Atypical antipsychotics have mostly replaced the older ‘typical’ antipsychotics because they are more effective for treating the negative symptoms of schizophrenia, and have better patient acceptability.

Atypical antipsychotics include risperidone (Risperdal®), olanzapine (Zyprexa®), quetiapine (Quetapril®, Seroquel®), amisulpride (Soliat®, aripiprazole (Abilify®) and ziprasidone (Zeldox®). Clozapine is also an atypical antipsychotic which has a specific adverse reaction profile and higher risks associated with its use (visit www.saferx.co.nz to view the clozapine bulletin for more information).

There is a large variability in individual patient response with these medicines. In general, start at a low dose and carefully titrate upwards; adverse effects are often dose-related. Combinations should be avoided (unless during switching) due to an increased risk of adverse events.

**BE AWARE OF METABOLIC SYNDROME; IT IS THE MOST IMPORTANT CLINICAL PROBLEM**

An increase in body weight, hyperglycaemia and type 2 diabetes has been observed in some patients taking atypical antipsychotics. The risk is greatest with clozapine and olanzapine, but cases have also been reported with risperidone and quetiapine. The risk of metabolic syndrome appears to be lower with amisulpride, ziprasidone and aripiprazole.

All patients prescribed antipsychotics, regardless of risk factors, should be given advice on diet and lifestyle interventions, monitored for the emergence of diabetes, and have lipid levels checked.

**MONITOR FOR ADVERSE EFFECTS AND MANAGE EARLY**

**Cardiovascular effects**

Current users of typical or atypical antipsychotics have an increased risk of sudden cardiac death compared with non-users, and former-users of such medicines. Atypical antipsychotic medicines can prolong the QT interval and lead to ventricular tachyarrhythmias. Prolongation of QT interval has been observed mostly with ziprasidone, and to a lesser extent with risperidone and aripiprazole. Tachycardia has been observed with risperidone, olanzapine, quetiapine, and less so with ziprasidone.

An increased risk of stroke has been associated with all antipsychotic medicines. Patients with pre-existing cardiovascular disease or cardiovascular risk factors may require an ECG prior to initiating treatment with antipsychotic medications. All patients with schizophrenia should have an annual cardiovascular disease risk assessment.

**Postural hypotension and hypertension**

Postural hypotension can occur when initiating or up-titrating risperidone, olanzapine, and quetiapine. Ensure that older patients and their caregivers are informed of the increased risk of falls. There have also been cases of severe hypertension leading to collapse following risperidone use.

**Movement disorders**

‘Typical’ antipsychotics should never be used in patients with Parkinson’s disease; atypical agents should be used very cautiously due to the potential exacerbation of symptoms. Higher doses of risperidone and amisulpride are associated with tremor, muscular rigidity and acute dystonia. Risperidone, amisulpride and olanzapine may cause akathisia (including agitation and restlessness).

Although new-onset tardive dyskinesia is less likely to occur with atypical, compared with typical antipsychotics, it can occur in up to 3% of patients taking risperidone.

**Other adverse effects**

Anticholinergic effects such as dry mouth, constipation and blurred vision can occur particularly with clozapine and olanzapine. Sedation has been especially associated with clozapine, olanzapine and quetiapine.

Sexual dysfunction is one of the main causes of non-adherence to antipsychotic medicines, especially with risperidone. Dose reductions or switching medications may be necessary. The antipsychotic drugs with the lowest risk of sexual dysfunction are aripiprazole, ziprasidone and quetiapine.

➥ continued
UNDERSTAND THAT THERE ARE SOME POTENTIALLY SERIOUS ADVERSE EFFECTS

Neuroleptic Malignant Syndrome (NMS)
This is a rare but potentially fatal adverse effect of all antipsychotic medications. It is more common in young male patients taking higher doses and is often associated with hot weather and exercise. It is also more likely to occur with risperidone. Symptoms include muscular rigidity, pyrexia, confusion, disorientation, tachycardia and increased sweating. Patients with these symptoms require urgent assessment, cessation of antipsychotics, and supportive treatment. Please remember that like the older antipsychotics, atypicals are also associated with raised hepatic enzymes and blood dyscrasias. Arrange blood counts if unexplained infection or fever develops.

Weight gain
Weight gain is most common with olanzapine. If there is weight gain of over 2kg within the first 2 weeks of starting any atypical antipsychotic medicine, consider a change of agent.

Diabetes
People with schizophrenia have an increased risk of diabetes. Avoid olanzapine in particular if there are risk factors such as obesity or a family history of diabetes. Monitor all patients for symptoms of diabetes during treatment.

Lipids
If the patient has a pre-existing abnormal lipid profile, use atypical antipsychotic medications with caution. Monitor lipids during treatment for all patients.

TAKE CARE WITH PATIENTS AT RISK OF DEMENTIA
There is an increased risk of mortality and stroke in elderly patients with dementia who are prescribed antipsychotic medication. Start with half the adult dose, or less, and review for efficacy and the emergence of adverse effects at each visit. Antipsychotics are ineffective for wandering, social withdrawal, shouting, pacing, touching, or cognitive defects.

Note: Risperdone is the only atypical antipsychotic officially indicated for BPSD.

Off-label prescribing
Atypical antipsychotics are frequently prescribed for anxiety, and have also been used for sedation, and post traumatic stress disorder. These indications are ‘off-label’ so prescribers must discuss the decision to prescribe with the patient (and their family), obtain consent and document this in the patient’s notes.

MONITORING RECOMMENDATIONS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Blood Count</td>
<td>Initially, then annually</td>
<td></td>
</tr>
<tr>
<td>Urea and Electrolytes</td>
<td>Initially, then annually</td>
<td></td>
</tr>
<tr>
<td>Liver Function Test</td>
<td>Initially, then annually</td>
<td>Not required for amisulpride</td>
</tr>
<tr>
<td>Lipid Profile</td>
<td>Initially, at 3 months, and annually</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>Initially, regularly during first 3 months, then annually</td>
<td>If taking clozapine or olanzapine, monitor every 3 months for the rest of the first year</td>
</tr>
<tr>
<td>Fasting Blood Glucose</td>
<td>Initially, at 4-6 months, then annually</td>
<td>If taking clozapine or olanzapine, also test after the first month</td>
</tr>
<tr>
<td>ECG</td>
<td>Initially (if risk-factors present)</td>
<td>Refer to individual datasheets</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Initially and during dose titration</td>
<td>Not mandatory for amisulpride and aripiprazole</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Initially, at 6 months, then annually</td>
<td>Check sooner if indicated by clinical presentation</td>
</tr>
<tr>
<td>CVD Risk Assessment</td>
<td>Annually</td>
<td>For all patients with schizophrenia</td>
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</tbody>
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ACKNOWLEDGEMENTS

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REFERENCES