SAMULIN® 70/30
(Human Insulin rDNA Origin)

1. NAME OF THE PRODUCT
SAMULIN® 70/30 (Human Insulin rDNA Origin) 100 IU/ml Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
SAMULIN® 70/30 100 IU/ml Injection
Each ml contains:
Human Insulin.....100 IU
70% Human Insulin Isophane Suspension, 30% Human Insulin Injection (rDNA Origin)

3. PHARMACEUTICAL FORM
Injection

Appearance: A white or almost white suspension which on standing deposits a white or almost white sediment and leaves a colorless or almost colorless supernatant, the sediment is readily suspended by gentle shaking. The particles are seen to be rod shaped crystals under microscope, the majority with a maximum dimension greater than 1µm but rarely exceeding 60µm, free from large aggregates.

4. CLINICAL PARTICULARS
4.1. THERAPEUTIC INDICATIONS:
For the treatment of patients with diabetes mellitus who require insulin for the maintenance of glucose homeostasis.

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:
SAMULIN® 70/30 should be given by subcutaneous injection but may, although not recommended, also be given by intramuscular injection. This formulation 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 in order to reduce the risk of lipodystrophy and cutaneous amyloidosis. Care should be taken when injecting any SAMULIN® 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. SAMULIN® 70/30 Mixture 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.

Instructions for use and handling SAMULIN® 70/30 Vials:

A suspension for injection in a 10ml vial to be used in conjunction with an appropriate syringe (100IU/ml markings).

a) Preparing a dose

Vials containing SAMULIN® 70/30 formulation should be rotated several times in the palms of the hands before use to completely resuspend the insulin, until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Do not shake vigorously as this may cause frothing, which may interfere with the correct measurement of the dose. The vials 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 vial, giving a frosed appearance. Prepare your syringe prior to injection, as directed by your physician. Use an insulin syringe marked for the strength of insulin being administered.

b) Injecting a dose

Inject the correct dose of insulin, as directed by your physician. Use of the injection sites should be rotated so that the same is not used more than approximately once a month.

Instructions for use and handling SAMULIN® 70/30 Cartridges:

To prevent the possible transmission of disease, each cartridge must be used by one patient only, even if the needle on the delivery device is changed. The cartridges should only be used in conjunction with a suitable insulin pen and should not be used with any other reusable pen as the dosing accuracy has not been established with other pens.

a) Preparing a dose

Cartridges containing SAMULIN® 70/30 formulation should be rolled in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend the insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Do not shake vigorously as this may cause frothing, which may interfere with the correct measurement of the dose. 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 afrosted appearance. The cartridges are not designed to allow any other insulin to be mixed in the cartridge. Cartridges are not designed to be refilled.

b) Injecting a dose

Inject the correct dose of insulin, as directed by your physician. Use of the

injection sites should be rotated so that the same is not used more than approximately once a month.

4.3. CONTRAINDICATIONS:

- Hypoglycaemia.
- Hypersensitivity to the active substance or to any of the excipients, unless used as part of a desensitisation programme.
- Under no circumstances should **SAMULIN®** formulation 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 (soluble, isophane, mixture), 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. 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.

Combination of human insulin with pioglitazone: Cases of cardiac failure have been reported when pioglitazone 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 pioglitazone 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. Pioglitazone should be discontinued, if any deterioration in cardiac symptoms occurs.

Excipients: This medicinal product contains less than 1mmol sodium (23mg) per dose, i.e., essentially “sodium-free”.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORM OF INTERACTIONS:

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. 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, beta$_2$ - sympatomimetics (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:

Fertility: Not available.

Pregnancy: 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.

Breast-feeding: 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). 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 insulin, 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). Skin and subcutaneous tissue disorders: Frequency “unknown”: Cutaneous amyloidosis.

Skin and subcutaneous tissue disorders: 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. Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

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. PHARMACODYNAMIC PROPERTIES:

Pharmacotherapeutic group: Insulins and analogues for injection, intermediate acting combined with fast acting.

ATC code: A10A D01.

Mechanism of action: SAMULIN® 70/30 is a premixed suspension of rapid and intermediate acting insulin. 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.

5.2. PHARMACOKINETICS:

The pharmacokinetics of insulin do not reflect the metabolic action of that hormone. Therefore, it is more appropriate to examine glucose utilisation curves when considering the activity of insulin. Individual variability will depend on factors such as size of dose, site of injection temperature and physical activity of the patient.

5.3. PRECLINICAL SAFETY DATA:

SAMULIN® 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:

- Phenol
- Meta-Cresol
- Glycerin
- Zinc Oxide

- Protamine Sulphate
- Disodium Hydrogen Phosphate Heptahydrate
- Hydrochloric Acid
- Sodium Hydroxide
- Water for Injection

6.2. INCOMPATIBILITIES:

SAMULIN® preparations should not be mixed with insulins produced by other manufacturers or with animal insulin preparations.

6.3. SHELF LIFE:

See expiry on the pack.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:

Store at 2 to 8°C, and protect from heat, light and freezing.
Improper storage may deteriorate the medicine.
Keep out of reach of chlildren.
For Vial: Once in use, the vial can be kept at room temperature (up to 25°C) for up to 6 weeks. Do not use beyond this period.
For Cartridge: Once in use, the cartridge can be kept at room temperature (up to 25°C) for up to 28 days. Do not use beyond this period.
Injection should not be used if vial/cartridge is leaking or suspension is discolored.

6.5. NATURE AND CONTENTS OF CONTAINER:

SAMULIN® 70/30 100 IU/ml Injection (Vial): 10ml clear glass vial (USP Type-I) with bromobutyl rubber stopper, sealed with flip off seal, pack size is 1x10ml.
SAMULIN® 70/30 100 IU/ml Injection (Cartridge): Clear, glass cartridge USP Type-I with bromobutyl rubber plunger and lined seal. Pack size is 5x3ml.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL OF A USED PRODUCT:

Do not use needles. Dispose of the needle in the responsible manner. Needles must not be shared. Vials/Cartridges can be used until empty, then properly discard. Any unused medicinal product or waste material product or waste material should be disposed of in accordance with local requirements.

6.7. DRUG PRODUCT SPECIFICATIONS:

Ph. Eur. Specs.

7. REGISTRATION / MARKETING AUTHORISATION HOLDER

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, Off Hub River Road, S.I.T.E., Karachi-Pakistan
www.samipharma.com
Mfg Lic. No. 000072

8. REGISTRATION / MARKETING AUTHORISATION NUMBER(S)

SAMULIN® 70/30 100 IU/ml Injection (Vial): 120490
SAMULIN® 70/30 100 IU/ml Injection (Cartridge): 126177

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

SAMULIN® 70/30 100 IU/ml Injection (Vial): 24th May, 2024
SAMULIN® 70/30 100 IU/ml Injection (Cartridge): 28th March, 2025

10. DATE OF REVISION OF THE TEXT

سیمولِن® ۷۰/۳۰ انجکشن

(ہیومن انسولین)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔ صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو ۲ سے ۸ ڈگری سینٹی گریڈ پر رکھیں اور گرمی، روشنی اور منجمد ہونے سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔

برائے وائل: زیر استعمال وائل کو ۲۵ ڈگری سینٹی گریڈ درجہ حرارت پر ۶ ہفتے تک رکھا جا سکتا ہے۔

مقررہ مدت کے بعد استعمال نہ کریں۔

برائے کارٹریج: زیر استعمال کارٹریج کو ۲۵ ڈگری سینٹی گریڈ درجہ حرارت پر ۲۸ دن تک رکھا جا سکتا ہے۔

مقررہ مدت کے بعد استعمال نہ کریں۔

وائل یا کارٹریج کے لیک ہونے یا سسپینشن کا رنگ تبدیل ہونے کی صورت میں ہرگز استعمال نہ کریں۔