

Insulin glargine (Lantus) for type 1 and 2 diabetes mellitus

(IN-su-lin GLAR-gene)

Summary

- Insulin glargine is a long-acting insulin analogue that can be used in type 1 and 2 diabetes mellitus.
- Insulin glargine has similar efficacy to that of isophane insulin in controlling blood glucose.
- Insulin glargine can reduce the overall incidence of hypoglycaemia, mostly at night, compared with isophane insulin. The risk of severe hypoglycaemia is similar to that with isophane insulin.
- Inform patients that insulin glargine is a clear, not a cloudy, solution. It should not be confused with clear short- or rapid-acting insulins.
- Insulin glargine can be given once daily, which may be more convenient for patients or carers who need to inject intermediate-acting insulin more than once daily.
- If switching from twice-daily isophane insulin to insulin glargine, use an initial dose that is 20% less than the total previous dose of isophane insulin, and titrate upwards if needed.

PBS listing

Insulin glargine is listed on the Pharmaceutical Benefits Scheme (PBS) as an unrestricted benefit. Insulin glargine can be prescribed on the PBS for adults and children with type 1 diabetes mellitus and adults with type 2 diabetes mellitus who require insulin.

Reason for PBS listing

Insulin glargine was listed on a cost-effectiveness basis compared with isophane insulin.¹ The Pharmaceutical Benefits Advisory Committee accepted that the improvement in hypoglycaemic event rates with insulin glargine, albeit in a population that cannot be defined, was cost effective at the price proposed.^{1,2}

Place in therapy

Insulin glargine is a long-acting analogue of human insulin. It controls blood glucose levels for up to 24 hours without a peak in insulin levels.^{3–6} Insulin glargine is an alternative to intermediate-acting insulin (isophane or lente) for treating type 1 and 2 diabetes mellitus.^{3,6,7}

Insulin glargine has similar efficacy to that of isophane insulin but can benefit some patients by reducing the overall incidence of hypoglycaemia.^{2,8–19} It may allow for tighter blood glucose control in patients who have frequent hypoglycaemia with isophane insulin.

Insulin glargine is as effective as isophane insulin

Intermediate- or long-acting insulin can be used in type 1 and 2 diabetes.^{6,7} Insulin glargine may not provide additional benefit in type 2 diabetes if blood glucose is adequately controlled with isophane insulin. However, it may be a convenient option for patients or carers who need to inject intermediate-acting insulin more than once daily.

In studies of patients with type 1 diabetes, insulin glargine once daily provided similar reductions in levels of glycated haemoglobin A_{1c} (HbA_{1c}) to those for isophane insulin (given at least once daily), but slightly lower mean fasting blood glucose (FBG) levels (7.5–8.0 mmol/L vs 8.0–9.0 mmol/L, respectively).^{8–10,18–23} This was in patients with an HbA_{1c} > 7% and baseline FBG > 8 mmol/L despite their previous insulin regimen (mostly isophane insulin twice daily with pre-meal short-acting insulin).^{8–10,18,19,21–23}

There is no difference between insulin glargine and isophane insulin in reducing HbA_{1c} or FBG levels in type 2 diabetes, when used either alone or in combination with oral hypoglycaemic agents.^{12–17,20} About one-third of patients in studies achieved target HbA_{1c} ≤ 7%¹¹ and FBG levels ≤ 7 mmol/L^{13,14} with either insulin glargine once daily, or isophane insulin once or twice daily.

These studies were unblinded, because insulin glargine is a clear solution and isophane insulin is cloudy. It cannot be excluded that bias may have occurred when titrating insulin doses according to FBG levels, and in reporting hypoglycaemia not confirmed by FBG levels. Studies ranged from 4 to 52 weeks' duration, so the long-term effects of insulin glargine on diabetes complications could not be assessed.

Consider insulin glargine for patients who have frequent episodes of hypoglycaemia with isophane insulin

Insulin glargine reduces the overall incidence of hypoglycaemia, mostly at night, compared with isophane insulin in patients with type 1 and 2 diabetes (see Safety issues). It may improve glycaemic control in some patients if a lower risk of hypoglycaemia enables more intensive dose titration so that target HbA_{1c} levels can be reached.

There is some evidence in type 2 diabetes that a smaller proportion of patients with HbA_{1c} levels ≤ 7% experiences nocturnal hypoglycaemia with insulin glargine (39%) compared with isophane insulin (49%).¹¹ This was seen in patients with mean baseline HbA_{1c} ≤ 9%.

Safety issues

Insulin glargine was generally as well tolerated as isophane insulin in studies. As with other insulins, adverse effects include hypoglycaemia, injection-site reactions, weight gain, headache, diarrhoea and infections.^{3,8–10,12–17,21–24} Insulin glargine may cause more pain at the injection site than isophane insulin (up to 6% vs 1% of patients, respectively).^{3,4,9,13,21} Injection-site reactions were generally mild and did not result in cessation of treatment.

Report suspected adverse reactions to the Adverse Drug Reactions Advisory Committee (ADRAC) online (see www.tgasime.health.gov.au) or by using the 'Blue Card' distributed with *Australian Prescriber*. For information about reporting adverse drug reactions, see the Therapeutic Goods Administration website (www.tga.gov.au).

Insulin glargine reduces, but does not eliminate, the risk of hypoglycaemia

As can be seen in Table 1, hypoglycaemia:

- remains a risk with insulin glargine
- is more common in type 1 than type 2 diabetes
- is slightly less frequent with insulin glargine compared with isophane insulin
- occurs at a similar rate between these insulins for severe events.

Table 1: Proportion of patients with at least one hypoglycaemic event in studies of insulin glargine compared with isophane insulin^{8–18,21–23}

Hypoglycaemic event*	Insulin glargine	Isophane insulin
Type 1 diabetes		
All symptomatic events	40–100%	49–98%
• Nocturnal events	18–81%	27–86%
• Severe events	0–11%	0–15%
Type 2 diabetes		
All symptomatic events	22–61%	32–67%
• Nocturnal events	7–31%	19–40%
• Severe events	0–7%	0–10%

* Definitions of hypoglycaemic events varied between studies: symptomatic (clinical symptoms confirmed or unconfirmed by FBG < 2.0–4.2 mmol/L), nocturnal (symptomatic hypoglycaemia occurring during sleep between bedtime and getting up in the morning, i.e. before morning pre-breakfast FBG measurement and morning insulin injection), severe (symptomatic hypoglycaemia requiring assistance from another person, with either FBG < 2.0–3.1 mmol/L or prompt recovery after administration of oral carbohydrate, intravenous glucose or glucagon).

Insulin glargine mainly reduces the incidence of hypoglycaemia at night.^{9,15–19} Studies of up to 1 year found that insulin glargine reduced the proportion of patients with at least one episode of nocturnal hypoglycaemia by 5–20% compared with isophane insulin.^{8–15} In patients with type 1 diabetes, absolute rates of nocturnal hypoglycaemia were reported as 1–2 episodes per month with insulin glargine and 3–4 episodes per month with isophane insulin.^{18,19} The absolute rates for patients with type 2 diabetes were 4–5 episodes per year with insulin glargine and 7–8 episodes per year with isophane insulin.^{16,17}

Lower incidence of hypoglycaemia is more apparent with insulin glargine compared with once-daily isophane insulin

The incidence of hypoglycaemia appears lowest when insulin glargine is compared with isophane insulin once daily^{10,20,23,24}; this is likely due to once-daily doses being higher than individual doses of isophane insulin twice daily. In one 4-week study of type 1 diabetes¹⁰ the proportion of patients with at least one episode of nocturnal hypoglycaemia was 36% with insulin glargine, 44% with isophane insulin twice daily, and 66% with isophane insulin once daily. In a 28-week study of type 2 diabetes^{13,24} there was less symptomatic hypoglycaemia with insulin glargine but only when compared with the subgroup of patients given isophane insulin once daily (46% vs 60%, respectively).

Dosing issues

Insulin glargine is usually injected subcutaneously once daily at bedtime.³ The initial dose and time of administration is determined on an individual basis and adjusted according to blood glucose levels.³

Switching from other insulins to insulin glargine

When changing treatment from another intermediate- or long-acting insulin to insulin glargine, the dose of rapid-

or short-acting insulin, or oral hypoglycaemic agents, may need adjustment.³

Patients who previously used once-daily isophane insulin can generally be switched to insulin glargine using the same dose. However, some patients who used twice-daily isophane insulin reported increased hypoglycaemia during dose titration with insulin glargine.^{21–23} If switching such patients to insulin glargine, use an initial dose that is 20% less than the total previous dose of twice-daily isophane insulin, and titrate upwards if needed.³

Information for patients

Inform patients and/or carers that insulin glargine:

- is a long-acting insulin for lowering blood glucose levels between meals
- is a clear solution — not to be confused with rapid- and short-acting insulins, which are also clear solutions
- is usually given as a once-daily injection
- must not be mixed with any other insulin or be diluted
- can lower the risk of, but not prevent, episodes of hypoglycaemia
- has a prolonged effect, which may delay recovery from hypoglycaemia.³

Advise about the factors that increase the risk of hypoglycaemia with insulins, including:

- inappropriate use of high doses
- missing or delaying meals
- insufficient carbohydrate intake
- drinking alcohol
- unaccustomed or unplanned exercise.^{4,6}

Suggest or provide the Lantus consumer medicine information (CMI) leaflet.

References

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The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.