# Figures and Tables

## Fig.1.

Simplified flowchart for American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE) 2009 glycemic control algorithm. Pathways are provided for patients with hemoglobin Ale (A1C) in 3 ranges: 6.5% to 7.5%, >7.6% to 9.0%, and >9.0%. There is a progression from rnonotherapy, to dual therapy, to triple therapy, to insulin therapy with or without additional agents. The order of presentation of regimens indicates general priorities that should be customized to the individual patient, with consideration of contraindications and precautions, allergies, comorbid conditions, drug-drug interactions, and drug-laboratory interactions. Physicians must be thoroughly familiar with complete prescribing information before selection of therapy. In each case, response to therapy should be monitored closely (determination of A1C every 2 to 3 months), and titration of dosages or changes of regimen should be implemented in a timely manner. Rx = treatment. Note accompanying Table of Annotated Abbreviations for Figure 1.

## Table of Annotated Abbreviations for Figure 1(a)

| **Abbreviation** | **Class** | **Generic name** | **Trade name** |
|---|---|---|---|
| AGI | α-Glucosidase inhibitor | Acarbose<br>Miglitol | Precose<br>Glyset |
| DPP4 | Dipeptidyl-peptidase-4 (DPP-4) inhibitor | Sitagliptin<br>Saxagliptin | Januvia<br>Onglyza |
| GLP-1 | Incretin mimetics (glucagonlike peptide-1 agonist) | Exenatide | Byetta |
| MET | Biguanide | Metformin | Metformin (generic), Glucophage XR, Glumetza, Riomet, Fortamet |
| SU | Sulfonylurea | Glyburide | DiaBeta, Glynase, Micronase |
| | | Glipizide | Glipizide (generic), Glucotrol, Glucotrol XL |
| | | Glimepiride | Amaryl |
| TZD | Thiazolidinedione | Rosiglitazone | Avandia |
| | | Pioglitazone | Actos |
| **Abbreviation** | **Definition** | **Comment** | |
| FPG | Fasting plasma glucose | After overnight fast of at least 8 hours | |
| PPG | Postprandial glucose | 2 hours after a meal | |

a The following single-tablet combinations of agents are available:
sitagliptin + metformin (Janumet), pioglitazone + metformin (ActoPlus Met),
rosiglitazone + metformin (Avandamet), repaglinide + metformin (PrandiMet),
glipizide + metformin (Metaglip and generic), and glyburide + metfonnin (Glucovance and generic).

## Table AI. Outline of Various Types of Insulin

| **Type of insulin** | **Trade name** | **Comment** |
|---|---|---|
| **Rapid-acting insulin analogues** | | |
| Aspart<br>Lispro | NovoLog<br>Humalog | Superior to regular human insulin in terms of more rapid action profile |

| | | |
|---|---|---|
| Glulisine | Apidra | with reduced risk of hypoglycemia 2-5 hours after a meal or overnight |
| **Premixed insulin/protamine** | | |
| Aspart + aspart-protamine<br>Lispro + lispro-protamine | NovoLog Mix<br>Humalog Mix | Usually used twice a day before breakfast and dinner; provides postprandial coverage with 2 injections per day; less flexible than use of basal-bolus therapy with a combination of rapid-acting and long-acting analogues |
| **Long-acting insulin analogues** | | |
| Glargine | Lantus | Can be used with 1 injection per day in patients with type 2 diabetes |
| Detemir | Levemir | Can be used with 1 injection per day in patients with type 2 diabetes; excellent reproducibility of absorption profile within individuals; possibly less weight gain than with other insulins |
| **Not recommended** | | |
| Regular human insulin | Humulin R<br>Novolin R | Onset of action is too slow and persistence of effect is too long to mimic a normal prandial physiologic profile; the result is impaired efficacy and increased risk of delayed hypoglycemia |
| NPH insulin | Humulin N<br>Novolin N | Does not provide a sufficiently flat "peakless" basal insulin; highly variable absorption even within individuals; increased risk of hypoglycemia compared with the long-acting insulin analogues glargine or detemir |

## TableA2 Summary of Insulin Regimens

| **Insulin regimen** | **Components and frequency of administration** | **Injections per day** |
|---|---|---|
| Basal | Glargine or detemir (daily or twice a day) | 1 or 2 |
| Premixed | NovoLog Mix or Humalog Mix (usually twice a day; occasionally used daily or 3 times a day) | 2 |
| Prandial | NovoLog, Humalog, or Apidra (usually 3 times a day) | 3 |
| Basal-bolus (multiple daily injections) | NovoLog, Humalog, or Apidra (usually 3 times a day) in combination with glargine or detemir (daily) | 4 |
| Continuous subcutaneous insulin infusion | NovoLog, Humalog, or Apidra | Continuous |

## NOTES

| Generic | Brand | Dose | Onset<br>Duration | Price |
|---|---|---|---|---|
| **Biguanides** | | | | |
| Metformin | Generic | Start 500 mg po bid with meals or 850 mg po qd; Max 1000 mg po bid | Half-life: 6.2 h (plasma); 17.6 h (blood) | 500 mg #60 $13<br>850 mg #90 $78<br>1000 mg #30 $18 |
| Metformin | Glucophage | same | same | 500 mg #60: 70<br>850 mg #60 $114<br>1000 mg #60: $142 |
| Metformin | Generic ER | same | same | 500 mg #90 $21<br>750 mg #30: $33 |
| Metformin | Glucophage XR | same | same | 500 mg #60: $70<br>750 mg #30: $54 |
| **Dipeptidyl-Peptidase-4 Inhibitors (DDP-4)** | | | | |
| Sitagliptin | Januvia | 100 mg po qd | Half-life: 12.4 h | 25 mg #90 $646<br>50 mg #30 $221<br>100 mg #30 $216 |
| Sitagliptin-Metformin | Janumet | Start 50-500 mg po bid; Max 50 mg-1000 mg po bid | | 50-500 mg #60 $217<br>50-1000 mg #60 $216 |
| Sitagliptin-Metformin | Janumet XR | Start 100-2000 mg po hs; Max 50/1000 mg 2 tabs po hs | | Not available |
| Linagliptin-Metformin | Jentadueto | Start 2.5-500 mg po bid; Max 2.5-1000 mg 2 tabs po bid | | Not available |
| Sitagliptin-Simvastatin | Juvisync | Start 100-40 mg po hs; adjust after 4 wks | | Not available |
| Saxagliptin | Onglyza | 2.5-5.0 mg po qd | Half-life 2.5 h, 3.1 h (metabolite) | 2.5 mg #30: $240<br>5 mg #30: $230 |
| Saxagliptin-Metformin | Kombiglyze XR | Start 5-500 mg po qd; Max 5-500 2 tabs po qd | | 2.5-1000 mg #30 $120<br>5-500 mg #30: $240<br>5-1000 mg #30: $230 |
| Linagliptin | Tradjenta | 5 mg po qd | Half-life: 12 h | 5 mg #30: $230 |
| **Glucose-Like Peptide-1 (GLP-1)** | | | | |
| Exenatide | Byetta | Start 5 mcg sc <1h before meals bid x1mo, then inc to 10 mcg sc bid | Half-life: 2.4 h | 10 mcg/0.04ml (1 pen, 2.4 ml): $282<br>5 mcg/0.02ml (1 pen, 1.2 ml): $330 |
| Exenatide | Bydureon | 2 mg sc qwk | Half-life: 2.4 h | Not available |
| Liraglutide | Victoza | Start 0.6 mg sc qd x1wk then 1.2 mg sc qd, max 1.8 mg/day | Half-life: 13 h | 18 mg/3ml (1 box, 6 ml): $306<br>18 mg/3ml (1 box, 9 ml): $432 |
| **Long-acting Insulins** | | | | |

| | | | | |
|---|---|---|---|---|
| Insulin glargine | Lantus | Start: 0.5-1u/kl/day sc hs; then adjust according to fasting glucose readings | Onset 1h; no peak; duration 24h | 100 u/ml (1 vial, 10 ml): $119<br>100 u/ml (1box, 15ml): $225 |
| Insulin detemir | Levemir | 0.1-0.2 u/kg sc hs; then adjust as above | Onset 5-7h; no peak; duration 24h | 100 u/ml (1 vial, 10 ml): $136<br>100 u/ml (5 pens, 3 ml): $242 |
| **Short-acting analog insulins** | | | | |
| Insulin aspart | NovoLog | Cover meals with 5 units/gram CHO < 15 min before meals; adjust according to the two hour after-meal glucose reading; may add a sliding scale | Onset < 0.,25 h, Peak 1-3 h, Duration 3-5 h | 100 u/ml (1 vial, 10 ml): $141<br>100 u/ml (1 box, 15 ml): $258<br>100 u/ml (5 cartridges, 3 ml): $265 |
| Insulin aspart protamine-Insulin aspart | Novolog Mix 70/30 | Cover meals with 5 units per gram of CHO * 70% total; adjust according to next pre-meal glucose reading; adjust 30% total according to 12 hour after-meal glucose reading | Onset < 0.25 h, Peak 1-2 h, Duration 12-24 h | 100 u/ml (1 vial, 10 ml): $138<br>100 u/ml (5 pens, 3 ml): $258 |

Abbreviations: / means a ratio such as numerator divided by denominator, u/ml means units per mililiter; # means number as in dispensing;< means less than; bid means twice a day; CHO means carbohydrateER means extended release; h means hour; hs means hour of sleep, or bedtime; kg means kilograms; Max means maximummin means minute; ml means mililiter; po means orallyqd menas dailyqwk means once a weeksc means subcutaneous;tabs means tablets u means units; XR means extended release.