Prescribing information for olanzapine for the treatment of schizophrenia and bipolar disorder

**Licensed Indication**

Olanzapine is indicated for the treatment of schizophrenia.

Olanzapine is effective in maintaining the clinical improvement during continuation therapy in patients who have shown an initial treatment response.

Olanzapine is indicated for the treatment of moderate to severe manic episode.

In patients whose manic episode has responded to olanzapine treatment, olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder.

**Dosage and administration**

Schizophrenia: The recommended starting dose for olanzapine is 10 mg/day.

Manic episode: The starting dose is 15 mg as a single daily dose in monotherapy or 10 mg daily in combination therapy.

Preventing recurrence in bipolar disorder: The recommended starting dose is 10 mg/day. For patients who have been receiving olanzapine for treatment of manic episode, continue therapy for preventing recurrence at the same dose. If a new manic, mixed, or depressive episode occurs, olanzapine treatment should be continued (with dose optimisation as needed), with supplementary therapy to treat mood symptoms, as clinically indicated.

During treatment for schizophrenia, manic episode and recurrence prevention in bipolar disorder, daily dosage may subsequently be adjusted on the basis of individual clinical status within the range 5-20 mg/day. An increase to a dose greater than the recommended starting dose is advised only after appropriate clinical reassessment and should generally occur at intervals of not less than 24 hours.

Olanzapine can be given without regards for meals as absorption is not affected by food. Gradual tapering of the dose should be considered when discontinuing olanzapine.

**Elderly patients**

A lower starting dose (5 mg/day) is not routinely indicated but should be considered for those 65 and over when clinical factors warrant.

**Patients with renal and/or hepatic impairment**

A lower starting dose (5 mg) should be considered for such patients. In cases of moderate hepatic insufficiency (cirrhosis, Child-Pugh Class A or B), the starting dose should be 5 mg and only increased with caution.

**Communication**

**BACK-UP ADVICE AND SUPPORT**

Back-up advice on the above is available at all times: See covering letter for contact details

**NB** As part of the recovery focus, patients may be discharged but only with a relapse plan including details of how to easily and quickly return to specialist services. Please refer to Psychosis Care Pathway.

Contact details

<table>
<thead>
<tr>
<th>Contact details</th>
<th>Telephone No.</th>
<th>Bleep:</th>
<th>Fax:</th>
<th>Email address:</th>
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<tbody>
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<td>T&amp;W CMHT</td>
<td>0300 3031601</td>
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<td>Redwoods Pharmacy Dept:</td>
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<td>Other:</td>
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In line with NICE Clinical Guideline 178, the Mental Health team will 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.

### Monitoring (on-going)

<table>
<thead>
<tr>
<th>Monitoring by</th>
<th>Time Period</th>
<th>Drug/ Class</th>
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<tbody>
<tr>
<td>Secondary care (or primary care where agreed*)</td>
<td>Prior to initiation = baseline</td>
<td>Olanzapine - Antipsychotic</td>
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<td></td>
<td></td>
<td>Fasting glucose or HbA1c</td>
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<td></td>
<td>Lipids (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides)</td>
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<td>U&amp;Es, LFTs, FBC</td>
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<td>Prolactin (if signs and symptoms of hyperprolactinaemia)</td>
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<td>BP and pulse</td>
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<td>BMI and waist circumference</td>
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<td>ECG (if CV risk identified, personal history of CV disease or in-patient)</td>
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<td></td>
<td></td>
<td>Assessment of movement disorders</td>
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<td></td>
<td>Assessment of nutritional status, diet and level of physical activity</td>
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<td></td>
<td>1 month</td>
<td>Fasting glucose, HbA1c</td>
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<td>3 months</td>
<td>Fasting glucose or HbA1c</td>
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<td>BMI</td>
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<td>12 months</td>
<td>Fasting glucose or HbA1c</td>
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<td>Lipids</td>
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<td>BP</td>
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<td>BMI and waist circumference</td>
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<tr>
<td>Primary care</td>
<td>Annually after first year</td>
<td>Fasting Glucose or HbA1c (Patients with Diabetes Mellitus (DM) or with risk factors for DM should be monitored every 6 months)</td>
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<td>Lipids (cholesterol or QRISK)</td>
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<td>BP and pulse</td>
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<td>BMI and waist circumference</td>
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<td>Prolactin (if signs and symptoms of hyperprolactinaemia)</td>
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<td>Assess for adherence and presence of movement disorders</td>
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<td>Physical examination including CV risk assessment</td>
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*There may be circumstances where the GP has agreed in advance to take over the care of the patient sooner but the rationale for this will be clear and documented.

The above tests can be undertaken more frequently if the patient’s clinical situation indicates.

### In addition to the annual NHS Health Check** assessments the physical health assessment for people with SMI should include:

- Ensure access to the relevant national screening and immunisation programmes, as recommended by Public Health England (PHE)
- Medicines reconciliation and review
- General physical health enquiry into
  - sexual health
  - oral health
- Assessment of
  - alcohol consumption
  - smoking status
  - illicit substance/non prescribed drugs
  - nutritional status
  - diet and level of physical activity

**the NHS Health Check should be offered annually to all age groups on the SMI register

Contraindications
Hypersensitivity to olanzapine or to any of the excipients. Patients with known risk for narrow-angle glaucoma.

Special Precautions
Olanzapine is not recommended for use in patients with dementia-related psychosis and/or behavioural disturbances because of an increase in mortality and the risk of cerebrovascular accident.
The use of olanzapine in the treatment of dopamine agonist associated psychosis in patients with Parkinson's disease is not recommended.
Hyperglycaemia and/or development or exacerbation of diabetes occasionally associated with ketoacidosis or coma has been reported uncommonly, including some fatal cases. In some cases, a prior increase in body weight has been reported which may be a predisposing factor.
Caution should be exercised in patients with low leukocyte and/or neutrophil counts for any reason, in patients receiving medicines known to cause neutopenia, in patients with a history of drug-induced bone marrow depression/toxicity, in patients with bone marrow depression caused by concomitant illness, radiation therapy or chemotherapy and in patients with hypereosinophilic conditions or with myeloproliferative disease. Neutropenia has been reported commonly when olanzapine and valproate are used concomitantly.
Given the primary CNS effects of olanzapine, caution should be used when it is taken in combination with other centrally acting medicines and alcohol.
Olanzapine should be used cautiously in patients who have a history of seizures or are subject to factors which may lower the seizure threshold. Seizures have been reported to occur uncommonly in patients when treated with olanzapine. In most of these cases, a history of seizures or risk factors for seizures were reported.

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with olanzapine. Nevertheless, because human experience is limited, olanzapine should be used in pregnancy only if the potential benefit justifies the potential risk to the foetus.
New born infants exposed to antipsychotics (including olanzapine) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Breast-feeding
In a study in breast-feeding, healthy women, olanzapine was excreted in breast milk. Mean infant exposure (mg/kg) at steady state was estimated to be 1.8% of the maternal olanzapine dose (mg/kg). Patients should be advised not to breast-feed an infant if they are taking olanzapine.

Adverse Effects
The most frequently (seen in ≥ 1% of patients) reported adverse reactions associated with the use of olanzapine in clinical trials were somnolence, weight gain, eosinophilia, elevated prolactin, cholesterol, glucose and triglyceride levels, glucosuria, increased appetite, dizziness, akathisia, parkinsonism, leukopenia, neutropenia (see section 4.4), dyskinesia, orthostatic hypotension, anticholinergic effects, transient asymptomatic elevations of hepatic aminotransferases, rash, asthenia, fatigue, pyrexia, arthralgia, increased alkaline phosphatase, high gamma glutamyltransferase, high uric acid, high creatine phosphokinase and oedema.

Neuroleptic malignant syndrome (NMS) – hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated CPK levels is an extremely rare adverse effect of all antipsychotics

Should a patient develop signs suggestive of neuroleptic malignant syndrome immediate referral to hospital is required and all antipsychotics should be discontinued immediately.
Drug Interactions

See product SPC for full list of drug interactions (www.medicines.org.uk)

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions. Please refer to full prescribing data in the Summary of Product Characteristics (www.medicines.org.uk) or the British National Formulary (www.bnf.org).

Specialist Services Responsibilities

Assess the patient, establish a diagnosis and determine a management strategy to include the establishment of a Care Programme Approach [CPA] (if appropriate) and involvement of the CPN/community mental health teams

If the patient is subject to a CPA, then an individual care programme will be defined for them and the GP will receive a copy of this. A named key worker and mental health team input will have to be organized (ensure that the key worker has drawn up a Care Programme involving the GP).

Baseline tests will be the responsibility of the specialist services before transfer to GP. The specialist service will undertake baseline monitoring and communicate results to the GP, or agree with the GP that they undertake these (according to local arrangements).

Send a letter to the GP indicating that the patient’s condition is stable from the date of the covering letter. Communicate to the GP, monitoring results to date and what needs to be monitored next and when. To inform GP if indication or use is off label for the product.

The patient will receive supplies of antipsychotic from the Trust for at least the first 3 months of stable treatment. Specialist services will review the patient as clinically appropriate.

Specialist Services will provide advice about and any alteration of antipsychotic dosage according to clinical parameters. Evaluation of adverse events reported by the GP, and identification of any specific monitoring required. Restarting antipsychotic therapy should this be necessary.

GP Responsibilities

GP to ‘SNOMED’ or ‘Read Code’ as appropriate on their e-system

Monitoring the patient’s overall health and well-being

Specific monitoring agreed with specialist

Prescribing antipsychotic

Adverse drug reaction/interaction monitoring

Immediate referral to hospital is required if patients develop signs of Neuroleptic Malignant Syndrome (hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated CPK levels)

Note: Neuroleptic Malignant Syndrome is an extremely rare adverse effect of all antipsychotics.

Keeping the key worker/mental health team informed of progress

Inform specialist of all relevant medical information regarding the patient and any changes to the patient’s medication irrespective of indication.

The information contained in this information is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. For further information please refer to the relevant Summary of Product Characteristics and NICE guidance or contact your local Specialist or Drug Information Centre.