### 1st LINE
In ADDITION to lifestyle measures

<table>
<thead>
<tr>
<th><strong>METFORMIN</strong>*</th>
<th><strong>EFFICACY</strong></th>
<th><strong>MODERATE</strong></th>
<th><strong>CV BENEFIT</strong></th>
<th><strong>YES</strong></th>
<th><strong>HYPOGLYCAEMIA RISK</strong></th>
<th><strong>LOW</strong></th>
<th><strong>WEIGHT</strong></th>
<th><strong>REDUCTION</strong></th>
<th><strong>MAIN ADVERSE EVENTS</strong></th>
<th><strong>GASTROINTESTINAL</strong></th>
<th><strong>IN CKD STAGE 3A</strong></th>
<th><strong>MAXIMUM 2 g DAILY</strong></th>
</tr>
</thead>
</table>

**ONCE OSMOTIC SYMPTOMS RESOLVED, ADD**

### 2nd LINE
In ADDITION to lifestyle measures

<table>
<thead>
<tr>
<th><strong>SULPHONYLUREA</strong>*</th>
<th><strong>EFFICACY</strong></th>
<th><strong>HIGH</strong></th>
<th><strong>SULPHONYLUREA</strong>*</th>
<th><strong>MODERATE</strong></th>
<th><strong>SULPHONYLUREA</strong>*</th>
<th><strong>LOW/MODERATE</strong></th>
<th><strong>SULPHONYLUREA</strong>*</th>
<th><strong>MODERATE</strong></th>
<th><strong>PIOGlitAZONE</strong>*</th>
<th><strong>MODERATE</strong></th>
<th><strong>CV BENEFIT</strong></th>
<th><strong>NO</strong></th>
<th><strong>HYPOGLYCAEMIA</strong></th>
<th><strong>LOW</strong></th>
<th><strong>WEIGHT</strong></th>
<th><strong>LOSS</strong></th>
<th><strong>MAIN ADVERSE EVENTS</strong></th>
<th><strong>GENITAL MYCOTIC</strong></th>
<th><strong>IN CKD STAGE 3A</strong></th>
<th><strong>CAREFUL MONITORING</strong></th>
</tr>
</thead>
</table>

**IF NOT REACHING TARGET AFTER 3−6 MONTHS, REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE**

**ADD ONE OF:**

- **SULPHONYLUREA***  
- **SGLT2 INHIBITOR***  
- **DPP-4 INHIBITOR***  
- **PIOGlitAZONE***

### 3rd LINE
In ADDITION to lifestyle measures

**IF NOT REACHING TARGET AFTER 3−6 MONTHS, REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE**

**ADD EITHER AN ADDITIONAL ORAL AGENT FROM A DIFFERENT CLASS**

**OR AN INJECTABLE AGENT**

** IF BMI >30 kg/m² **

<table>
<thead>
<tr>
<th><strong>SULPHONYLUREA</strong>*</th>
<th><strong>EFFICACY</strong></th>
<th><strong>HIGH</strong></th>
<th><strong>GLP-1 AGONIST</strong>*</th>
<th><strong>HIGH</strong></th>
<th><strong>BASAL INSULIN</strong>*</th>
<th><strong>HIGH</strong></th>
<th><strong>CV BENEFIT</strong></th>
<th><strong>YES (SPECIFIC AGENTS)</strong></th>
<th><strong>LOW</strong></th>
<th><strong>WEIGHT</strong></th>
<th><strong>LOSS</strong></th>
<th><strong>MAIN ADVERSE EVENTS</strong></th>
<th><strong>GASTROINTESTINAL</strong></th>
<th><strong>IN CKD STAGE 3A</strong></th>
<th><strong>DOSE UNCHANGED</strong></th>
</tr>
</thead>
</table>

**IF BMI <30 kg/m²**

- **GLP-1 AGONIST***  
- **BASAL INSULIN***

** IF BMI >30 kg/m² **

- **stop DPP-4 inhibitor**  
- **consider reducing sulphonylurea**  
- **continue metformin**  
- **can continue pioglitazone**  
- **can continue SGLT2 inhibitor**

** IF BMI <30 kg/m² **

- **inject before bed**  
- **use NPH (isophane) insulin - or longer-acting analogues according to risk of hypoglycaemia**  
- **can continue metformin, pioglitazone, DPP-4 inhibitor or SGLT2 inhibitor**  
- **can reduce or stop sulphonylurea**

### 4th LINE
In ADDITION to lifestyle measures

**IF NOT REACHING TARGET AFTER 3−6 MONTHS, REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE ADD ADDITIONAL AGENT(S) FROM 3rd LINE OPTIONS (NEED SPECIALIST INPUT)**

** IF INSULIN INTENSIFICATION REQUIRED (NEED SPECIALIST INPUT)**

**ADD PRANDIAL INSULIN OR SWITCH TO TWICE-DAILY MIXED BIPHASIC INSULIN**

*Continue medication at each stage if EITHER individualised target achieved OR HbA1c falls more than 0.5% (5.5 mmol/mol) in 3−6 months. Discontinue if evidence that ineffective.*

**NOTES:** 1. Consider dose reduction. 2. Do not delay if first line options not tolerated / inappropriate. 3. See guideline pages 23 & 26-27. 4. See BNF: specific agents can be continued at reduced dose. 5. See BNF: no dose reduction required for lixisenatide. 6. Pioglitazone is contraindicated in people with (or with a history of) heart failure or bladder cancer. 7. Do not combine dapagliflozin with pioglitazone. 8. Caution with exenatide when eGFR<50 ml/min/1.73 m². 9. Adjust according to response. 10. Driving, occupational hazards, risk of falls, previous history.

**ABBREVIATIONS:** CKD 3A = chronic kidney disease stage 3A (estimated glomerular filtration rate 45−59 ml/min/1.73 m²) CV = cardiovascular