INSULIN GLARGINE
GLYSOLIN® G DispoPen-2
100 IU / mL
SOLUTION FOR INJECTION (SC)
INSULINS AND ANALOGUES

Drugs That May Blunt Signs and Symptoms of Hypoglycemia

Drugs: beta-blockers, clonidine, guanethidine, and reserpine.

Intervention: Increased frequency of glucose monitoring may be required when Insulin Glargine (GLYSOLIN® G) is co-administered with these drugs.

OVERDOSE AND TREATMENT

Excess insulin administration may cause hypoglycemia and hypokalemia. Mild episodes of hypoglycemia can usually be treated with oral carbohydrates. Adjustments in drug dosage, meal patterns, or exercise may be needed.

More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. After apparent clinical recovery from hypoglycemia, continued observation and additional carbohydrate intake may be necessary to avoid recurrence of hypoglycemia. Hypokalemia must be corrected appropriately.

It is therefore recommended that the diabetic patient constantly carry some sugar lumps, sweets, biscuits, or sugary fruit juice. Adjustments in drug dosage, meal patterns, or exercise, may be needed.

STORAGE CONDITION

Store at temperatures between 2- 8°C. Do not freeze.

When in case, Dispopen should be kept below 30°C for up to 4 weeks.

Do not expose to excessive heat or direct sunlight. Insulin Glargine DispoPen-2 must be kept out of reach of children.

Insulin Glargine (GLYSOLIN® G) must only be used if the solution is clear and colourless with no particles visible.

Insulin Glargine (GLYSOLIN® G) must not be mixed with any other Insulin nor be diluted. Mixing or diluting can change its time/action profile and mixing can cause precipitation.

Remove the needle from the Pen after each injection.

Do not refill the Insulin Glargine DispoPen-2.

Insulin Glargine DispoPen-2 should never be used after the expiry date.

When Wockhardt DispoPen-2 is in cool storage, take it out 1 or 2 hours before you inject to allow it to arrive at room temperature. Cold insulin is more painful to inject.

CAUTION

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription. For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction.

AVAILABILITY

USP Type I clear glass cartridge x 3 mL with pen delivery device (Box of 1's)

BRP-037-01

Date of First Authorization: March 3, 2014

Date of Last Revision of Package Insert: January 25, 2024

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100 IU/mL Solution for Injection (SC)
Insulins and Analogues

Instruction Leaflet

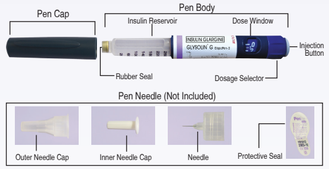
Your healthcare professional has decided that Wockhardt Disposable Insulin Pen is right for you. Talk with your healthcare professional about proper injection technique before using Wockhardt Disposable Insulin Pen.

Read these instructions carefully before using your Wockhardt Disposable Insulin Pen. If you are not able to follow all the instructions completely on your own, Kindly take the help of your registered medical practitioner.

Follow these instructions completely each time you use Wockhardt Disposable Insulin Pen to ensure that you get an accurate dose. If you do not follow these instructions you may get too much or too little insulin, which may affect your blood glucose. Do not share your Disposable Insulin Pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

Wockhardt Disposable Insulin Pen is a disposable pen for the injection of insulin. Each Wockhardt Disposable Insulin Pen contains in total 300 units of insulin. You can set doses from 1 to 60 units in steps of 1 unit.

Keep this leaflet for future reference.



Important Information for Use of Disposable Pen:

- Always attach a new needle before each use.
- Use 32G, 4mm needle with Wockhardt Disposable insulin pen. These are sold separately by Needle manufacturers. Contact your healthcare professional for further information.
- Always perform the safety test before each injection.
- This pen is only for your use. Do not share it with anyone else.
- If your injection is given by another person, special caution must be taken by this person to avoid accidental needle injury and transmission of infection.
- Never use Wockhardt Disposable Insulin Pen if it is damaged or if you are not sure that it is working properly.
- Always have a spare Wockhardt Disposable Insulin Pen in case your Wockhardt Disposable Insulin Pen is lost or damaged.

Step 1. Check the Insulin

A. The Recombinant Insulin Glargine (GLYSOLIN® G) Injection is contained in Wockhardt's Disposable Insulin Pen with Dark Blue Colour injection button.

B. Take off the pen cap.

C. Check the appearance of your insulin. Recombinant Insulin Glargine (GLYSOLIN® G) Injection is a clear insulin solution. Do not use this Wockhardt Disposable Insulin Pen if the insulin solution is cloudy, colored or has particles.

Step 2. Attach the Needle

Always use a new sterile needle for each injection. This helps prevent contamination, and potential needle blocks.

A. Wipe the Rubber Seal with alcohol.

B. Remove the protective seal from a new needle.

C. Line up the needle with the pen, and keep it straight as you attach it (screw or push on, depending on the needle type).



- If the needle is not kept straight while you attach it, it can damage the rubber seal and cause leakage, or break the needle.



Step 3. Perform a Safety Test

Always perform the Safety test before each injection.

Performing the safety test ensures that you get an accurate dose by:

- ensuring that pen and needle work properly
- removing air bubbles

A. Select a dose of 2 units by turning the dosage selector.



B. Take off the outer needle cap and keep it to remove the used needle after injection. Take off the inner needle cap and discard it.



C. Hold the pen with the needle pointing upwards.

D. Tap the insulin reservoir so that any air bubbles rise up towards the needle.

E. Press the injection button all the way in. Check if insulin comes out of the needle tip.



You may have to perform the safety test several times before insulin is seen.

- If no insulin comes out, check for air bubbles and repeat the safety test two more times to remove them.
- If still no insulin comes out, the needle may be blocked. Change the needle and try again.
- If no insulin comes out after changing the needle, your Wockhardt Disposable Insulin Pen may be damaged. Do not use this Wockhardt Disposable Insulin Pen.

Step 4. Select the Dose

You can set the dose in steps of 1 unit, from a minimum of 1 unit to a maximum of 60 units. If you need a dose greater than 60 units, you should give it as two or more injections.

A. Check that the dose window shows "0" following the safety test.

B. Select your required dose (in the example below, the selected dose is 30 units). If you turn past your dose, you can turn back down.



- Do not push the injection button while turning, as insulin will come out.
- It is possible to set a dose larger than the amount of insulin left in the cartridge.

At the end of an injection, the number in the window should be '0'. If it is not, this is the amount of insulin you did NOT receive. Remember this number and complete your dose with a new Wockhardt Disposable Insulin Pen.

Step 5. Inject the Dose

A. Use the injection method as instructed by your healthcare professional.

B. Insert the needle into the skin.



C. Deliver the dose by pressing the injection button in all the way. The number in the dose window will return to "0" as you inject.



D. Keep the injection button pressed all the way in. **Slowly count to 10 before you withdraw the needle from the skin.** This ensures that the full dose will be delivered.

Step 6. Remove and Discard the Needle

Always remove the needle after each injection and store Wockhardt Disposable Insulin Pen without a needle attached. This helps to prevent:

- Contamination and/or infection
- Entry of air into the insulin reservoir and leakage of insulin, which can cause inaccurate dosing.

A. Put the outer needle cap back on the needle, and use it to unscrew the needle from the pen. To reduce the risk of accidental needle injury, never replace the inner needle cap.

- If your injection is given by another person, special caution must be taken by this person when removing and disposing the needle. Follow recommended safety measures for removal and disposal of needles (e.g. a one handed capping technique) in order to reduce the risk of accidental needle injury and transmission of infectious diseases.

B. Dispose of the needle safely. Used needles should be placed in sharps containers (such as red biohazard containers), hard plastic containers (such as detergent bottles), or metal containers (such as an empty coffee can). Such containers should be sealed and disposed of properly.

- If you are giving an injection to a third person, you should remove the needle in an approved manner to avoid needle-stick injuries.

C. Always put the pen cap back on the pen, then store the pen until your next injection.

- If your Wockhardt Disposable Insulin Pen is in cool storage, take it out 1 to 2 hours before you inject to allow it to arrive at room temperature. Cold insulin is more painful to inject.

Storage Instructions

Keep Wockhardt Disposable Insulin Pen out of the reach and sight of children.

Keep your Wockhardt Disposable Insulin Pen in cool storage (36°F - 46°F [2- 8°C]) until first use. Do not allow it to freeze.

Do not put it next to the freezer compartment of your refrigerator, or next to a freezer pack.

Once you take your Wockhardt Disposable Insulin Pen out of cool storage, for use or as a spare, you can use it for up to 28 days. During this time it can be safely kept at room temperature up to 86°F (30°C). Do not use it after this time.

Wockhardt Disposable Insulin Pen in use must not be stored in a refrigerator.

Do not use Wockhardt Disposable Insulin Pen after the expiration date printed on the label of the pen or on the carton.

Protect Wockhardt Disposable Insulin Pen from light.

Discard your used Wockhardt Disposable Insulin Pen as required by your local authorities.

Maintenance

Protect your Wockhardt Disposable Insulin Pen from dust and dirt.

You can clean the outside of your Wockhardt Disposable Insulin Pen by wiping it with a damp cloth.

Do not soak, wash or lubricate the pen as this may damage it.

Your Wockhardt Disposable Insulin Pen is designed to work accurately and safely. It should be handled with care. Avoid situations where Wockhardt Disposable Insulin Pen might be damaged. If you are concerned that your Wockhardt Disposable Insulin Pen may be damaged, use a new one.

GLYSOLIN® G DispoPen-2 is a registered Trademark of Wockhardt

WOCKHARDT

Manufactured by:
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For more details on Diet & Diabetes, visit www.wockhardtdiabetes.com

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

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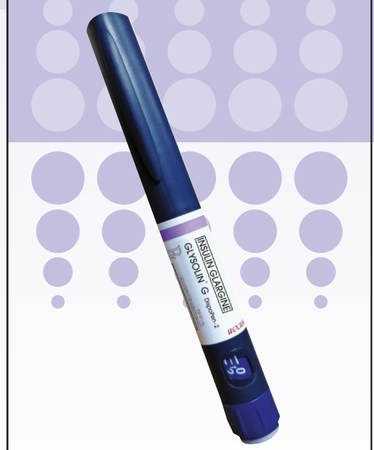

WOCKHARDT

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FORMULATION

Each pen delivery device contains one 3 mL cartridge of Insulin Glargine.

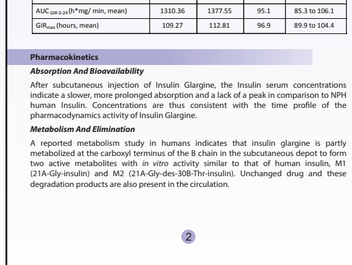
Each mL of cartridge contains:
Insulin Glargine (rDNA).....100 IU
m-Cresol USP .....0.27% w/v
Water for Injection..... q.s

DESCRIPTION

Insulin Glargine (GLYSOLIN® G) is a sterile solution of insulin glargine for subcutaneous use. Insulin glargine is a recombinant human insulin analog that is a long-acting, parenteral blood-glucose-lowering agent. Insulin glargine has low aqueous solubility at neutral pH. At pH 4 insulin glargine is completely soluble. After injection into the subcutaneous tissue, the acidic solution is neutralized, leading to formation of microprecipitates from which small amounts of Insulin Glargine (GLYSOLIN® G) are slowly released, resulting in a relatively constant concentration/time profile over 24 hours with no pronounced peak. This profile allows once daily dosing as basal insulin. Insulin Glargine (GLYSOLIN® G) is produced by recombinant DNA technology utilizing a non-pathogenic laboratory strain of *Escherichia coli* as the production organism. Insulin glargine differs from human insulin in that the amino acid asparagine at position A21 is replaced by glycine and two arginines are added to the C-terminus of the B-chain.

Chemically, insulin glargine is 21A-Gly-30Ba-L-Arg-3030b-L-Arg-human insulin and has the empirical formula $C_{267}H_{404}N_{72}O_{78}S_6$ and a molecular weight of 6063. Insulin glargine has the following structural formula:

CLINICAL PHARMACOLOGY



Pharmacotherapeutic group: Antidiabetic agent (Long acting human insulin analogue)
ATC (Anatomical Therapeutic Chemical) Classification Code: A10AE04

Mechanism of Action

The primary activity of insulin, including insulin glargine, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis, and enhances protein synthesis.

Pharmacodynamics

The glucose-lowering effect on a molar basis (i.e., when given at the same doses) of intravenous Insulin Glargine (GLYSOLIN® G) is approximately the same as that for human insulin. Insulin Glargine differs because of its unique structure providing a smooth and peakless profile with a prolonged duration of action of 24 hours (end of observation period) compared to 14.5 hours for NPH human Insulin. The onset of action of Insulin Glargine (GLYSOLIN® G) is slower than NPH human Insulin.

The duration of action of insulin glargine after abdominal, deltoid, or thigh subcutaneous administration is reportedly similar. The time course of action of insulins, including Insulin Glargine (GLYSOLIN® G), may vary between individuals and within the same individual.

Comparative Pharmacodynamics of Glysolin® G with Innovator*

Pharmacodynamics of Insulin Glargine (GLYSOLIN® G) was compared with that from Innovator in two separate studies – one in healthy volunteers (n=40 in two-way cross-over design) and second in patients of type 1 diabetes mellitus (n = 111 in parallel group design) with successful achievement of bioequivalence of Insulin Glargine (GLYSOLIN® G) to Innovator as displayed in the tables below.

Table 1: Pharmacodynamic comparison of Insulin Glargine (GLYSOLIN® G) to Innovator in healthy volunteers

Pharmacodynamic Parameter	Geometric LSM		T/R Ratio	90% CI of T/R
	Glysolin® G (T, N=69)	Innovator (R, N=65)		
GIR_{max} (mg/kg/min, mean)	1.82	1.85	0.98	0.87 to 1.11
$AUC_{GIR\,0\text{-}24h}$ (h*mg/kg/min, mean)	20.99	21.63	0.97	0.83 to 1.14
GIR_T_{max} (hours, median)	12.83	12.83	P value 0.74	

Table 2: Pharmacodynamic comparison of Insulin Glargine (GLYSOLIN® G) to Innovator in Type 1 Diabetic patients (After exclusion of outlier values)

Parameter	Geometric LSM		T/R Ratio	90% CI of T/R
	Glysolin® G (T, N=94)	Innovator (R, N=94)		
$AUC_{GIR\,0\text{-}24}$ (h*mg/ min, mean)	1310.36	1377.55	95.1	85.3 to 106.1
GIR_{max} (hours, mean)	109.27	112.81	96.9	89.9 to 104.4

Pharmacokinetics

Absorption And Bioavailability

After subcutaneous injection of Insulin Glargine, the Insulin serum concentrations indicate a slower, more prolonged absorption and a lack of a peak in comparison to NPH human Insulin. Concentrations are thus consistent with the time profile of the pharmacodynamics activity of Insulin Glargine.

Metabolism And Elimination

A reported metabolism study in humans indicates that insulin glargine is partly metabolized at the carboxyl terminus of the B chain in the subcutaneous depot to form two active metabolites with *in vitro* activity similar to that of human insulin, M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin). Unchanged drug and these degradation products are also present in the circulation.

Special Populations

Age, Race, And Gender.

Effect of age, race, and gender on the pharmacokinetics of Insulin Glargine (GLYSOLIN® G) has not been evaluated. However, in reported clinical studies in adults and pediatric patients, subgroup analyses based on age, race, and gender did not show differences in safety and efficacy between insulin glargine and NPH insulin.

Obesity

Effect of Body Mass Index (BMI) on the pharmacokinetics of Insulin Glargine (GLYSOLIN® G) has not been evaluated.

INDICATIONS

For the treatment of type-1 and type-2 diabetes mellitus patients who require basal (long - acting) insulin for the control of hyperglycemia.

Limitations of Use

Insulin Glargine (GLYSOLIN® G) is not recommended for the treatment of diabetic ketoacidosis.

DOSAGE AND ADMINISTRATION

Important Administration Instructions

- Administer Insulin Glargine (GLYSOLIN® G) subcutaneously once daily at any time of day but at the same time every day.
- Prior to initiation of Insulin Glargine (GLYSOLIN® G), train patients on proper use and injection technique.
- Patient should follow the Instructions for Use of pen device to correctly administer Insulin Glargine (GLYSOLIN® G) from cartridge.
- Administer Insulin Glargine (GLYSOLIN® G) subcutaneously into the abdominal area, thigh, or deltoid, and rotate injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy [see **ADVERSE DRUG REACTIONS**].
- Visually inspect Insulin Glargine (GLYSOLIN® G) cartridges for particulate matter and discoloration prior to administration. Only use if the solution is clear and colorless with no visible particles.
- Refrigerate unused (unopened) Insulin Glargine (GLYSOLIN® G) cartridges.
- Do not administer intravenously or via an insulin pump.
- Do not dilute or mix Insulin Glargine (GLYSOLIN® G) with any other insulin or solution.
- The cartridges to be used in pen device are for single patient use only [see **WARNINGS AND PRECAUTIONS**].

General Dosing Instructions

- Individualize and adjust the dosage of Insulin Glargine (GLYSOLIN® G) based on the individual's metabolic needs, blood glucose monitoring results and glycemic control goal.
- Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), during acute illness, or changes in renal or hepatic function. Dosage adjustments should only be made under medical supervision with appropriate glucose monitoring [see **WARNINGS AND PRECAUTIONS**].

Initiation of GLYSOLIN G Therapy

Type 1 Diabetes

- In patients with type 1 diabetes, Insulin Glargine (GLYSOLIN® G) must be used concomitantly with short-acting insulin. The recommended starting dose of (GLYSOLIN® G) in patients with type 1 diabetes should be approximately one-third of the total daily insulin requirements.

Short-acting, premeal insulin should be used to satisfy the remainder of the daily insulin requirements.

Type 2 Diabetes

- The recommended starting dose of Insulin Glargine (GLYSOLIN® G) in patients with type 2 diabetes who are not currently treated with insulin is 0.2 units/kg or up to 10 units once daily. One may need to adjust the amount and timing of short- or rapid-acting insulins and dosages of any oral Antidiabetic drugs.

Changing To Insulin Glargine (GLYSOLIN® G) From Other Insulin Therapies

- If changing patients from once daily insulin glargine 300 Units/mL to once daily Insulin Glargine (GLYSOLIN® G), the recommended initial (GLYSOLIN® G) dose is 80% of the insulin glargine 300 Units/mL dose that is being discontinued. This dose reduction will lower the likelihood of hypoglycemia.
- If changing from a treatment regimen with an intermediate or long-acting insulin to a regimen with Insulin Glargine (GLYSOLIN® G), a change in the dose of the basal insulin may be required and the amount and timing of the shorter-acting insulins and doses of any oral antidiabetic drugs may be needed to be adjusted.
- If changing patients from once-daily NPH insulin to once-daily (GLYSOLIN® G), the recommended initial Insulin Glargine (GLYSOLIN® G) dose is the same as the dose of NPH that is being discontinued.
- If changing patients from twice-daily NPH insulin to once-daily Insulin Glargine (GLYSOLIN® G), the recommended initial Insulin Glargine (GLYSOLIN® G) dosage is 80% of the total NPH dose that is being discontinued. This dosage reduction will lower the likelihood of hypoglycemia.

CONTRAINDICATIONS

Insulin Glargine (GLYSOLIN® G) is contraindicated

- During episodes of hypoglycemia.
- In patients with hypersensitivity to or one of its excipients.

WARNINGS AND PRECAUTIONS

Never Share An Insulin Glargine (GLYSOLIN® G) Cartridge Or Needle Between Patients

Insulin Glargine (GLYSOLIN® G) cartridges must never be shared between patients, even if the needle is changed. Patients using Insulin Glargine (GLYSOLIN® G) must never reuse or share needles with another person. Sharing poses a risk for transmission of blood-borne pathogens.

Hyperglycemia Or Hypoglycemia With Changes In Insulin Regimen

Changes in insulin strength, manufacturer, type, or method of administration may affect glycemic control and predispose to hypoglycemia or hyperglycemia. These changes should be made cautiously and only under close medical supervision, and the frequency of blood glucose monitoring should be increased. For patients with type 2 diabetes, dosage adjustments of concomitant oral and Antidiabetic products may be needed.

Hypoglycemia

Hypoglycemia is the most common adverse reaction associated with insulin, including Insulin Glargine (GLYSOLIN® G). Severe hypoglycemia can cause seizures, may be life-threatening or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery).

Hypoglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Symptomatic awareness of hypoglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers), or in patients who experience recurrent hypoglycemia.

Risk Factors For Hypoglycemia

The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As

with all insulin preparations, the glucose lowering effect time course of Insulin Glargine (GLYSOLIN® G) may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature. Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to co-administered medication. Patients with renal or hepatic impairment may be at higher risk of hypoglycemia.

Risk Mitigation Strategies For Hypoglycemia

Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.

The long-acting effect of Insulin Glargine (GLYSOLIN® G) may delay recovery from hypoglycemia.

Medication Errors

Accidental mix-ups among insulin products, particularly between long-acting insulins and rapid-acting insulins, have been reported. To avoid medication errors between Insulin Glargine (GLYSOLIN® G) and other insulins, instruct patients to always check the insulin label before each injection.

Hypersensitivity And Allergic Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including Insulin Glargine (GLYSOLIN® G). If hypersensitivity reactions occur, discontinue Insulin Glargine (GLYSOLIN® G); treat per standard of care and monitor until symptoms and signs resolve. Insulin Glargine (GLYSOLIN® G) is contraindicated in patients who have had hypersensitivity reactions to Insulin Glargine (GLYSOLIN® G) or one of the excipients.

Hypokalemia

All insulin products, including Insulin Glargine (GLYSOLIN® G), cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Monitor potassium levels in patients at risk for hypokalemia if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations).

Fluid Retention And Heart Failure With Concomitant Use Of PPAR-gamma Agonists

Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists, 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 Insulin Glargine (GLYSOLIN® G), 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.

Use In Specific Populations

Pregnancy

There are no well-controlled clinical studies of the use of Insulin Glargine (GLYSOLIN® G) in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

All pregnancies have a background risk of birth defects, loss, or other adverse outcome regardless of drug exposure. This background risk is increased in pregnancies complicated by hyperglycemia and may be decreased with good metabolic control. It is essential for patients with diabetes or history of gestational diabetes to maintain good metabolic control before conception and throughout pregnancy. In patients with diabetes or gestational diabetes, insulin requirements may decrease during the first trimester, generally increase during the second trimester, and rapidly decline after delivery. Careful monitoring of glucose control is essential in these patients. Therefore, female patients should be advised to tell their physicians if they intend to become, or if they become pregnant while taking Insulin Glargine (GLYSOLIN® G).

Nursing Mothers

Endogenous insulin is present in human milk; it is unknown whether insulin glargine is excreted in human milk. Because many drugs, including human insulin, are excreted in human milk, caution should be exercised when Insulin Glargine (GLYSOLIN® G) is administered to a nursing woman. Use of Insulin Glargine (GLYSOLIN® G) is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their insulin doses.

Pediatric Use

The safety and effectiveness of Insulin Glargine (GLYSOLIN® G) have been established in pediatric patients (age 2 to 15 years) with type 1 diabetes in reported clinical studies. The safety and effectiveness of insulin glargine in pediatric patients younger than 2 years of age with type 1 diabetes and pediatric patients with type 2 diabetes have not been established.

The dosage recommendation when changing to Insulin Glargine (GLYSOLIN® G) in pediatric patients (age 2 to 15 years) with type 1 diabetes is the same as that described for adults [see DOSAGE AND ADMINISTRATION]. As in adults, the dosage of Insulin Glargine (GLYSOLIN® G) must be individualized in pediatric patients (age 2 to 15 years) with type 1 diabetes based on metabolic needs and frequent monitoring of blood glucose.

In the reported pediatric clinical study, pediatric patients (age 2 to 15 years) with type 1 diabetes had a higher incidence of severe symptomatic hypoglycemia compared to the adults in studies with type 1 diabetes.

Geriatric Use

Caution should be exercised when Insulin Glargine (GLYSOLIN® G) is administered to geriatric patients. In elderly patients with diabetes, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in the elderly.

Hepatic Impairment

The effect of hepatic impairment on the pharmacokinetics of Insulin Glargine (GLYSOLIN® G) has not been studied. Frequent glucose monitoring and dose adjustment may be necessary for Insulin Glargine (GLYSOLIN® G) in patients with hepatic impairment.

Renal Impairment

The effect of renal impairment on the pharmacokinetics of Insulin Glargine (GLYSOLIN® G) has not been studied. Some studies with human insulin have shown increased circulating levels of insulin in patients with renal failure. Frequent glucose monitoring and dose adjustment may be necessary for Insulin Glargine (GLYSOLIN® G) in patients with renal impairment.

Obesity

Subgroup analyses based on BMI in reported controlled clinical studies, did not show differences in safety and efficacy between insulin glargine and NPH.

ADVERSE DRUG REACTIONS

The following adverse reactions are discussed elsewhere:

- **Hypoglycemia** [see **WARNINGS AND PRECAUTIONS**]
- **Hypersensitivity and allergic reactions** [see **WARNINGS AND PRECAUTIONS**]
- **Hypokalemia** [see **WARNINGS AND PRECAUTIONS**].

Peripheral Edema

Some patients taking insulin glargine have experienced sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

Lipodystrophy

Administration of insulin subcutaneously, including Insulin Glargine (GLYSOLIN® G), has resulted in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue) in some patients.

Insulin Initiation And Intensification Of Glucose Control

Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy.

Weight Gain

Weight gain has occurred with some insulin therapies including Insulin Glargine (GLYSOLIN® G) and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

Allergic Reactions

Local Allergy

As with any insulin therapy, patients taking Insulin Glargine (GLYSOLIN® G) may experience injection site reactions, including redness, pain, itching, urticaria, edema, and inflammation.

Systemic Allergy

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including insulin glargine and may be life threatening.

Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. All insulin products can elicit the formation of insulin antibodies. The presence of such insulin antibodies may increase or decrease the efficacy of insulin and may require adjustment of the insulin dose.

Medication errors have been reported in which other insulins, particularly rapid-acting insulins, have been accidentally administered instead of insulin glargine. To avoid medication errors between Insulin Glargine (GLYSOLIN® G) and other insulins, patients should be instructed to always verify the insulin label before each injection.

Other adverse event reported in patients administered with Insulin Glargine (GLYSOLIN® G) include upper respiratory tract infection, peripheral edema, hypertension, influenza, sinusitis, cataract, bronchitis, arthralgia, pain in extremity, back pain, cough, urinary tract infection, diarrhea, depression, headache, accidental injury, infection and retinal vascular disorder.

DRUG INTERACTIONS

Drugs That May Increase the Risk of Hypoglycemia

Drugs: Antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, propoxyphene, salicylates, somatostatin analogs (e.g., octreotide), and sulfonamide antibiotics.

Intervention: Dose reductions and increased frequency of glucose monitoring may be required when Insulin Glargine (GLYSOLIN® G) is co-administered with these drugs.

Drugs That May Decrease the Blood Glucose Lowering Effect of Insulin Glargine (GLYSOLIN® G)

Drugs: Atypical antipsychotics (e.g. olanzapine and clozapine), corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (e.g. in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g. albuterol, epinephrine, terbutaline), and thyroid hormones.

Intervention: Dose increases and increased frequency of glucose monitoring may be required when Insulin Glargine (GLYSOLIN® G) is co-administered with these drugs.

Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of Insulin Glargine (GLYSOLIN® G)

Drugs: Alcohol, beta-blockers, clonidine, and lithium salts. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.

Intervention: Dose adjustment and increased frequency of glucose monitoring may be required when Insulin Glargine (GLYSOLIN® G) is co-administered with these drugs.