to current standards of care, and discontinuation or dose reduction of the PPAR-gamma agonist must be considered

Special Populations As with other insulins, the dose requirements for INSUGEN®50/50 may be reduced in

patients with renal or hepatic impairment. se adjustment for INSUGEN[®]-50/50 is recommended in paediatrics and geriatrics (see logy and Method of Administration section)

Drug Interactions A number of medications affect glucose metabolism that may require insulin dose adjustment and particularly close monitoring for hypoglycaemia or worsening glycaemic

The following are examples of medications that may increase the blood glucose-low effect of insulin and increase susceptibility to hypoglycaemia: oral antidiabetic medications, pramlintide acetate, angiotensin converting enzyme (ACE) inhibitors Honowaski, Antonia Markan, Antone - anguata ang Anguata ang Anguata ang Anguata ang effect of insulin, leading to worsening of glycaemic control; corticosteroids, niacin danazol, diuretics, sympathomimetic agents (e.g., epinephrine, salbutamol, terbutaline), isoniazid, phenothiazine derivatives, somatropin, thyroid hormones, estrogens, progestogens (e.g., in oral contraceptives), and atypical antipsychotics. Beta-blockers, clonidine, and lithium salts may either potentiate or weaken the blood glucose lowering effect of insulin.

Alcohol can increase susceptibility to hypoglyca

Pentamidine may cause hypoglycaemia, which may sometimes be followed by hyperglycaemia. The signs of hypoglycaemia may be reduced or absent in patients taking sympatholytic

medications such as beta-blockers, clonidine, guanethidine, and reserpine

Pregnancy and Lactation

There are no restrictions on treatment of diabetes with insulin during pregnancy, as insulin does not pass the placental barrier. Both hypoglycaemia and hyperglycaemia, which can occur in inadequately controlled diabetes therapy, increase the risk of malformations and death *in utero*. Intensified control in the treatment of pregnant women with diabetes is therefore recommended

Environment of programment of programment representation of the second and the contemplating pregnancy. Insulin requirements usually fall in the first trimester and subsequently increase during the second and third trimesters.

After delivery, insulin requirements return rapidly to pre-pregnancy values. Insulin treatment of the nursing mother presents no risk to the baby. However, the INSUGEN⁵ 50/50 docsage may need to be adjusted.

Effects on Ability to Drive and Use Machines

The patient's ability to Drive and USE watchings 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.

Undesirable Effects

of diabetic retinopathy.

transitory nature.

Immune system disorders: Urticaria, rash

As for other insulin products, in general, hypoglycaemia is the most frequently occurring undesirable effect. Weight gain is common when taking insulin. It may occur if the insulin drose is too high in relation to the insulin requirement. In clinical trials and during marketed use, the frequency varies with patient population and dose regimens. Therefore, no specific frequency can be presented. Severe hypoglycaemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent uneaccount of brain function or even death. Frequencies of adverse drug reactions from clinical trials that are considered related to biphasic insulin are listed below. Within each frequency grouping, undestable effects are presented in order of decreasing seriousness. Side effects reported uncommonly (≥1/1,000 to <1/100) Nervous system disorders (Peripheral neuropathy); Fast improvement in blood glucose

control may be associated with a condition termed "acute painful neuropathy", which is

Diabetic retinopathy: Long-term improved glycaemic control decreases the risk of

progression of diabetic retinopathy. However, intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening

Skin and subcutaneous tissue disorders (Lipodystrophy): Lipodystrophy may occur at the

injection site as a consequence of failure to rotate injection sites within an area. General disorders and administration site conditions (injection site reactions). Injection site reactions (redness, swelling, itching, pain and haematom at the injection site) may

occur during treatment with insulin. Most reactions are transitory and disappear during

Oedema: it may occur upon initiation of insulin therapy. These symptoms are usually of

Side effects reported very rarely (<1/10,000) Eve disorders (Refraction disorders): Refraction anomalies may occur upon initiation of

Anaphylactic reactions: Symptoms of generalised hypersensitivity may include

insulin therapy. These symptoms are usually of transitory nature.