# Example of Therapeutic Management of Type 2 Diabetes

Check A1c 6 to 12 weeks after initiation or dose change

Reinforce lifestyle changes in addition to medications. Metformin to maximum dose (2,000 to 2,550 mg/day) unless not tolerated or contraindicated

A1c <7% or below individualized target

A1c <9% but above target goal

A1c ≥9%

Add second agenta from Table 1 or insulin therapya,b based on patient-specific factors.c Otherwise, discuss and assist provider with treatment options from Table 2. Check A1c in 6 to12 weeks.

Continue current therapy or de-escalate therapy as appropriate

Consider insulin therapya,b

A1c <7% or below individualized target?

Continue current therapy or de-escalate therapy

as appropriate

Add third agenta from Table 1 or insulin therapya,b based on patient-specific factors.c Otherwise, discuss and assist provider with treatment options from Table 2.

Check A1c in 6 to 12 weeks.

A1c <7% or below individualized target?

Discuss and assist primary care provider with next steps in therapy

Continue current or de-escalate therapy as appropriate

a Primary care provider (PCP) will be notified via notes in EMR; PCP will co-sign prescriptions.

b Refer to insulin initiation and insulin adjustment protocols, below.

c Patient-specific factors include anticipated efficacy of antihyperglycemic agents at achieving A1c goal, hypoglycemia risk, weight gain, side effects, and costs.

**Table 1. Noninsulin antihyperglycemic agents for the treatment of type 2 diabetes**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Generic**  **(Brand Name)** | **Strength (mg)** | **Initial Dose (mg)** | **Max Dose (mg)** | **Usual Dose (mg)** |
| *Biguanide* | | | | |
| Metformin  (Glucophage) | 500, 850, 1000 | 500 or 850  daily | 2550 daily | 1500-2000  divided (BID) |
| Metformin extended-release  (Glucophage XR/Fortamet) | 500, 750 | 500 daily with evening meal | 2500 daily | 1500-2000 daily or divided |
| *DPP-4 inhibitors* | | | | |
| Sitagliptin  (Januvia) | 25, 50, 100 | 50-100 daily | 100 daily | 100 daily |
| Saxagliptin  (Onglyza) | 2.5, 5 | 2.5-5 daily | 5 daily | 2.5-5 daily |
| Linagliptin (Trajenta) | 5 | 5 daily | 5 daily | 5 daily |
| Alogliptin (Nesina) | 6.25, 12.5, 25 | 25 daily | 25 daily | 25 daily |
| *GLP-1 agonists* | | | | |
| Liraglutide  (Victoza) | Multidose pen | 0.6 daily | 1.8 daily | 1.8 daily |
| Albiglutide  (Tanzeum) | 30, 50 | 30 weekly | 50 weekly | 30-50 weekly |
| Dulaglutide  (Trulicity) | 0.75, 1.5 | 0.75 weekly | 1.5 weekly | 0.75-1.5 mg weekly |
| Exenatide (Byetta) | 5 mcg, 10 mcg | 5-10 mcg BID | 10 mcg BID | 10 mcg BID |
| Exenatide extended-release (Bydureon) | 2 | 2 weekly | 2 weekly | 2 weekly |
| Lixisenatidea (Adlyxin) | 10 mcg, 20 mcg | 10 mcg daily | 20 mcg daily | 20 mcg daily |
| *Sulfonylureas (Second Generation)* | | | | |
| Glimepiride  (Amaryl) | 1, 2, 4 | 1-2 daily | 8 daily | 4 daily |
| Glipizide  (Glucotrol) | 5, 10 | 2.5, 5 daily | 40 divided (BID) | 10-20 divided (BID) |
| Glipizide ER  (Glucotrol XL) | 2.5, 5, 10 | 5 daily | 20 daily or divided (BID) | 5-20 daily or divided (BID) |
| Glyburideb  (Diabeta, Micronase) | 1.25, 2.5, 5 | 2.5-5 daily | 20 daily or divided (BID) | 5-20 daily or divided (BID) |

BID, twice daily.

a Expected to be available late 2016.

b Use glyburide with caution (higher risk of prolonged hypoglycemia in older adults and those with renal impairment).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Generic**  **(Brand Name)** | **Strength (mg)** | **Initial Dose (mg)** | **Max Dose (mg)** | **Usual Dose (mg)** |
| *Thiazolidinedione* | | | | |
| Pioglitazone (Actos) | 15, 30, 45 | 15-30 daily | 45 | 15-45 daily |
| *Alpha-glucosidase inhibitor* | | | | |
| Acarbose (Precose) | 25, 50, 100 | 25 daily with meal | 300 | 50-100 TID before meals |
| Miglitol (Glyset) | 25, 50, 100 | 25 daily with meal | 300 | 25-100 TID |
| *Non-sulfonylurea insulin secretagogues* | | | | |
| Repaglinide (Prandin) | 0.5, 1.2 | 0.5 with meals | 16 | 0.5-4 AC to QID |
| Nateglinide (Starlix) | 60, 120 | 60-120 with meal | 360 | 60-120 AC |
| *Sodium-glucose cotransporter 2 (SGLT-2) inhibitors* | | | | |
| Empagliflozin (Jardiance) | 10, 25 | 10 daily | 25 | 10-25 daily |
| Canagliflozin (Invokana) | 100, 300 | 100 daily | 300 | 300 daily |
| Dapagliflozin (Farxiga) | 5, 10 | 5 daily | 10 | 5 in morning |

**Table 1 continued. Noninsulin antihyperglcemic options for the treatment of type 2 diabetes**

AC, *ante cibum* before meals; QID, four times a day; TID, three times a day.

**Table 3. Combination noninsulin antihyperglycemic agents for the treatment of type 2 diabetes**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Generic**  **(Brand Name)** | **Strength (mg)** | **Initial Dose (mg)** | **Max Daily Dose (mg)** | **Usual Dose (mg)** |
| Glipizide/metformin  (Metaglip) | 2.5/250,  2.5/500,  5/500 | 2.5/250 daily-2.5/500 BID or 2.5/500-5/500 BID | 10/2000  or  20/2000 | Titrate to effective dose (not over max) |
| Glyburide/metformin (Glucovance) | 1.25/250,  2.5/500,  5/500 | 1.25/250 daily-BID  or 2.5/500-5/500 BID | 10/2000  or  20/2000 | 2.5/500-10/1000  daily-BID |
| Repaglinide/metformin  (PrandiMet) | 1/500,  2/500 | 1/500 BID within 15 min prior to meal | 10/2500 | Titrate to effective dose (not over max) |
| Pioglitazone/metformin (Actoplus Met) | 15/500,  15/850 | 15/500-15/850 daily-BID | 45/2550 | Titrate to effective dose (not over max) |
| Pioglitazone/metformin ER (Actoplus Met XR) | 15/1000,  30/1000 | 15/1000-30/1000 daily | 45/2000 | Titrate to effective dose (not over max) |
| Sitagliptin/metformin (Janumet) | 50/500,  50/1000 | 50/500 BID or  50/1000 BID | 100/2000 | Titrate to effective dose (not over max) |
| Sitagliptin/metformin ER  (Janumet XR) | 50/500,  50/1000,  100/1000 | 50/500 BID or  50/1000 BIDor 100/1000 daily | 100/2000 | Titrate to effective dose (not over max) |
| Linagliptin/metformin (Jentadueto) | 2.5/500,  2.5/850,  2.5/1000 | 2.5/500 BID  or  2.5/850 BID  or  2.5/1000 BID | 5/2000 | 2.5-5/2000 mg daily |
| Linagliptin/metformin ER (Jentadueto XR) | 2.5/1000, 5/1000 | 2.5/1000 daily  or 5/1000 daily | 5/1000 | 2.5-5/1000 mg daily |
| Saxagliptin/metformin ER (Kombiglyze XR) | 2.5/1000,  5/500,  5/1000 | 2.5/1000 daily or  5/500 daily or  5/1000 daily | 5/2000 | 2.5-5/2000 mg daily |
| Alogliptin/metformin (Kazano) | 12.5/500,  12.5/1000 | 12.5/500 BID or  12.5/1000 BID | 25/2000 | 25/2000 mg daily |
| Canagliflozin/metformin (Invokamet) | 50/500,  150/500,  50/1000,  150/1000 | 50/500 BID  or 150/500 BID  or  50/1000 BID  or  150/1000 BID | 300/2000 | 100-300/2000 mg  daily |
| Dapagliflozin/metformin ER  (Xigduo XR) | 5/500,  10/500,  5/1000,  10/1000 | 5/500 daily-BIDor  5/1000 daily-BID or  10/500 daily  or  10/1000mg daily | 10/2000 | 5-10/2000 mg daily |
| Empagliflozin/metformin (Synjardy) | 5/500,  5/1000,  12.5/500,  12.5/1000 | 5/500 BID  or  5/1000 BID  or  12.5/500 BID  or  12.5/1000 BID | 25/2000 | 10-25/2000 mg daily |

Example protocol for initiating insulin

1. Start with NPH, detemir, or glargine.
2. The choice may vary depending on endogenous insulin secretion, need for mealtime insulin coverage, cost and convenience.
3. All patients started on insulin should demonstrate use of a glucometer and be educated about recognizing and treating hypoglycemia.

*NPH, detemir, or glargine insulin*

* 1. Continue metformin ± sulfonylurea depending on preprandial glucose.
  2. Add 10-20 units of NPH, detemir, or glargine insulin daily.
  3. Then increase insulin by 10% or 2-4 units every 3 days until attaining the goal fasting blood glucose of <130 mg/dL without hypoglycemia.
  4. Once fasting glucose is at goal, check post-prandial glucose; if >180 mg/dL, consider adding either rapid-acting or regular insulin before meals.

*NPH or detemir insulin (BID)*

1. Continue metformin, discontinue sulfonylurea.
2. Add 5-10 units of NPH or detemir insulin at breakfast and dinner (or bedtime).
3. Then increase insulin by 10% or at least 2 units every 3 days until attaining the goal fasting blood glucose and pre-dinner glucose of <130 mg/dL without hypoglycemia.
4. Once fasting glucose is at goal, check post-prandial glucose; if >180 mg/dL, consider adding either rapid or regular insulin before meals.

*Premixed insulin (intermediate and short-acting or rapid-acting mixtures)*

1. Continue metformin, discontinue sulfonylurea.
2. Add 10 units of pre-mixed insulin at breakfast and dinner.
3. Then increase pre-breakfast and/or pre-dinner insulin by 10% or at least 2 units every 3 days until attaining the goal fasting and pre-meal glucose level of <130 mg/dL without hypoglycemia.

## Sample protocol for adjusting insulin

|  |  |
| --- | --- |
| If overnight or before breakfast glucose is above/below target… | Adjust the dinner or bedtime dose of NPH or glargine |
| If before lunch glucose is above/below target… | Adjust the breakfast dose of regular or rapid-acting insulin |
| If before dinner glucose is above/below target… | Adjust the breakfast dose of NPH or adjust the lunch dose of regular or rapid-acting insulin |
| If before bedtime glucose is above/below target… | Adjust the dinner dose of regular or rapid-acting insulin |
| If fasting glucose levels are significantly higher than bedtime levels (i.e., twice as high), consider nocturnal hypoglycemia. Have the patient check glucose levels around 3:00 a.m. for two days during the week. If the glucose levels are: | |
| Normal in the middle of the night… | Increase the NPH dinner dose |
| Low in the middle of the night… | Decrease the NPH dinner dose |

*Disclaimer: Please note that clinical guidelines change frequently and this document is meant to serve as an example only. The therapeutic management of type 2 diabetes protocol flow chart can be modified so you can update it based on your patient population and current guidelines. This content is provided for informational purposes only and is not intended as medical advice, or as a substitute for the medical advice of a physician.*

Example provided courtesy of the University of Michigan Medical Group.

Source: *AMA.* *Practice transformation series: improve care for patients with type 2 diabetes. 2017.*