# Step-Wise Dosing and Titration of Oral Medications for Type 2 Diabetes

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| 7-8 | Less than 1.4 | Start single agent  
- Metformin 500 mg twice a day with food  
If on max tolerated dose of metformin, add 2nd oral agent  
- Add sulfonylurea (preferred due to cost)  
- Add pioglitazone | Increase every 1-2 weeks  
- Metformin: by 500 mg daily if preprandial blood glucose values are greater than 130-150.  
  o **Note:** slow titration is needed to decrease GI side effects  
  o **Note:** metformin use is contraindicated in renal dysfunction (Scr>1.5mg/dL in men or Scr>1.4mg/dL in females) and should not be used in patients aged >80 unless a measured creatinine clearance is within normal limits.  
- Glipizide or Glyburide: add 2.5 mg in the evening and then increase by 2.5 mg in the morning alternating with increasing evening dose if preprandial blood glucose values are greater than 130-150.  
- Glimepiride: by 1 mg daily if preprandial blood glucose values are greater than 130-150  
- Pioglitazone: by 15 mg per day if A1C is greater than 7 in 3 months.  
  o **Note:** slower dose titration for pioglitazone  
  o **Note:** Rosiglitazone has been associated with increased incidence of adverse events.  
    (American Diabetes Association: Consensus 2009 and 2007 Black Box Warning) |
| 7-8 | 1.4-2 | Start single agent sulfonylurea OR pioglitazone  
If on a single agent, add 2nd oral agent  
- Add sulfonylurea if patient already on pioglitazone  
- Add pioglitazone if patient already on sulfonylurea | Increase sulfonylurea or pioglitazone according to dosing titration above  
**Note:** glipizide max dose = 20 mg per day in 1-2 doses due to renal insufficiency  
  glyburide = Avoid use of glyburide in CrCl<50ml/min  
  glipizide = Avoid use of glipizide in CrCl <10ml/min |
| Greater than 2 | Start single agent pioglitazone  
If on a single agent, consider basal insulin | Increase pioglitazone according to dosing titration above  
See insulin table for titration of doses |

**Name**  
- Metformin - 1000 mg BID  
- Glipizide - 20 mg BID  
- Glyburide - 10 mg BID  
- Glimepiride - 8 mg daily  
- Pioglitazone - 45 mg daily

This serves as a guideline. Physician discretion to be used for management. Developed by DITTO Team, J Hariharan MD, I O'Shaughnessy, MD, Debbie Gillard RPH, L Guddie, RPH - 2006 ©

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*Medical College of Wisconsin*
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**A1C** | **S Creatinine** | **Medications** | **Dosing and Titration guidelines** – *(Recheck A1C in 3 months)*  
---|---|---|---  
8-9 | Less than 1.4 | Start combination therapy:  
- Metformin 500 mg twice a day with food **AND**  
- Sulfonylurea starting doses:  
  - Glipizide 5 mg BID before meals  
  - Glyburide 5 mg BID before meals  
  - Glimepiride 2 mg daily before breakfast **OR**  
- Metformin 500 mg twice a day with food **AND**  
- Pioglitazone 15-30 mg per day (Metformin w/sulfonylurea is preferred)  
| Increase every 1-2 weeks  
- Metformin: by 500 mg daily if preprandial blood glucose values are greater than 130-150.  
  - **Note:** slow titration is needed to decrease GI side effects  
  - **Note:** metformin use is contraindicated in renal dysfunction (Scr>1.5mg/dL in men or Scr>1.4mg/dL in females) and should not be used in patients aged >80 unless a measured creatinine clearance is within normal limits.  
- Glipizide or glyburide: add 2.5 mg in the morning alternating with increasing evening dose if preprandial blood glucose values are greater than 130-150 up to max dose.  
- Glimepiride: by 1 mg daily if preprandial blood glucose values are greater than 130-150 up to max dose.  
- Pioglitazone: by 15 mg per day if A1C is greater than 7 in 3 months.  
  - **Note:** slower dose titration for pioglitazone  
  - Rosiglitazone has been associated with increased incidence of adverse events.  
  (American Diabetes Association: Consensus 2009 and 2007 Black Box Warning)  
  (MAX doses listed above in yellow section)  
  
8-9 | 1.4-2 | Start combination therapy with sulfonylurea **and** pioglitazone  
| Increase sulfonylurea or pioglitazone according to dosing titration above  
**Note:** glipizide max dose = 20 mg per day in 1-2 doses due to renal insufficiency  
  glyburide = Avoid use of glyburide in CrCl<50ml/min  
  glipizide = Avoid use of glipizide in CrCl <10ml/min  
8-9 | Greater than 2 | Start single agent pioglitazone **OR** Begin basal insulin, basal insulin with pre-meal boluses, or premixed insulin  
| Increase pioglitazone according to dosing titration above  
| See insulin table for titration of doses  

**Byetta®** (exenatide) - Can consider if patient fails sulfonylurea and/or metformin; BMI greater than 27; and Creatinine clearance greater than 30mL/min  
Dosing- 5 mcg SQ BID for 1 month and then increase to 10 mcg SQ BID (MAX dose) if preprandial blood glucose values are greater than 130-150  

**A1C** | **S Creatinine** | **Medications** | **Dosing and Titration guidelines** – *(Recheck A1C in 3 months)*  
---|---|---|---  
Greater than 9 | Less than 1.4 | Begin combination therapy: metformin **AND** basal insulin, basal insulin with pre-meal boluses or premixed insulin  
| Increase metformin according to dosing titration above  
| See insulin table for titration of doses  
Greater than 9 | Greater than 1.4 | Begin basal insulin, basal insulin with pre-meal boluses or premixed insulin  
| See insulin table for titration of doses  

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