GENERAL RECOMMENDATIONS

- Start insulin if A1C and glucose levels are above goal despite optimal use of other diabetes medications. (Consider insulin as initial therapy if A1C very high, such as > 10.0%) 6,7,8
- Start with BASAL INSULIN for most patients 6,7,8
- Consider the following goals1,6
  ADA A1C Goals:
  - A1C < 7.0 for most patients
  - A1C > 7.0 (consider 7.0-7.9) for higher risk patients
  1. History of severe hypoglycemia
  2. Multiple co-morbid conditions
  3. Long standing diabetes
  4. Limited life expectancy
  5. Advanced complications or 6. Difficult to control despite use of insulin

  ADA Glucose Goals*: Fasting and premeal glucose < 130
  Peak post-meal glucose (1-2 hours after meal) < 180
  Difference between premeal and post-meal glucose < 50
  *for higher risk patients individualize glucose goals in order to avoid hypoglycemia

BASAL INSULIN

- Long-acting:
  - Glargine (Lantus®)
  - Detemir (Levemir®)

- Intermediate-acting:
  - NPH Note: NPH insulin has elevated risk of hypoglycemia so use with extra caution6,8,15,17,25,32

- Basal insulin is best starting insulin choice for most patients (if fasting glucose above goal). 6,7,8
- Start one of the intermediate-acting or long-acting insulins listed above. 6,7,8 Start insulin at night. 8
- When starting basal insulin: Continue secretagogues. Continue metformin. 7,8,20,29
- Note: if NPH causes nocturnal hypoglycemia, consider switching NPH to long-acting insulin. 17,25,32

STARTING DOSE:

Start dose: 10 units6,7,8,11,12,13,14,16,19,20,21,22,25
Consider using a lower starting dose (such as 0.1 units/kg/day32) especially if patient is thin or has a fasting glucose only minimally above goal.

TITRATION

Teach patient to self titrate ↑ by 1 units every 1 day until average fasting glucose < 130*16
(*Inform patient to hold titration until further evaluation if develops any hypoglycemia)

or

Titrated 1 time per week as per table below until average fasting glucose < 13010,11,13,14,15,17,18,20,21,26,28

- Fasting glucose > 180 increase 8u
- Fasting glucose 160-180 increase 6u
- Fasting glucose 140-160 increase 4u
- Fasting glucose 130-140 increase 2u
- Fasting glucose 70-130 no change
- Fasting glucose < 70 decrease 2u or 10%

Within one to two months, evaluate post-meal glucose pattern6,7,8

If post-meal glucose levels > 50 mg/dl above premeal: consider ADD PRANDIAL INSULIN6,7,8

Note: If patient unable to do multiple daily injections, consider switching to MIXED INSULIN instead of adding prandial insulin (see pg. 3 for switching to mixed insulin). (Mixed insulin is more likely to cause hypoglycemia6,10 and generally requires a fixed meal schedule6)
**PRANDIAL INSULIN**

Rapid Acting: Lispro (Humalog®)  
Aspart (Novolog®)  
Glulisine (Apidra®)  

Short Acting: Regular  

Note: Regular insulin has longer peak and extra risk of hypoglycemia so use with caution.

- **TITRATE:**  
  Adjust insulin to carb ratio as appropriate per below until post-meal glucose < 180.  
  - 1 unit to 15 gm  
  - 1 unit to 12 gm  
  - 1 unit to 10 gm  
  - 1 unit to 7 gm  
  - 1 unit to 5 gm  
  - 1 unit to 4 gm  
  - 1 unit to 3 gm

- **Alternate adjustment:**  
  Adjust insulin to carb ratio per 500 rule.

- **NOTE:**  
  If post-meal pattern low, back up the scale.

**MIXED INSULIN**

75/25 Lispro Mix (Humalog® Mix) or 50/50 Lispro Mix (Humalog® Mix)  
70/30 Aspart Mix (Novolog® Mix)  
70/30 NPH/Regular  

Note: 70/30 NPH/Regular insulin has elevated risk of hypoglycemia so use with extra caution.

- Mixed insulin is an option for patients who are unable to do multiple injections and who have fixed meal schedules.
- Mixed insulin is more likely to cause hypoglycemia compared to basal and prandial insulins.
- Start one of the mixed insulins listed above.
- When starting mixed insulin: Stop secretagogues. Continue metformin. (If already on other insulin, then see guideline for switching to mixed insulin on page 3).

**STARTING DOSE:**  
4 units qAC  

- May consider start with largest meal only.
- Instruct patients to eat carb consistent meals when first starting prandial insulin.

**Alternate choice:**  
If meals vary in size and patient is accurate at counting carbs

- **TITRATE:**  
  Titrated 1-2 units every 2-3 days until post-meal glucose < 180.  
  (May consider different doses for different meals)

- **ALTERNATE STARTING DOSE:**  
  1 unit to 15 grams carbs qAC.

  Note: may consider calculate insulin to carb (I:C) ratio = 500 / total daily dose (TDD) of insulin (500 rule).

  *May also consider add I:C ratio to snacks.

- **Consider adding pre-meal Correction Factor (CF):**  
  Add 1 unit for each 50 that pre-meal glucose is > 130

- **ALTERNATIVE STARTING DOSE:**  
  Add 1 unit for each 50 that pre-meal glucose is > 130

  *Alternate method to determine pre-meal correction factor:  
  Correction factor (CF) = 1800 / total daily dose of insulin (1800 rule)

  *May also consider correction factor at bedtime using target of 150.

- **MIXED INSULIN:**
  75/25 Lispro Mix (Humalog® Mix) or 50/50 Lispro Mix (Humalog® Mix)  
  70/30 Aspart Mix (Novolog® Mix)  
  70/30 NPH/Regular

  Note: 70/30 NPH/Regular insulin has elevated risk of hypoglycemia so use with extra caution.

- Mixed insulin is an option for patients who are unable to do multiple injections and who have fixed meal schedules.
- Mixed insulin is more likely to cause hypoglycemia compared to basal and prandial insulins.
- Start one of the mixed insulins listed above.
- When starting mixed insulin: Stop secretagogues. Continue metformin. (If already on other insulin, then see guideline for switching to mixed insulin on page 3).

**STARTING DOSE:**  
PRE-DINNER dose 6-10 units  
(may adjust depending on previous basal insulin dose)

Target glucose for titration is fasting glucose.  
(may also consider post-dinner glucose when titrating dose)

**STARTING DOSE:**  
PRE-BREAKFAST dose: 6-10 units  
(may adjust depending on previous basal insulin dose)

Target glucose for titration is pre-dinner glucose.  
(may also consider post-breakfast glucose when titrating dose)

**TITRATE:**  
Titrated 1-2 units every 2-3 days until average target glucose < 130.

**OR**

Titrated 1-2 times per week such as per table below until average target glucose < 130.

- Target glucose > 200  
  ↑ by 4 units
- Target glucose 131-200  
  ↑ by 2 units
- Target glucose 70-130  
  No change
- Target glucose < 70  
  ↓ by 2-4 units or by 10%

- May require different doses for pre-breakfast and pre-dinner.
- May consider adding pre-lunch dose as well if needed.

Sutter Medical Foundation. February, 2011
Switching Mixed Insulin to Basal/Prandial Insulin

Selection of Patients:
- Patient has persistent hypoglycemia episodes or
- Patient has excess glucose variability or
- Patient wants a more flexible meal schedule

- Determine total daily mixed insulin dose (TDD)
- Stop mixed insulin
- Start basal insulin qHS and prandial insulin qAC.

Starting dose of prandial insulin:
10% TDD (total daily mixed insulin dose) qAC
Note: This is essentially = to the current prandial component of mixed insulin

Starting dose of basal insulin:
50% TDD (total daily mixed insulin dose) qHS
Note: This is essentially = to 80% of the current basal component of mixed insulin

Titrating per BASAL Insulin guideline
Titrating per PRANDIAL Insulin guideline

Switching from Basal or Basal/Prandial Insulin to Mixed Insulin

Selection of Patients:
- Difficulty taking multiple injections daily
- Stable consistent meal schedule
- Stable glucose pattern and no hypoglycemia episodes

- Determine total daily insulin dose (TDD)
- Stop both Basal and Prandial insulin
- Start Mixed insulin before breakfast and before dinner.

Starting dose of dinner dose:
30-40% of total daily insulin dose
Target glucose for titration is fasting glucose.
(may also consider post-dinner glucose when titrating dose)

Starting dose of breakfast dose:
30-40% of total daily insulin dose
Target glucose for titration is pre-dinner glucose.
(may also consider post-breakfast glucose when titrating dose)

Titrating per MIXED Insulin guideline

Switching Insulin Types

Switching from NPH to Lantus/Levemir:
consider if patient has nocturnal hypoglycemia or persistent day time hyperglycemia:
Start Lantus/Levemir before bed at 50%-70% of total daily NPH dose* (then titrate per basal insulin guideline)

Switching from Lantus/Levemir to NPH:
consider if patient needs to switch due to cost
Start NPH before bed at 40% of total daily Lantus/Levemir dose* (then titrate per basal insulin guideline)
Caution:
- Watch for nocturnal hypoglycemia
- Evaluate day time glucose levels. If necessary consider add morning NPH dose as well.
- If adding morning NPH dose, consider lower lunch prandial insulin due to midday NPH peak

Switching from Regular to Humalog/Novolog/Apidra:
consider if patient has day time hypoglycemia
Start Humalog/Novolog/Apidra at 80% of current Regular Insulin mealtime dose* (then titrate per prandial insulin guideline)

Switching from Humalog/Novolog/Apidra to Regular Insulin:
consider if patient needs to switch due to cost
Start Regular Insulin at 80% of current mealtime Humalog/Novolog/Apidra dose* (then titrate per prandial insulin guideline)
Caution:
- Watch for day time hypoglycemia
- Need to take Regular Insulin injection 30 minutes before meals

*NOTE: consider alternate dose adjustment if low or high glucose levels on current insulin dose!

Pre-Operative Diabetes Guidelines

General Recommendations
Day before surgery: Take all regular diabetes pills and oral medications (except hold evening metformin dose). Take Byetta, Victoza and Symlin as usual.
Day of surgery*: Hold all regular diabetes pills and oral medications. Hold Byetta, Victoza and Symlin.

*Tell patient to treat any hypoglycemia with 15 gms of glucose gel or glucose tabs or 4 ozs of clear juice such as apple or cranberry.

Adjusting Insulin
Day before surgery:
- Basal Insulin: Take 80% of usual nighttime dose*
- Prandial Insulin: Take as usual
- Mixed Insulin: Take 80% of usual nighttime dose*

Morning of surgery:
- Basal Insulin: Take 80% of usual morning dose*
- Prandial Insulin: Hold
- Mixed Insulin: Hold

*NOTE: may consider alternate dose adjustment if low or high glucose levels on current insulin dose!
ADDITIONAL INFORMATION:

Alternate self titration for basal insulin: 
May consider self titrating basal insulin by increasing dose 2 unit every 2-3 days until average fasting glucose is < 130. Self titration of 2 unit intervals may be easier for patients using insulin syringes.

Other diabetes medication in combination with insulin:
- **Metformin**: Continue if able because helps prevent weight gain when patient on insulin.
- **Secretagogues**: (sulfonylureas and meglitinides): Consider continuing when patient is on basal insulin only. Stop when patient is on prandial or mixed insulin.
- **Other Diabetes Medications**: decision to continue or discontinue other diabetes medications should be made with consideration of multiple individual patient characteristics.

**Note**: once patient’s glucose levels are controlled with insulin, it may occasionally be possible to stop insulin and continue or switch to oral medications depending of the stage of the diabetes and changes in other individual patient characteristics.

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**Example of correction factor using 1800 Rule**

Patient on 60 units basal insulin. Total Daily Dose (TDD) is 60 units. Correction Factor (CF) = 1800 / 60 = 30. If pre-meal glucose = 230, blood glucose is 150 mg/dl above goal of 130; Correction is 150/30 = 5 units. Give 5 units in addition to prandial insulin dose being used to cover meal.

**Example of Insulin with prandial dose of 4 units and correction factor of 1:50, correcting down to 130**

<table>
<thead>
<tr>
<th>Pre-meal Glucose Level</th>
<th>Prandial Insulin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-130</td>
<td>4 units</td>
</tr>
<tr>
<td>130-180</td>
<td>5 units</td>
</tr>
<tr>
<td>180-230</td>
<td>6 units</td>
</tr>
<tr>
<td>230-280</td>
<td>7 units</td>
</tr>
<tr>
<td>280-330</td>
<td>8 units</td>
</tr>
<tr>
<td>330-380</td>
<td>9 units</td>
</tr>
<tr>
<td>380-430</td>
<td>10 units</td>
</tr>
<tr>
<td>&gt;430</td>
<td>11 units</td>
</tr>
</tbody>
</table>

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**Example of carbohydrate ratio using 500 Rule**

Patient on 50 units basal insulin daily. Total Daily Dose (TDD) is 50 units. Insulin to Carbohydrate Ratio (I:C Ratio): 500/50 = 1:10 units. For a 60 gm carbohydrate meal = 60/10 = take 6 units.

**Mealtime Advice**
- Take rapid acting prandial and mixed insulins just before a meal. At restaurants only take once food actually arrives at table.
- Take Regular insulin 30 minutes before meals.

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**Hypoglycemia**
- Tell patient to carry rapidly absorbed carbohydrate source at all times and teach friends and family about how to treat low glucose. Treat low glucose (<70) as per **Rule of 15's**: Give 15 gm of rapidly absorbed carbohydrate (ie: 1/2 cup juice or 4 glucose tabs). Recheck glucose level in 15 minutes. Give another 15 gm of carbohydrate if glucose still < 70. Repeat until the glucose level higher than 70. Once glucose level returns to normal, consider follow with a snack or meal. Inform provider of hypoglycemia episodes at next appointment. If severe (unconscious, seizures) call 911 and give glucagon (1.0 for adult, 0.5 for child < 50 lbs) if available. Prescribe glucagon kit for high risk patient to have at home.

**Identification**
- Carry personal ID and wear medical ID.

**Insulin Device**
- Consider insulin pen if able for patients with vision, dexterity or cognition difficulties or for patient convenience. Note insulin pens cost more than insulin vials. However, total cost of insulin pen is potentially lower than vial if patient’s daily insulin dose is low (since less unused insulin needs to be discarded at end of month). Insulin pens may not be covered by insurance.

**Storage**
- Refrigerate insulin until opened. Discard after expiration date. Once opened can be kept at room temperature. Avoid heat. Replace insulin vial or pen as required per specific insulin package insert.

**Syringes and Needles**
- For pen consider use pen needles that are 31 or 32 gauge and 5 mm to 8 mm. For vials consider use syringes that are 0.3-1.0 cc with ultrafine 5/16” 31 gauge needles. Instruct patient to leave needle in skin for 5 or more seconds after injection completed.

**Exercise**
- Low glucose levels may occur during or after exercise. Carry glucose source when exercising. Check glucose before and during exercise. If patient has low glucose levels associated with exercise: consider decreasing preceding prandial insulin dose (if within several hours before exercise) and/or taking extra carbohydrates before or during exercise.

**Education**
- All patients should receive Diabetes Self Management Training (DSMT) and Medical Nutrition Therapy (MNT) by certified diabetes educator if possible.

Sutter Medical Foundation. February 2011
LITERATURE SEARCH AND RATING PROCESS

The identification and rating of the body of evidence to support the Type 2 Diabetes Insulin Guidelines followed a three-step process:

1. Pertinent articles for review were by identified by a Medline search including the key words: Diabetes Mellitus, Type 2/drug therapy, Hypoglycemic Agents, Insulin, Algorithms, Titration, Titration, Bolus, and Basal. The search was limited to 2005-2010 and the language English. Older clinical trials evaluating Regular insulin were included, since none were available from 2005-2010. The most recent ADA and AACE consensus statements, position statements and technical reviews on diabetes care topics were also identified. Insulin package insert recommendations were obtained from Lexi-Comp, Online.

2. Experts in diabetes care then examined the list of articles and included only those that were identified as randomized controlled clinical trials examining the initiation and titration of insulin, the most recent general consensus statements, technical reviews, or position statements by ADA and AACE, the most recent insulin review article by the American Academy of Family Practice, and the Lexi-Comp online insulin package insert recommendations.

3. The articles were reviewed and the body of evidence was rated using a system adopted from the ADA grading system for clinical practice recommendations. American Diabetes Association Standards of medical care in diabetes--2010. Diabetes Care. 2010 Jan;33 Suppl 1:S12.

(A) Clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered, including:
- Evidence from a well-conducted multicenter trial
- Evidence from a meta-analysis that incorporated quality ratings in the analysis
- Compelling non-experimental evidence, i.e., “all or none” rule developed by Center for Evidence Based Medicine at Oxford
- Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including:
  - Evidence from a well-conducted trial at one or more institutions
  - Evidence from a meta-analysis that incorporated quality ratings in the analysis

(B) Supportive evidence from well-conducted cohort studies:
- Evidence from a well-conducted prospective cohort study or registry
- Evidence from a well-conducted meta-analysis of cohort studies

(C) Supportive evidence from a well-conducted case-control study
- Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results
- Evidence from observational studies with high potential for bias (such as case series with comparison to historical controls)
- Evidence from case series or case reports

Conflicting evidence with the weight of evidence supporting the recommendation

Expert consensus or clinical experience

GENERAL INFORMATION: Consensus Statements and Reviews


BASAL INSULIN (A-level evidence)

PRANDIAL INSULIN (A-level evidence)

Anderson J H; Brunelle R L; Koivisto V A; Pfutzner A; Trautmann M E; Vignati L; DiMarchi R. Reduction of postprandial hyperglycemia and frequency of hypoglycemia in IDDM patients on insulin-analogue treatment. Multicenter Insulin Lispro Study Group. Diabetes Feb 1997 46 (2) p265-70.


MIXED INSULIN (A-level evidence)


Robbins DC, et al. Mealtime 50/50 basal + prandial insulin analogue mixture with a basal insulin analogue, both plus metformin, in the achievement of target HbA1c and postprandial blood glucose levels in patients with type 2 diabetes: a multinational, 24-week, randomized, open-label, parallel-group comparison. Clin Ther. 2007 Nov;29(11):2349-64.