STATUS FORMAT FOR APPROVAL OF ARTWORK		**M. J. BIOPHARM PVT. LTD.** L-7, MIDC Indl. Area, Taloja, Dist. Raigad - 410 208, Maharashtra, INDIA.
SOP No. : QAP - 001	**Format No. : QAP:001:F2:02**	

Product Name		**Country**	Export
Generic Name	Insulin Injection	**Size**	220 x 180 mm
PM Item	PIL	**Supersedes**	-----
Language	English	**New Item code**	LF0XXXX
Manufactured by	M. J. Biopharm Pvt. Ltd.	**Colour Shades**	■ Black
Manufactured for:/ Marketed By	Generix Laboratories Pvt. Ltd.		
Specifications:	60 gsm JK maplitho paper		

Insulin Injection

Vial

COMPOSITION:

1. Insulin Injection, Soluble Ph. Eur
Each ml contains

Insulin Human Ph. Eur. (Human Insulin rDNA origin)	100 IU
Meta-cresol (as preservative) USP	0.25 % W/V
Water for Injection USP	qs

2. Insulin Injection, Isophane Ph. Eur
Each ml contains

Insulin Human Ph. Eur. (Human Insulin rDNA origin)	100 IU
Meta-cresol (as preservative) USP	0.16 % W/V
Phenol (as preservative) USP	0.065% W/V
Water for Injection USP	qs

3. Insulin Injection, Biphasic Isophane Ph. Eur
Each ml contains

Insulin Human Ph. Eur. (Human Insulin rDNA origin) (30% as Soluble Insulin Injection & 70% as Isophane Insulin Injection)	100 IU
Meta-cresol (as preservative) USP	0.16 % W/V
Phenol (as preservative) USP	0.065% W/V
Water for Injection USP	qs

QUALITATIVE & QUANTITATIVE COMPOSITION:
1 ml contains 100IU of human insulin (produced in E. coli by recombinant DNA technology)
One vial contains 10 ml equivalent to 1000 IU of human insulin for 100 IU vials respectively.

DOSAGE FORM:
Solution for injection: **Insulin Injection, Soluble Ph. Eur**
Suspension for injection: **Insulin Injection, Isophane Ph. Eur, Insulin Injection, Biphasic Isophane Ph. Eur**

CLINICAL PHARMACOLOGY:
Therapeutic Indication:
Insulin is indicated for the treatment of patient with Diabetes Mellitus, Maintain normal glucose homeostasis in patient with diabetes.

Posology and administration
Posology
The dosage should be determined by the physician, according to the need of the patient.
Method of administration
All Insulin vial preparations are for subcutaneous injection. Additionally Insulin Injection Soluble may be administered by intravenous infusion.
Use sterile 100 IU syringe.
While administering through subcutaneously (in abdominal wall, thigh, upper arm, or buttocks), Rotate injection sites to reduce risk of lipodystrophy and localized cutaneous amyloidosis. Individualize and adjust dosage based on metabolic needs, blood glucose monitoring results and glycemic control goal.
If intravenous infusion is chosen for Insulin Injection Soluble then it should be administered ONLY under medical supervision at concentrations from 0.1 unit/mL to 1 unit/mL in infusion systems containing 0.9% sodium chloride.

When administered subcutaneously care should be taken when injecting to ensure that a blood vessel has not been entered. After injection, the site of injection should not be massaged. Patients must be educated to use the proper injection techniques.

Contraindications
Hypoglycemia (low blood sugar)
Hypersensitivity to human insulin or any of the excipients
Under no circumstances should any Insulin formulation other than Insulin Injection Soluble be given intravenously.

Special Warning and Precautions for Use
Any change of insulin (e.g. Brand, source, purity, and strength) should be made with caution and only under medical supervision. Dose adjustments may be required. Appropriate testing should be conducted prior to initiation of Insulin treatment in patients who have previously developed generalized allergic reactions to insulin preparations.
The requirement of insulin may be affected by high fever; severe infection; emotional stress; gastrointestinal disorders, especially nausea, vomiting and diarrhea; pituitary, adrenal or thyroid gland disorders. The usual dose should be reviewed by a doctor in these conditions, and the patient should monitor glucose levels in blood/urine frequently. The most frequent adverse reactions experienced by insulin users is hypoglycemia (Low blood sugar). If this condition is severe, immediate medical help is necessary. Early warning symptoms of hypoglycemia may be less pronounced or different under certain conditions e.g. changing form animal insulin to human insulin, long duration of diabetes, diabetic neuropathy, and use of beta-blockers. The onset and intensity of the symptoms may vary between patients. If such symptoms occur frequently, even if they are mild, patients should seek medical advice to change the insulin dose or diet. If uncertain about the symptoms, the patient should learn to monitor the level of glucose in blood and urine frequently to familiarize themselves with the symptoms of hypoglycemia.

Patients who intend to travel across more than two time zones should consult their doctor concerning adjustments in insulin injection schedule. Exercise may lower the body's requirement for insulin during and for some time after the activity. It may also speed up onset of effect of an insulin dose, especially if the area of injection site is involved. Patients should discuss with the doctor concerning changes in dosing regimen to accommodate exercise e.g. not to inject insulin into a thigh before running. It is not known if correct dosing of Insulin may affect the ability to drive or operate machinery.
However, hyperglycemia may lead to disturbances of the central nervous system affecting vision and distance assessment. Patients should be cautious when driving or using machinery in situations where considerable differences in blood glucose concentration may occur, such as at the commencement of insulin treatment, change of insulin preparation, when under stress, and during excessive physical exertion.
Combination of human insulin with thiazolidinediones Cases of cardiac failure have been reported with the usage of thiazolidinediones in combination with insulin, especially in patients with multiple risk factors predisposing to cardiac heart failure. If treatment in combination of insulin and pioglitazone is considered patients should be observed for signs and symptoms of heart failure, weight gain and edema.
Discontinue thiazolidinediones, if any deterioration in cardiac symptoms occurs.
Avoid sharing of needles or syringes between patients in order to avoid transmission of blood-borne pathogens.

Drug Interactions: Drugs interacting with human insulin may increase the risk of hypoglycemia or may decrease the blood glucose lowering effect of human insulin or may increase/decrease blood glucose lowering effect of human insulin or may blunt the signs and symptoms of hypoglycemia.

The following substances may interact with the insulin preparations: Oral hypoglycaemics, beta-blockers, ACE inhibitors, MAO inhibitors (antidepressants), methyldopa, salicylates, alcohol, anabolic steroids, sulfonamide antibiotics, tetracycline, antibacterial quinolones, alpha-adrenalin, isoniazid phenothiazides, -2 stimulants (such as salbutamol, terbutaline), lithium salts, clonidine, alcohol.

USE IN SPECIAL POPULATION:
Use in renal and hepatic impairment: Insulin is metabolized mainly in liver and kidneys. Its duration of action is prolonged in patients with kidney or liver impairment. Dose reduction of Insulin is required in these patients.
Use in Pregnancy: It is essential to maintain continuous good control of glycaemia among diabetics requiring insulin throughout the pregnancy as hyperglycemia may harm the fetus. Management of the condition may be more difficult since insulin requirement changes during pregnancy. Patients who are pregnant or planning to become pregnant should consult the doctor.
Use in lactation: There are no restrictions on treatment of diabetes with Insulin during lactation. Insulin treatment of the nursing mother is not expected to affect the baby. However, the dosages of Insulin may need to be adjusted.
Use in Geriatrics: Patients with advanced age using any insulin, including Insulin may be at risk of hypoglycaemia due to co-morbid disease and polypharmacy.

EFFECT ON PATIENT'S ABILITY TO DRIVE AND USE MACHINE: Patient's ability concentrate and react may be impaired as a result of hypoglycemia. This may constitute risk in situations where these abilities are of special importance (e.g. car driving or operating machine). Advise patients for taking precautions to avoid hypoglycemia while doing activities like driving or operating machinery, importantly in particular to those who lack awareness of the warning sign of hypoglycemia or have frequent episodes of hypoglycemia.

UNDESIRABLE EFFECTS:
Hypoglycaemia
Symptoms of hypoglycemia usually occur suddenly. They may include hyperhidrosis, dizziness, trembling, sensation of hunger, anxiety, and tingling sensation in hands, feet, lips or tongue, concentration disturbance, sleepiness, sleep disturbances, loss of self-control, dilation of the pupils, visual disorders, speech disturbances, and irritability. Severe hypoglycemia may lead to unconsciousness and may result in temporary or permanent impairment of brain function or even death.
Hypokalemia:
Human insulin can cause a shift in potassium from the extracellular to intracellular space, leading to hypokalemia Peripheral Edema: Human insulin may cause sodium retention and edema, particularly, if previously poor metabolic control is improved by intensified insulin therapy. Weight Gain: Weight gain can occur with insulin therapy, including human insulin and has been attributed to the anabolic effects of insulin.
Lipodystrophy:
Other adverse events that occasionally occur during treatment with biosynthetic insulin are: allergy to insulin, insulin resistance, post-insulin lipodystrophy (atrophy or over growth of fat tissue in the area of injection). However, lipodystrophy may be minimized by rotating the site of injection. Patients should inform their doctor if they experience any adverse reaction while using the product.
Localized Cutaneous Amyloidosis (LCA):
LCA at the injection has occurred. Hyperglycemia has been reported with repeated insulin injections into areas of localized cutaneous amyloidosis; hypoglycemia has been reported with a sudden change to an unaffected injection site.
Immunogenicity: As with all therapeutic peptides, insulin administration may cause anti-insulin antibodies to form. The incidence of antibody formation with human insulin is unknown.

OVERDOSE
Overdose may cause hypoglycemia and hypokalemia. Treatment of mild to moderate hypoglycemia: If the patient is conscious and co-operative, a readily available sugar-containing food (or small quantity of glucose powder) should be offered. This should then be followed by a longer acting carbohydrate (such as a sandwich or dried fruit).
Treatment of severe hypoglycemia: Glucagon is generally used for treating hypoglycemia outside hospital. For adults and children 5 years and above who are unable to take oral food or fluids the dose of glucagon is 1 mg injected subcutaneously or intramuscularly. If intravenous access is available, 20 to 30 ml glucose 50% should be administered through a securely positioned catheter.
For children under 5 years, the dose of glucagon is 0.5 mg injected intramuscularly or subcutaneously followed by oral feeding when conscious. If intravenous access is available, a 2 ml/kg bolus 10% glucose solution should be given, followed by 0.1 ml/kg/minute until the patients is fully conscious.

PHARMACOLOGICAL PROPERTIES
Mechanism of action: Insulin lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat and by inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis, and enhance protein synthesis. The administration of appropriate doses of insulin to patients with diabetes mellitus along with controlled diet and exercise, temporarily restores their ability to metabolize carbohydrates, fats and proteins, store glycogen in the liver, and convert glucose to fat. When given to a diabetic patient at appropriate doses and dosage intervals, the blood glucose level is maintained within a reasonable range, urine remains relatively

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QA Packaging	**RA**	**F & D**	**Production**	**Purchase**

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L-7, MIDC Indl. Area, Taloja, Dist. Raigad - 410 208,
Maharashtra, INDIA.

Product Name		**Country**	Export
Generic Name	Insulin Injection	**Size**	220 x 180 mm
PM Item	PIL	**Supersedes**	-----
Language	English	**New Item code**	LF0XXXX
Manufactured by	M. J. Biopharm Pvt. Ltd.	**Colour Shades**	■ Black
Manufactured for:/ Marketed By	Generix Laboratories Pvt. Ltd.		
Specifications:	60 gsm JK maplitho paper		

free from glucose and ketone bodies, and diabetic complications like acidosis and coma are prevented.

Pharmacodynamics:
Insulin Injection, Soluble Ph. Eur: Regular short acting insulin
Insulin Injection, Isophane Ph. Eur: Intermediate acting insulin
Insulin Injection, Biphasic Isophane Ph. Eur: Mixture of intermediate acting insulin with short acting insulin.

The primary activity of insulin Human r-DNA is the regulation of glucose metabolism. In addition, insulins have 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.

Pharmacokinetics:
In healthy subjects, approximately 5% of Insulin is bound to plasma proteins. Insulin can also be detected in cerebrospinal fluid at a concentration of approximately 25% of total serum insulin concentration. Insulin is metabolized by the liver and kidneys, and to a lesser extent in fat and muscle tissue. It is eliminated by the kidneys, and minute quantities are also eliminated in bile. The elimination half-life is approximately 4 minutes. Hepatic or renal impairment, which is often associated with ageing patients, may delay insulin elimination. The various preparations of Insulin are formulated to provide short intermediate and biphasic therapeutic action. In clinical practice, the duration of Insulin action may vary from that specified below. As with all insulin preparations, variations between and within patients may occur depending upon injection site, dosage, diet, temperature and physical activity.

Presentation	Onset of effect	Maximum effect	Duration of effects
Insulin Injection, Soluble Ph.Eur. 100 IU/ml	Within 30 minutes	1-3 hours	Upto 08 hours
Insulin Injection Isophane Ph.Eur. 100 IU/ml	Within 1.5 hours	3-10 hours	Upto 24 hours
Insulin Injection Biphasic Isophane Ph.Eur. 100 IU/ml	Within 30 minutes	2-8 hours	Upto 24 hours

NON-CLINICAL PROPERTIES:
In in vitro tests, including binding to insulin receptor sites and effects on growing cells, insulin Human r-DNA behaved in a manner that closely resembled human insulin. Acute, one month and twelve month toxicology studies produced non-significant toxicity findings. Insulin Human r-DNA did not induce fertility impairment, embryo toxicity or teratogenicity in animal studies.

DESCRIPTION:
Insulin vial contains insulin produced by recombinant DNA technology using a special non-disease- producing strain of Escherichia coli bacteria.
The insulin molecule in Insulin vial is mono component and is identical to natural human insulin in composition and in three - dimensional confirmation.
Insulin Injection, Soluble Ph.Eur. in is a short acting human insulin. Isophane insulin Injection is an intermediate acting human insulin.
Insulin Injection Biphasic Isophane Ph.Eur. is a mixture of Soluble Insulin 30% and Isophane insulin 70%.

PHARMACEUTICAL PARTICULARS:
List of excipients

Insulin Injection Biphasic Isophane Ph.Eur. 100 IU/ml	Insulin Injection Isophane Ph.Eur. 100 IU/ml	Insulin Injection, Soluble Ph.Eur. 100 IU/ml
• Liquid phenol (Distilled) • Metacresol (Distilled) • Glycerin • Protamine sulphate equivalent to protamine base. • Zinc oxide (anhydrous) equivalent to zinc ion • Dibasic sodium hydrogen phosphate (anhydrous) • Water for injection • 10% Hydrochloric acid solution • 10% sodium hydroxide solution.	• Liquid phenol (Distilled) • Metacresol (Distilled) • Glycerin • Protamine sulphate equivalent to protamine base. • Zinc oxide (anhydrous) equivalent to zinc ion • Dibasic sodium hydrogen phosphate (anhydrous) • Water for injection • 10% Hydrochloric acid solution • 10% sodium hydroxide solution.	• Metacresol (Distilled) • Glycerin • 10% hydrochloric acid solution • 10% sodium hydroxide solution • Water for injection.

Incompatibilities
Insulin preparations should not be mixed with insulin produced by other manufacturers or with animal insulin preparations.

SHELF LIFE
2 Years

STORAGE & HANDLING INSTRUCTIONS:
Store between 2 °C and 8 °C in a refrigerator. Do not freeze. Protect from light.
Keep out of reach of children.
Opened vials can be stored at temperature upto to 25 °C for 28 days.

PACKAGING INFORMATION
10 ml USP type 1 glass vial, labelled and packed in a carton along with a package insert.

STORAGE CONDITIONS:
Insulin preparation can be stored at temperature of 2-8 °C.

PATIENT COUNSELLING INFORMATION
Never share syringe between patients. Advise patients using Insulin Injection vials not to share needles or syringes with another person. Sharing posess a risk for transmission of blood-borne pathogens.
Instruct patients on self-management procedures including glucose monitoring, proper injection technique, and management of hypoglycaemia and hyperglycaemia especially at initiation of Insulin therapy. Instruct patients on handling of special situations such as intercurrent conditions (illness, stress, or emotional disturbances), an inadequate or skipped insulin dose, inadvertent administration of an increased insulin dose, inadequate food intake, and skipped meals. Instruct patients on the management of hypoglycaemia.
Inform patients that their ability to concentrate and react may be impaired as a result of hypoglycemia. Advise patients who have frequent hypoglycaemia or reduced or absent warning signs of hypoglycemia to use caution when driving or operating machinery.
Advice patients that changes in insulin regimen can predispose to hyperglycaemia or hypoglycaemia and that changes in insulin regimen should be made under close medical supervision.
Inform patients that accidental mix-ups between Insulin Injection have been reported. Instruct patients to always carefully check that they are administering the correct insulin (e.g., by checking the insulin label before each injection) to avoid medication errors between Insulin Injection and other insulins. . Do not freeze them. Do not expose Insulin vial to excessive heat or direct sunlight.
Insulin vial must be kept out of reach of children.

Advise patients that hypersensitivity reactions have occurred with Insulin Injection. Inform patients on the symptoms of hypersensitivity reactions. Instruct patients to visually inspect Insulin Injection before use and to use Insulin Injection only if it contains no particulate matter and appears uniformly cloudy after mixing.

Manufactured for:
GENERIX LABORATORIES PRIVATE LIMITED
BT-54 Basement, Somdatt Chamber- II-9,
Bhikaji Cama Place, Delhi -110066, India.

Manufactured by:
M. J. BIOPHARM PVT. LTD.
L-7, MIDC Indl. Area, Taloja,
Dist. Raigad - 410 208,
Maharashtra, INDIA.

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DATE OF REVISION OF PACKAGE INSERT – June 2024

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QA Packaging		**RA**	**F & D**	**Production**	**Purchase**