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<thead>
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<th>CHANGE RECORD</th>
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Medicines Management Tool for Antipsychotics

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Background

There is evidence to suggest that some antipsychotics are more effective than others: Clozapine is the treatment of choice for refractory illness, and olanzapine Amisulpride, and perhaps risperidone are more effective than other first and second generation antipsychotics\(^1\). Individual antipsychotic drugs differ by the range and extent of their side effect profile, principally in the following areas.

- Weight gain
- Hyperprolactinaemia
- Sedation
- EPSE
- Hyperlipidaemia
- Postural hypotension
- Other cardiovascular effects
- Hyperglycaemia

This Medicines Management tool is intended to be used assist clinicians and practitioners with the making of prescribing decisions, to target prescribing to produce a care plan that fits the individuals’ holistic needs.

The tool is a summary of current evidence for the selection of antipsychotics. Suggested monitoring parameters are included, as well as strategies for the prevention and management of side effects. There are a range of baseline and yearly monitoring parameters which vary dependent on which medications are being taken.

**Any tests and monitoring are the responsibility of the prescriber.**

The secondary care team should maintain responsibility for monitoring service users’ physical health and the effects of antipsychotic medication for at least the first 12 months or until the person's condition has stabilised, whichever is longer. Thereafter, the responsibility for this monitoring may be transferred to primary care under shared care arrangements. [new 2014]

The presence of adverse effects of medication should be considered on each occasion that an individual is reviewed.

\(^{1}\) Maudsley Guidelines in Psychiatry 12\(^{th}\) edition
Weight Gain

<table>
<thead>
<tr>
<th>Risk/extent of weight gain</th>
<th>Antipsychotics</th>
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<tbody>
<tr>
<td>Low</td>
<td>Lurasidone</td>
</tr>
<tr>
<td>Mild</td>
<td>Amisulpride, aripiprazole, fluphenazine, haloperidol, sulpiride, paliperidone, quetiapine, risperidone, flupenthixol</td>
</tr>
<tr>
<td>High</td>
<td>Clozapine, olanzapine, chlorpromazine</td>
</tr>
</tbody>
</table>

**Background**
People with schizophrenia are at increased risk of weight gain. There is no evidence that antipsychotics have any direct metabolic effect but many antipsychotics increase appetite although some of the newer agents to a lesser degree.

**Predisposing factors include:**
- Younger age
- Lower BMI

**Monitoring of Weight**

- Baseline waist circumference, weight and measurement of BMI
- An online calculator is also available
  [http://www.nhs.uk/Tools/Pages/Healthyweightcalculator.aspx](http://www.nhs.uk/Tools/Pages/Healthyweightcalculator.aspx)

- Ranges of body mass index: weight(Kg)/height²(m²) taken from NHS website link above
  - <18.5 - underweight
  - 18.5-25 - desirable
  - 25-30 - mildly overweight (grade I obesity)
  - 30-40 - grade II obesity
  - >40 - grade III obesity

- Cardiovascular risk is increased if waist circumference exceeds following values
  - Men- 94cm (37 inches)  •  Asian Men- 90cm (35 inches)
  - Women- 80cm (31.5 inches)  •  Asian women- 80cm (31.5 inches)
- Cardiovascular risks are increased if BMI is over 25 (ideal BMI = 18.5 to 24.9) Measure waist circumference, weigh and calculate BMI monthly for the first 6 months
- Weekly monitoring of weight is recommended early in treatment
- Monitor waist circumference, weight and BMI every 3 months after first 6 months
- GPs and other primary healthcare professionals should monitor at least once a year
- Consider need for more frequent monitoring if increased weight is identified

**Strategies for Minimisation of Weight Gain**

- Choose low association agent whenever possible
- Prior to commencement discuss expected benefits and drawbacks of medication
- Discuss information regarding the potential for weight gain
- Encourage low fat, high fibre diet rich in fruit, vegetables and complex carbohydrates
- Educate on link between sugary drinks and weight gain
- Encourage exercise that builds on the individuals usual activities
- Promote good sleep patterns
Management of Weight Gain

Assess for possible causes of increased weight

Medication Review
- Consider contribution of antipsychotic
- Consider role of other medication

Pregnancy

Follow Trust Guidelines for the Prescribing of Medication in Pregnancy

Recent smoking cessation

Physical Considerations
- Thyroid function
- FBC
- LFTs
- Albumin
- Electrolytes

Normal

Abnormality detected

Stabilise physical parameters

Consider switch to antipsychotic with lower association with weight gain

Dietary advice not sufficient or decision not to switch

Switch

Weight gain unresolved

- Follow Guidelines for Antipsychotic Medication Switches
- Assess mental state regularly e.g. BPRS
- Increased monitoring
- Consider referral to Primary Care for weight management
- Dietary advice
- Lifestyle changes
- Cognitive techniques
Hyperprolactinaemia

| Incidence/severity of hyperprolactinaemia | Aripiprazole, clozapine, lurasidone | Olanzapine, quetiapine | Amisulpride, flupentixol, paliperidone, risperidone, sulpiride, zuclopenthixol | Chlorpromazine, fluphenazine, haloperidol, pipotiazine, trifluoperazine, |

**Background**

While there is no consistent correlation between antipsychotic dose, prolactin concentration and the occurrence of symptoms, elevated prolactin levels can be manifested by the following symptoms:

- Sexual dysfunction - such as reduced libido, impotence and anorgasmia
- Amenorrhea
- Galactorrhoea - breast milk production in the male or female
- Osteoporosis
- Infertility
- Gynaecomastia

Prolactin elevating drugs (Amisulpride, sulpiride, risperidone FGAs) should ideally be avoided in patients under 25 yrs (ie before peak bone mass), patients with osteoporosis and patients with a history of hormone-dependent breast cancer.

**Monitoring for the Effects of Raised Prolactin**

- Consider baseline prolactin - especially when using agents known to elevate prolactin
- Check against current reference values
- Complete sexual history and details of menstrual difficulties when appropriate
- Use a recognised, evidence based tool for screening of sexual side effects - SESCAM
- Reassess when symptoms suggestive of hyperprolactinaemia present

**Strategies for Minimisation of Hyperprolactinaemia**

- Choose low association agent whenever possible
- Prior to commencement discuss expected benefits and drawbacks of medication
- Discuss information regarding the potential for side effects associated with hyperprolactinaemia
- Addition of Aripiprazole to existing treatment in symptomatic patients
Management of Hyperprolactinaemia

Assess possible causes of symptoms associated with hyperprolactinaemia

Prolactin level check-compare to baseline where one is available

Antipsychotic dose reduction  OR  Switch to lower association agent

- Monitor mental state – BPRS
- Inform female individuals of potential return of menstruation and offer support and contraceptive advice
- Review symptoms of hyperprolactinaemia at regular intervals

Resolution of symptoms of hyperprolactinaemia

Yes- and corrected

Physical cause identified

Symptoms of hyperprolactinaemia persist

Recheck prolactin

Investigate possible physical causes of hyperprolactinaemia E.g. prolactin secreting tumour

No
Sedation

<table>
<thead>
<tr>
<th>Incidence/severity of sedation</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>Amisulpride, aripiprazole</td>
</tr>
<tr>
<td>Low</td>
<td>Flupentixol, haloperidol, paliperidone, risperidone, sulpiride, trifluoperazine,</td>
</tr>
<tr>
<td>Medium</td>
<td>Fluphenazine, olanzapine, quetiapine, zuclopenthixol,</td>
</tr>
<tr>
<td>High</td>
<td>Chlorpromazine.</td>
</tr>
<tr>
<td>Very high</td>
<td>Clozapine</td>
</tr>
</tbody>
</table>

**Background**

Sedation can be separated into non-specific sedation, which is characterised by drowsiness and somnolence and specific sedation, which is characterised by psychomotor inhibition and psychic indifference. While the sedative properties of medication can be perceived useful for individuals who are very agitated or aggressive, they can adversely affect well being and functional capability.

- Negative aspects of the illness such as apathy should be differentiated from sedation.
- Consider the potential for depression.
- Sedation is more prominent during the early stages of treatment.
- Some degree of tolerance may develop.
- Degree of sedation can be such that the individual becomes unaware of the level of sedation that they are experiencing and perceive it normal.

**Monitoring for the Effects of Sedation**

- Consider a detailed assessment of the individual's current sleep pattern and history, especially if using atypical associated with high levels of sedation.
- Utilise sleep charts to identify problems.
- Assessment by the bed partner can provide additional information about the individual's behaviour whilst asleep, when appropriate.

**Strategies for Minimisation of Sedation**

- Inform individuals of the risks that medication may cause sedation and advise against driving or using machinery if affected.
- Advise that sedation is sometimes more common in the early stages of treatment.
- Emphasise the need to review, should they experience sedation.
Management of Sedation

Individual reports sedation → Allow 3 to 4 weeks on medication to allow for tolerance → Sedation resolved or does not impede on functional capability → Review antipsychotic dose and/or assess need for antidepressant → Symptoms:
- suggestive of negative features of schizophrenia
- suggestive of depression → Assess risks of medication → Consider:
- Taking once daily doses at bedtime?
- Asymmetrically splitting dose of twice daily doses, with majority of dose at bedtime
- Change to low association agent → Sedation unresolved
Extrapyramidal Side Effects (EPSE)

<table>
<thead>
<tr>
<th>Incidence/severity of EPSE</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>Clozapine, olanzapine, quetiapine</td>
</tr>
<tr>
<td>Low</td>
<td>Amisulpride, aripiprazole, paliperidone, risperidone (low dose), sulpiride</td>
</tr>
<tr>
<td>Medium</td>
<td>Chlorpromazine, flupentixol, pipotiazine, risperidone (above low dose), trifluoperazine</td>
</tr>
<tr>
<td>High</td>
<td>Fluphenazine, haloperidol, zuclopenthixol</td>
</tr>
</tbody>
</table>

**Background**
EPSE can be divided into four types:
- Dystonias- usually acute and within a few days of treatment
- Parkinsonian-usually appear in first few months of treatment
- Akathisia- can occur in first few weeks of treatment
- Tardive Dyskinesia- late onset, may be irreversible

There is evidence that certain groups are more susceptible to EPSE, even with the atypical antipsychotics. These include:
- Length of exposure to antipsychotics in the elderly
- Presence of affective or negative symptoms
- Being left handed
- Being diabetic
- Family history of schizophrenia + dyskinesia
- Previous head injury or organic brain disease

Males- acute dystonia

The risk of EPSE with all the atypical agents is much lower than with the conventional antipsychotics, but there is still the potential for individuals to experience a difficult side effect that society has little or no understanding of. The occurrence of EPSE plays a significant role in non-concordance.

**Monitoring for EPSE**
Careful monitoring is essential, especially with mild to moderate EPSE. The individual should be assessed prior to treatment using a validated assessment tool such as:

**Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS)**
- LUNSERS is a 41 symptom scale, covering psychological, neurological, autonomic, hormonal and other miscellaneous antipsychotic side-effects were included. An additional 10 “red herring” side-effects, which are not known to be associated with antipsychotic drugs, were included to help validate the test results.
Modified Abnormal Involuntary Movement Scale (AIMS- Munetz & Benjamin 1988)
- 12 item scale
- Assesses presence and severity of Tardive Dyskinesia
- Dependent mainly on examination and observer ratings
- Includes instruction for examination procedure

Monitoring should be carried at baseline and then biannually if asymptomatic. Should symptoms emerge the increased frequency of monitoring is established by the effectiveness of remedial strategies.

**Strategies for Minimisation of EPSE**
- Use lowest effective dose possible
- Use antipsychotic monotherapy wherever possible
- Re-assess need for antipsychotic regularly
- Consider withdrawing other drugs that may induce/exacerbate movement disorders

**Drug Treatment of EPSE**

The evidence for the effectiveness of drug treatment is more robust for the treatment of dystonia and parkinsonian type symptoms. The treatment of akathisia and tardive dyskinesia is largely based on small case reports.

**Dystonia**
- Oral, intramuscular (IM) or intravenous (IV) anticholinergic medication depending on severity of symptoms
  - Individual may be unable to swallow
  - Response to IV usually within 5 minutes
  - Response to IM usually around 20 minutes
  - Response to oral medication may take up to 2 hours

**Parkinsonian type**
- Oral anticholinergic medication
  - Do not prescribe at night (symptoms usually absent during sleep)
  - Majority of individuals do not require long term treatment
  - Review continued need at least 3 monthly
  - May induce dependence
  - May induce psychosis
  - Have a range of adverse side effects
  - Potentially lethal in overdose

**Akathisia**
- Anticholinergics are generally unhelpful
- All treatments are unlicensed-
  - Propranolol 30 to 80 mg daily
  - 5-HT2 antagonists such as mirtazapine, trazodone, mianserin
  - Cyproheptadine 16mg daily
  - Clonazepam 500 micrograms to 3mg daily

**Tardive dyskinesia**
- Anticholinergics may exacerbate
- Tetrabenazine started at 12.5mg daily and titrated to 25 to 200mg daily is the only licensed treatment
- Propranolol 40-120mg daily
- Amantadine

- Buspirone at up to 180mg/d
- Anticholinesterases eg donepezil 5-10mg od, galantamine 8-24mg/d
- Gabapentin
- Ginko Biloba
- Levetiracetam 500-3000mg daily
- Melatonin 10mg daily
Management of EPSE

Individual presents with symptoms suggesting EPSE

Assess using validated instrument
- LUNSERSAIMS

Consider relative risk of prescribed medication
- Antipsychotic
- Other medication

Consider switch to agent with lower association with EPSE

Monitor mental state

Consider drug treatment of EPSE

Strategies to minimise EPSE
- lowest effective dose possible
- monotherapy wherever possible
- assess need for continued antipsychotic
- withdraw other medication that may exacerbate EPSE

Resolution of symptoms or reduction to acceptable level

Yes

No associated risks

Medication has associated risks

NO

YES
Hyperlipidaemia

There are no large scale trials that quantify the effects of atypical antipsychotics on lipid metabolism. Several studies suggest that changes in lipid profile are concordant with weight changes and that clozapine and olanzapine tend to be associated with adverse changes in serum concentrations of triglyceride and cholesterol. This is reflected in the SPC for olanzapine therapy, reporting elevated serum cholesterol levels as common and elevated triglyceride levels as very common. Additionally changes from levels of total cholesterol (serum fasting levels) within desirable range at baseline to high levels post therapy were noted as common. The SPC for clozapine notes very rare hypercholesterolemia and for quetiapine the SPC notes evidence of adverse lipid profile in clinical studies. There are reports of hyperlipidaemia with phenothiazine therapy and included in the SPC for zuclopenthixol.

Background

Antipsychotic induced weight gain is known to be associated with hyperlipidaemia. Blood cholesterol has a log-linear relationship to the risk of CHD and is a key modifiable factor. Blood cholesterol can be reduced by dietary change, physical activity and medication. Treatment should be aimed at reducing overall CHD risk. A combined approach that addresses all risk factors yields most benefit. Elevated serum cholesterol is considered an independent risk factor for the development of CHD and a fasting lipid profile is recommended every 5 years for all individuals of 20 years and above, regardless of cardiovascular risk status.

It should be recognised that standard CVD risk scores will underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These groups include:

- people with serious mental health problems
- people taking medicines that can cause dyslipidaemia such as antipsychotic medication, corticosteroids or immunosuppressant drugs

Monitoring for Hyperlipidaemia

- Check fasting serum cholesterol prior to treatment
- Assessment should include Thyroid Stimulating Hormone (TSH) if dyslipidaemia is present
- Monitor as appropriate, depending on results and other risk factors as per NICE guidelines CG181 Cardiovascular disease: risk assessment and reduction, including lipid modification

Total cholesterol, HDL cholesterol and non-HDL cholesterol should be measured in all people who have been started on high-intensity statin treatment (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) at 3 months
of treatment and aim for a greater than 40% reduction in non-HDL cholesterol. If a greater than 40% reduction in non-HDL cholesterol is not achieved:

• discuss adherence and timing of dose

• optimise adherence to diet and lifestyle measures

• consider increasing the dose if started on less than atorvastatin 80 mg and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement. [new 2014]

Provide annual medication reviews for people taking statins.

• Use these reviews to discuss medicines adherence and lifestyle modification and address CVD risk factors.

• Consider an annual non-fasting blood test for non-HDL cholesterol to inform the discussion. [new 2014]

Discuss with people who are stable on a low- or middle-intensity statin the likely benefits and potential risks of changing to a high-intensity statin when they have a medication review and agree with the person whether a change is needed. [new 2014]
Classification of serum cholesterol levels

<table>
<thead>
<tr>
<th>Serum Lipid Concentration mmol/L</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low density lipoprotein- LDL</td>
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</tr>
<tr>
<td>&lt; 2.59</td>
<td>Optimal</td>
</tr>
<tr>
<td>2.59 to 3.34</td>
<td>Near or above optimal</td>
</tr>
<tr>
<td>3.36 to 4.11</td>
<td>Borderline high</td>
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<tr>
<td>4.14 to 4.89</td>
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<td>≥ 4.91</td>
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<tr>
<td>Total cholesterol- TC</td>
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</tr>
<tr>
<td>&lt; 4.0</td>
<td>Desirable</td>
</tr>
<tr>
<td>≥ 4.0</td>
<td>High</td>
</tr>
<tr>
<td>High density lipoprotein- HDL</td>
<td></td>
</tr>
<tr>
<td>&lt;1.0</td>
<td>Low</td>
</tr>
<tr>
<td>≥1.55</td>
<td>High</td>
</tr>
</tbody>
</table>

< = less than, > = more than and ≥ = greater than or equal to

The risk for CHD should be calculated using an appropriate risk calculator (NICE) see link below which in addition to current lipid levels takes account of other positive risk factors:

- Older age- 45 years and above in males, 55 years and above in female
- Smoking
- Obesity
- Hypertension- BP of or above 140/90 mmHg
- HDL concentration of less than 1.0 mmol/L in men or 1.2 mmol/L in women
- Family history of premature heart disease
- Ethnicity
- Abnormal fasting blood glucose levels

Diabetes is a risk factor equivalent to CHD

The risk factor is individual to the patient and should be recorded with primary care consultation records.

People with the following pre-existing conditions do not require risk assessment as they meet the requirement for secondary treatment:

- CHD or angina
- Stroke or TIA
- Peripheral Vascular Disease

Risk equations should not be used for people who are at high risk of CVD due to the following conditions, as they have specific treatment considerations:

- familial hypercholesterolemia – treated by specialist management
- diabetes – treated under NICE management of type 2 diabetes (update) CG 66

People older than 40 should have their estimate of cardiovascular (CVD) risk reviewed on an ongoing basis. Offer the patient information about the absolute risk of CVD and absolute benefits and harms of an intervention over a 10 year period.

https://www.qrisk.org/2017/
Strategies for Minimisation of Hyperlipidaemia

- Use low association agent when possible
- Encourage lifestyle changes
- Monitor weight regularly and take appropriate action in cases of weight gain
- Monitor serum cholesterol at appropriate intervals

Management of Hypercholesterolemia

Lifestyle changes appropriate for the improvement of lipid profile include:
- Increase physical activity, consider exercise referral systems
- Weight reduction
- Decreased dietary intake of saturated fat and cholesterol
- A cardioprotective diet (Including 5 portions of fruit and vegetables a day and 2 portions of oily fish a week as per NICE)

If lifestyle changes are insufficient then additional measures should be taken for an additional six weeks:
- Reinforcement of lifestyle changes
- Referral to a dietician

Before offering lipid modification therapy (statins) for primary prevention of CHD all other modifiable CVD factors should be considered and their management optimised if possible
- Control BP: The NHS defines high blood pressure as a result > 140/90mmHg. Between 120/80 and 140/90, patients are at greater risk of developing high blood pressure if measures are not taken to reduce this:
  - Smoking Cessation: Offer advice about how to stop smoking including advice on nicotine replacement therapy.
- Advice on other modifiable risk factors and personalised advice about how they can be reduced, including advice about physical activity, diet, alcohol consumption, weight and diabetes should be provided.

Should measures prove insufficient to reduce lipids and CHD risk then a change to a lower association atypical if possible, mental state should be monitored accordingly. If a change to a lower association agent is not possible pharmacological treatment for hypercholesterolemia may be necessary.

Pharmacological intervention

Statin therapy is recommended by NICE as part of the management strategy for primary prevention of CVD for adults who have a 10% or greater 10 year risk of developing CVD regardless of lipid level.
For secondary prevention (existing CVD/CHD) lipid modification therapy should be offered and not delayed by management of modifiable risk factors.
Treatment for primary CVD should be initiated with Atorvastatin 20mg

In secondary prevention statin treatment should be considered in people with CVD with atorvastatin 80 mg. Use a lower dose of atorvastatin if any of the following apply:
• potential drug interactions
• high risk of adverse effects
• patient preference. [new]
Postural Hypotension

<table>
<thead>
<tr>
<th>Incidence/severity of hypotension</th>
<th>Amisulpride, aripiprazole, flupentixol, olanzapine, sulpiride,</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Fluphenazine, haloperidol, paliperidone, quetiapine, risperidone, trifluoperazine zuclopenthixol,</td>
</tr>
<tr>
<td>High</td>
<td>Chlorpromazine, clozapine</td>
</tr>
</tbody>
</table>

**Background**
Postural hypotension is associated with antipsychotics that block alpha\(^1\) adrenoreceptors. It is likely to be more problematic in the following groups:
- Older individuals
- Individuals with cardiovascular disease
- Individuals on antihypertensive medication

Individuals exhibit varying degrees of tolerance to falls in blood pressure. A drop in systolic pressure in the region of 20 to 30mmHg within 3 minutes of standing, with associated symptoms is adequate for the diagnosis of postural hypotension.

Symptoms associated with postural hypotension include:
- Feeling faint or fainting
- Headache
- Neck pain
- Seizures- usually clonic jerks
- Weakness or buckling of the legs
- Angina- particularly after food
- Cognitive slowing
- Light headedness

**Monitoring for Postural Hypotension**
- Morning sitting and standing blood pressure after initiation and dose increments
- More frequent monitoring if symptomatic of postural hypotension

**Strategies for the Minimisation of Postural Hypotension**
- Choose agents with lower propensity for causing postural hypotension where possible
- Use standardised titrations for dose increments
- Consider more cautious titration in higher risk individuals and those who experience symptoms suggestive of postural hypotension

**Management of Postural Hypotension**
Individual presents with symptoms suggestive of postural hypotension

Educate individual to minimise postural hypotension
- Plan activity before meals
- Consume largest meal at night
- Decrease alcohol intake
- Eat low carbohydrate foods
- Avoid large meals
- Drinking water may improve symptoms
- Avoid prolonged recumbency
- Avoid prolonged exercise
- Care during hot weather
- Keep shower or bath temperature moderate
- Raise head of bed 5 to 20°

Further education

Symptoms continue

Switch to lower association agent and monitor mental state

Resolution of symptoms
**Other Cardiovascular Side Effects**

**Stroke**

In elderly patients with dementia, antipsychotic drugs are associated with a small increased risk of mortality and an increased risk of stroke or transient ischemic attack. All older individuals should be assessed for risk factors for cerebrovascular events (e.g. hypertension, atrial fibrillation), prior to commencement of any antipsychotic drug.

It is recommended that:

- Antipsychotic drugs should not be used in elderly patients to treat mild to moderate psychotic symptoms.
- Initial doses of antipsychotic drugs in elderly patients should be reduced (to half the adult dose or less), taking into account factors such as the patient’s weight, comorbidity, and concomitant medication.
- Treatment should be reviewed regularly
- Risperidone holds a licence for the short-term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer’s dementia unresponsive to non-pharmacological interventions and when there is a risk of harm to self or others.
- There is very limited evidence for the efficacy of atypical or typical antipsychotic drugs for the treatment of symptoms of psychosis in dementia.
- A clinically significant degree of improvement has only been demonstrated for aripiprazole, with NNT of 13.8

**Myocarditis and Cardiomyopathy**

Potentially fatal myocarditis (usually occurring in the first 2 months of treatment) and cardiomyopathy (occurring at anytime) are rare serious effects of clozapine. Individuals who have a history suggestive of heart disease should be assessed by a specialist before commencing treatment with clozapine.
Hyperglycaemia

<table>
<thead>
<tr>
<th>Incidence of hyperglycaemia/risk of developing/exacerbating diabetes mellitus</th>
<th>Minimal</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amisulpride, aripiprazole, asenapine</td>
<td>High potency first generation antipsychotics eg haloperidol</td>
<td>Quetiapine, risperidone, phenothiazines</td>
<td>Clozapine olanzapine</td>
<td></td>
</tr>
</tbody>
</table>

**Background**

The prevalence of diabetes mellitus among individuals with schizophrenia is around twice that in the general population. Traditional and atypical antipsychotics may further increase the risk of developing diabetes. Much of the information about the risk of hyperglycaemia is based on retrospective analyses of large databases. The difficulty in adjusting for confounding factors and there is a clear need for more robust evidence to assess the relative risks of individual antipsychotics. Most, but not all, analyses have suggested an increased risk with atypical antipsychotics as a group. Known risk factors for hyperglycaemia include:

- Age of 45 or more
- Positive family history
- Pre-existing obesity - ≥ 20% above desired body weight or BMI ≥ 25
- Physical inactivity
- Ethnic factors - African, Asian, Afro-Caribbean origin
- Impaired glucose tolerance - fasting plasma glucose of ≥ 5.55mmol/L but < 6.99mmol/L
- Hypertension - BP ≥ 140/90mmHg
- HDL cholesterol less than 0.9 and or triglycerides more than 2.82mmol/L
- History of gestational diabetes or delivery of baby weighing > 4kg
- Polycystic ovary syndrome or history of vascular disease

It is suggested that the risk of developing diabetes during therapy is cumulative and not associated with initial therapy alone.

**Monitoring for Hyperglycaemia**

- Baseline random or fasting plasma glucose prior to initiation
- Serum glucose concentration 3 to 4 monthly for first year to check for hyperglycaemia - glucose concentration ≥ 8.9mmol/L but < 11.0mmol/L
- Subsequently for high risk individuals - check serum glucose concentration 6 monthly
- Individuals with no additional risk factors - check serum glucose concentration 12 monthly

**Strategies for the Minimisation of Hyperglycaemia**

- Use low association agent where ever possible
- Advise individuals on prophylactic lifestyle changes when prescribing an atypical antipsychotic particularly those associated with weight gain or hyperglycaemia
- Advise individual to report first signs of polyuria (excess urination) and polydipsia (excess drinking)
**Management of Hyperglycaemia**

- **Monitoring indicates signs of hyperglycaemia**
  - **Encourage lifestyle changes**
    - **Switch to atypical with lower association with hyperglycaemia**
      - Already on low association agent or switch would adversely affect mental state
        - **Consider use of oral hypoglycaemic agent**
          - Levels maintained within normal limits

- **Monitor mental state**
  - **YES**
  - **NO**
    - **INEFFECTIVE**
    - **EFFECTIVE**
MONITORING FORMS:

- **INITIATION (First 12 months)**
- **MAINTENANCE (After first 12 months)**