Diabetes Medications

Type 1
Insulin is needed

Type 2
Oral Diabetes Medications
Or
Oral Diabetes Medications plus Insulin
Or
Insulin Alone

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Metformin

(Glucophage®, Glucophage XR®, Glumetza™)
Insulin sensitizer
Used world wide for diabetes control for many years
1st line therapy in type 2 diabetes
Weight neutral, modest improvement in lipids
Lower cost
Effective in combination therapy
Research shows CV event risk reduction

Thiazolidinedione (TZD’s)
Pioglitazone (Actos®) and Rosiglitazone (Avandia®)
Insulin sensitizers
Possible side effects: Weight gain, edema, fractures, bladder cancer concern with long term use
Contraindications:
Heart Disease (Black box warning CHF)
Liver disease
Kidney disease
Pregnancy

Insulin Secretagogues
Glipizide (Glucotrol®), Glipizide Extended Release, Glyburide (Diabeta®), Glimepiride (Amaryl®), Repaglinide (Prandin®), and Nateglinide (Starlix®)

Helps release insulin from the pancreas
Side effects: Hypoglycemia & weight gain
Contraindications:
Kidney disease (use with caution)
Liver disease
Pregnancy
Lab tests: Creatinine & ALT
"NEW KIDS ON THE BLOCK"

Incretin mimetics
Amylinomimetic
  DPP4 Inhibitors
SGLT2 transport inhibitors
Inhaled insulin

GLP-1 Agonists

GLP-1 is a type of hormone, known as an incretin, and it is found naturally in the body. When food is consumed, GLP-1 is released from the small intestines. GLP-1 has multiple actions in the body:
1) reduces appetite by suppressing receptors in the hypothalamus
2) slows gastric emptying —> makes you feel full —> decreases food intake
3) helps beta cells in pancreas produce insulin when blood glucose is high
4) helps suppress glucose output from liver during meals

GLP-1 AGONISTS

Byetta (Exenatide)
Twice a day

Victoza (Liraglutide)
Once a day

Bydureon (Exenatide ER)
Once a week

Tanzeum (Albiglutide)
Once a week

Trulicity (Dulaglutide)
Once a week

Symlin
pramlintide acetate injection

Synthetic analog of human amylin hormone made in the beta cells of the pancreas
■ Helps suppress glucagon secretion
■ Regulates gastric emptying

Dipeptidyl Peptidase-4 Inhibitor (DPP-4 Inhibitor)

Selective inhibitor of dipeptidyl peptidase-4 (DPP-4)
Increases GLP-1 levels 2-3 fold
Enhances insulin secretion, reduces glucagon levels, weight neutral
Side effects: Low risk of hypoglycemia
Contraindications: Kidney disease; use lower dose
  Pregnancy (Category B)

Sitagliptan (Januvia) Saxagliptan (Onglyza)
Linagliptin (Tradjenta) Alogliptin (Nesina)
Vildagliptin (Galvus)

SGLT Inhibitors

Canagliflozin (Invokana), Dapagliflozin (Farxiga),
Empagliflozin (Jardiance)

MOA: the kidneys reabsorb glucose via sodium glucose transporters primarily SGLT2. These drugs inhibit SGLT2, reducing glucose reabsorption and increasing urinary glucose excretion.
*Jardiance has demonstrated CV risk

Side effects: genital fungal infections, UTI, hypotension, hypoglycemia when taken with insulin or insulin secretagogues, impaired renal function, increased LDLc.
Contraindications: pregnancy, children or persons with renal impairment.

Insulin

- Protein hormone secreted by the pancreas
- Regulates the storage of glycogen in the liver
- Accelerates oxidation of glucose in cells

There are several different types of insulin and ways of delivery (vial & syringe, insulin pens, insulin pumps).

- The type of insulin and how it is delivered is dependent on the provider’s orders, glucose patterns, insurance coverage, and the ability of the patient to deliver the insulin.
- Some hospitals use only vial & syringe for giving insulin, while other hospitals use insulin pen devices.

Basal/Background Insulin

- In the fasting state a small amount of insulin is needed to match the glucose that is made by the liver.

Types of Insulin

<table>
<thead>
<tr>
<th>Insulin Types</th>
<th>Speed of Action</th>
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<tbody>
<tr>
<td>Lispro (Humalog)</td>
<td>• Rapid (Bolus or Mealtime)</td>
</tr>
<tr>
<td>Aspart (Novolog)</td>
<td>• Short</td>
</tr>
<tr>
<td>Glulisine (Apidra)</td>
<td>• Intermediate</td>
</tr>
<tr>
<td>Regular NPH</td>
<td>• Long (Basal or Background)</td>
</tr>
<tr>
<td>Detemir (Levemir)</td>
<td></td>
</tr>
<tr>
<td>Glargine (Lantus &amp; Toujeo)</td>
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BASAL INSULIN CONCEPT

- Basal Insulin:
  - Suppresses glucose production between meals and overnight.
  - 40-50% of daily needs
NPH INSULIN

Basal insulin
Daily bedtime dose – lowers fasting blood glucose
With Regular or rapid-acting analog – usually twice daily

Long-Acting Basal Insulins

Glargine (Lantus) and Detemir(Levemir)
Background insulin
Usually once daily – same time
Cannot be mixed
Cannot be pre-drawn
Less hypoglycemia than with NPH

Toujeo (insulin glargine injection)

Prescription Toujeo® is a long-acting insulin (300 units/ml) used to control blood sugar in adults with diabetes mellitus. Toujeo® contains 3 times as much insulin in 1 ml as standard insulin (100 Units/ml). Toujeo® is not for use to treat diabetic ketoacidosis. Toujeo® should not be used in children. Developed by Sanofi.

Degludec U 200 Insulin

- Insulin degludec (IDeg) is a new basal insulin that has an ultra-long and flat time-action profile with a half-life >42 hours.
- Great for shift workers as doses can be given as soon as 8 hours and as long as 42 hours apart.
- Works better than splitting Glargine or Detemir insulins as the second dose is often forgotten.
- U100 and U200 pens available.


Basaglar

• Basaglar® approved as a biosimilar insulin in the US
• FDA considers it a “follow-on” insulin glargine product
• Available only as a pen

BOLUS/MEALTIME INSULIN CONCEPT

Bolus Insulin is given with food intake
• Limits hyperglycemia after meals
• Immediate rise and sharp peak after 1 hour
• 10-20% of total daily insulin requirement at each meal
REGULAR INSULIN

- Short acting insulin
- Can be mixed with NPH insulin
- Peaks later than rapid acting analog
- Often used in pregnancy

RAPID ACTING ANALOGS

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
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<tbody>
<tr>
<td>lispro</td>
<td>Humalog</td>
</tr>
<tr>
<td>aspart</td>
<td>NovoLog</td>
</tr>
<tr>
<td>glulisine</td>
<td>Aprida</td>
</tr>
</tbody>
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Meal Coverage + compensatory coverage

Inhaled Insulin

Afrezza

Regular insulin
Patient must have a physical exam and a spirometry test before using.
Deep into the lungs in 1-2 seconds. Out of system in 180 minutes.
Two devices packaged in a box.

IMPORTANT SAFETY INFORMATION: Sudden lung problems (acute bronchospasm) have been seen in patients with asthma and COPD (chronic obstructive pulmonary disease) using Afrezza®.
Afrezza® is not to be used in patients with long-term lung disease such as asthma or COPD, or smokers.

Inhaled insulin continued...

Peaks levels about 20 minutes, Peak activity ~ 1 hour
Duration of action 2-3 hours

MIXED INSULINS

Novolin 70/30  Novolog Mix 70/30

Know the difference!
U500 INSULIN

- 500 units per ml
- Given to insulin resistant type 2 diabetics who are on > 200 units per day total daily dose
- Most closely mimics NPH insulin
- Injected 2-4 times a day
- Now available in pens
  - Dials in 5 unit increments
  - No dose conversion
  - Up to 300 units per injection

Xultophy

Insulin degludec 100 units/ml and Liraglutide 3.6mg/ml

- Type 2 diabetes
- Once a day dosing
- Provides basal insulin with GLP1 inhibitor
- Increased chance for getting to goal A1c
- Less weight gain than with insulin alone
- Contraindicated in persons with medullary thyroid cancer

Glargine lowers fasting bg while Lixi works better on post prandial blood sugars.

Fixed ratio combination of IGlar and Lixisenatide

IGlar 2 units and 1 μg lixisenatide
Max dose IGlar 60 units and 30 μg lixisenatide

Once a day dosing + no weight gain

Diabetes Care 2016 Aug; dc160917. https://doi.org/10.2337/dc16-0917

Continuous Subcutaneous Insulin Infusion: Pumps

Insulin pumps first developed in the 1970s.
Closely approximates normal physiological insulin delivery by continuously delivering a basal rate of rapid acting insulin and allows for bolus of insulin just prior to meals based on carbohydrate content.
Requires a motivated and capable patient. Intensive education is necessary up front and then close attention to monitoring of glucose patterns so appropriate adjustments can be safely made.

Several on the Market:

Professional: Medtronic Ipro and Dexcom G4
Personal:
Medtronic enlite with insulin pump
DEXCOM>approved for use by FDA to use for treatment decisions (without a fingerstick blood sugar).

Artificial Pancreas

Is it here yet?

Artificial pancreas device system (APDS)—an innovative device that automatically monitors blood glucose and provides appropriate insulin doses in people with diabetes who use insulin.

A computer-controlled algorithm connects the CGM and insulin infusion pump to allow continuous communication between the two devices. Sometimes an artificial pancreas device system is referred to as a “closed-loop” system.

Approved by FDA Oct 2016: Medtronic 670G hybrid closed loop system, automatically administers or withholds insulin in response to sensor glucose measurements. Approved for type 1 only over age 14.
Stem Cell Transplant

- Not available except for in clinical trials
- Limited by availability of stems cells
  - Autologous Hemapoetic Stem Cells (from your own bone marrow)
  - Adult stem cells (cadaver)
  - Placental stem cells (limited availability)
  - Embryonic stem cells (controversial)
- Some success was noted with autologous hemapoetic stem cell transplants in type 2 patients, they required less insulin.
- Possible risk of tumor formation


Pancreas Transplant

Each year, approximately 1,300 people with type 1 diabetes receive whole-organ pancreas transplants.
- 83% success rate at end of 1 year
- Limited availability dependent upon donors
- Must remain on anti-rejection drugs for the rest of their lives putting them at risk for other infections and diseases
- Often done in conjunction with kidney transplant