

Administration of small doses of glargine and detemir: Dilution and insulin dosing pens (update by Jacquie Rand)

Administering small doses of detemir and glargine cats to dogs and cats is problematic, and limits their use when doses of less than 1U are required. Information below will assist in administering small doses.

Insulin dosing pens such as the HumaPen Luxura HD (Eli Lilly) and the NovoPen Junior (USA) / Demi (other countries)(Novo Nordisk) are specifically designed for use in babies and children, and deliver accurate and precise insulin doses in 0.5 U increments.

However, with the pens currently available, smaller increments than 0.5 U are not possible. In some small dogs, use of detemir is limited because it is approximately 4 times more potent than other insulin in dogs (not cats). Despite these limitations, detemir provides excellent glycemic control in many dogs. In some cats, particularly those going into remission and regaining some beta cell function, dose adjustments for glargine and detemir are required in increments less than 0.5 U.

New information indicates that detemir and glargine can be diluted and mixed.

Detemir is a relatively stable insulin, and can be mixed with other shorter acting insulin eg lispro or NPH. A special diluting medium is also available from NovoNordisk, but in some countries (USA and Australia), the company will not supply veterinarians. Detemir can also be diluted with sterile water or saline (information from NovoNordisk). However, diluting with saline or water also dilutes the antimicrobial additive (meta-cresol). Therefore, because of the risk of bacterial contamination, it is recommended dilution is done just prior to administration of insulin. Having said that, veterinarians in the past have previously diluted other insulin in the bottle and kept it refrigerated, and discarded it in about 30 days. Based on experience with other insulin, with time, stability and action seemed to be adversely affected. Therefore, because of the risk of bacterial contamination and unknown changes in time with efficacy, diluting detemir in the bottle is not recommended.

For **glargine**, neither dilution or mixing is recommended by the manufacturer, and leads to formation of a cloudy precipitate in the syringe. However, human patients are mixing glargine with other insulin, and a publication (see Kaplan below) has shown that there was no adverse effect on glycemic control as measured by continuous glucose monitoring. Glargine is a relatively stable insulin, and therefore it would be expected that it could also be diluted with insulin or saline just prior to injection. Be aware that it will form a cloudy precipitate in the syringe. Mixing in the bottle is not recommended because of problems with accuracy of dosing when the insulin is a precipitate, bacterial contamination and the unknown effect on stability and efficacy.

In general, from the references below, mixing with a shorter-acting insulin will change the action profile, mainly of the shorter acting insulin compared to giving separately. Mixing detemir with a rapid-acting insulin analogue like insulin aspart will reduce and delay the maximum effect of the rapid-acting insulin compared to that observed following separate injections.

In general, unless smaller dose increments of 0.5 U are required, use of dosing pens is recommended for doses less than 2 U and will provide better accuracy, stability and minimize the risk of bacterial contamination compared to diluting insulin.

References:

Effects of Mixing Glargine and Short-Acting Insulin Analogs on Glucose Control

KAPLAN et al DIABETES CARE, VOLUME 27, NUMBER 11, NOVEMBER 2004

Conclusions: This study provides preliminary data that mixing glargine with lispro or aspart insulin in the same syringe and dividing the dose of glargine does not adversely affect glucose concentrations. Lower nocturnal blood glucose concentrations in study mixed versus study separate and basal, although not statistically significant, should alert physicians that the evening dose of lantus may need to be titrated to prevent hypoglycemia.

No serious adverse events occurred during the study. Although the mixtures turned cloudy, no complaints of

increased pain or injection difficulties were reported. Long-term effects of mixing glargine and SAIs on HbA1c were not assessed in this study.

In conclusion, our data suggest that mixing glargine with SAIs or twice-daily dosing does not affect short-term glycemic profile. Further studies are needed to evaluate the long-term effects of these regimens.

The Alteration of Aspart Insulin Pharmacodynamics When Mixed With Detemir Insulin

CENGIZ, DIABETES CARE, VOLUME 35, APRIL 2012

CONCLUSIONS— These data demonstrate that mixing aspart with detemir insulin markedly lowers the early PD action of aspart and prolongs its time-action profile as compared with the separate injection of these analogs. These changes in insulin PD should be weighed against the added convenience of mixing when considering such unlicensed use of these insulins in youth with type 1 diabetes.

Early Pharmacokinetic and Pharmacodynamic Effects of Mixing Lispro With Glargine Insulin

CENGIZ, DIABETES CARE, VOLUME 33, NUMBER 5, MAY 2010

CONCLUSIONS— These data demonstrate that mixing lispro with glargine markedly flattens the early pharmacodynamic peak of lispro and causes a shift to the right in the GIR curve changes that might lead to difficulties in controlling meal-related glucose excursions.

A 12-wk follow-up study to evaluate the effects of mixing insulin lispro and insulin glargine in young individuals with type 1 diabetes

Lucchesi et al. *Pediatric Diabetes* 2012

Conclusions: These data suggest that mixing IL with IG immediately before the SC injection decreases IL serum peak concentration without affecting the glycemic profile after 12 wk in this group with type 1 diabetes mellitus.