

Use of Insulin in the treatment of diabetes mellitus

insulin preparations	Pharmacokinetics		Uses & Other
1-Ultra-short acting insulins e.g. Lispro, aspart very fast onset and short duration	<ul style="list-style-type: none"> ✓ Clear solutions at neutral pH. ✓ Do not aggregate or form dimers or hexamers (<i>monomeric analogue</i>). ✓ Fast onset of action (5-15 min) ✓ Short duration of action (3-5 h) ✓ Reach peak level 30-90 min after injection. 	<ul style="list-style-type: none"> ✓ S.C. (5 min no more than 15 min before meal). ✓ I.V. in emergency. ✓ 2-3 times/day. ✓ Mimic the prandial mealtime insulin release ✓ Have the lowest variability of absorption 	-used to control post-prandial hyperglycemia and emergency ketoacidosis . <i>Advantages of Insulin Lispro vs Regular Insulin</i> <ul style="list-style-type: none"> • Rapid onset of action (<i>due to rapid absorption</i>) • Reduced risk of postprandial hypoglycemia (<i>due to short duration of action</i>)
2-Short acting insulins (regular insulin)	<ul style="list-style-type: none"> ✓ Soluble crystalline zinc insulin (stability -shelf half life) ✓ Clear solutions at neutral pH. ✓ Hexameric analogue ✓ Onset of action 30-45 min (s.c.). ✓ Peak 2-4 h. ✓ Duration 6-8 h. 	<ul style="list-style-type: none"> ● 2-3 times/day. ● S.C. 30 - 45 min before meal 	<ul style="list-style-type: none"> ✓ Control postprandial hyperglycemia & ketoacidosis. ✓ Can be used in pregnancy ✓ I.V. in emergency situations. <ul style="list-style-type: none"> – Management of ketoacidosis – After surgery – During acute infection
3-Intermediate acting insulins			
A) Isophane (NPH) Insulin	<ul style="list-style-type: none"> ✓ NPH, is a Neutral Protamine Hagedorn insulin in phosphate buffer. ✓ NPH insulin is combination of protamine & crystalline zinc insulin (1: 6 molecules). proteolysis release insulin. ✓ Peak serum level 5-7 h. ✓ Duration of action 13-18 h. 	<ul style="list-style-type: none"> ✓ Turbid suspension at neutral pH. ✓ Given S.C. only not i.v. ✓ Cannot be used in ketoacidosis or emergency ✓ Onset of action 1-2 h. 	<div style="border: 1px dashed black; padding: 5px;"> Insulin mixtures <ul style="list-style-type: none"> ✓ (NPL= NPH / lispro) (NPA= NPH / aspart) ✓ NPL & NPA have the same duration as NPH ✓ 75/25 - 70/30 - 50/50 (NPH/regular). </div>
B) Lente insulin	<ul style="list-style-type: none"> ✓ Mixture of: 30% semilente insulin (<i>amorphous precipitate of zinc insulin in acetate buffer</i>) & 70% ultralente insulin (<i>poorly soluble crystal of zinc insulin</i>) ✓ Turbid suspension at neutral pH ✓ Given S.C., <u>not intravenously</u> 	<ul style="list-style-type: none"> ✓ Delayed onset of action (1-3 h) ✓ Peak serum level 4-8 h. ✓ Duration of action 13-20 h. ✓ Lente is not used in diabetic ketoacidosis or emergency. ✓ Require several hours to reach therapeutic levels. 	<ul style="list-style-type: none"> ✓ Lente and NPH insulins are equivalent in activity.
Long acting insulins Insulin glargine (lantis)	<ul style="list-style-type: none"> ✓ Slow onset of action 2 h. ✓ Clear solution BUT forms precipitate (<i>depot</i>) at injection site. ✓ Less absorption rate than NPH & Lente. ✓ Given s.c., <u>not intravenously</u> 	<ul style="list-style-type: none"> ✓ Maximum effect after 4-5 h ✓ Produce broad plasma concentration plateau (low continuous insulin level). ✓ Prolonged duration of action (24 h). ✓ Used Once daily 	Advantages over intermediate-acting insulins: <ul style="list-style-type: none"> 1-Constant circulating insulin over 24 hr with no peak (<i>peakless profile</i>). 2-Sfer than NPH & Lente insulins (reduced risk of nocturnal hypoglycemia).

	Short-acting (regular) insulins e.g. Humulin R, Novolin R	Ultra-Short acting insulins e.g. Lispro, aspart, glulisine
Uses	postprandial hyperglycemia & emergency diabetic ketoacidosis	postprandial hyperglycemia & emergency diabetic ketoacidosis
Physical characteristics	Clear solution at neutral pH	Clear solution at neutral pH
chemistry	Hexameric analogue	Monomeric analogue
Route & time of administration	S.C. 30 – 45 min before meal I.V. in emergency (e.g. diabetic ketoacidosis)	S.C. 5 min (no more than 15 min) before meal I.V. in emergency (e.g. diabetic ketoacidosis)
Onset of action	30 – 45 min (S.C)	0 – 15 min (S.C)
Peak level	2 – 4 hr	30 – 90 min
Duration	6 – 8 hr	3 – 5 hr
Usual administration	2 – 3 times/day or more	2 – 3 times / day or more

- Ultrashort acting insulins & Short acting insulins (regular) are universal, NPH, lente, and glargine are only used in type I diabetes mellitus.
- lispro and aspart are faster than regular insulin.
- Regular insulin has high incidence of hypoglycemia compared with lispro and aspart.
- Both ultrashort acting insulin & Regular insulin can be used in case of pregnancy, because they don't have a teratogenic effect.
- None of the NPH, lente, and glargine can be used in emergencies (diabetic ketoacidosis).
- NPH, lente, and glargine are available in S.C. form only
- NPH can be mixed with regular insulin or lispro
- Glargine has a prolonged duration of action (24h.), so it's given once daily. And should not be mixed with other insulin.
- Advantages of Insulin glargine over intermediate-acting insulins:
 - Constant circulating insulin over 24 hr with no pronounced peak.
 - More safe than NPH & Lente insulins (Reduced risk of hypoglycemia).
- Hypoglycemia is the most common complication of insulin therapy.