Bupropion
(for depression)

Traffic light classification - Amber 2
Off-label use
Information sheet for Primary Care Prescribers

Licensed and Off-label Indications

- Bupropion is licensed an aid to smoking cessation in combination with motivational support in nicotine-dependent patients (RED classification)[1].
- Bupropion is not licensed for the treatment of depression in the UK but there is evidence for use as an antidepressant as an off-label indication (AMBER 2 classification)[2,5,7].
- Bupropion is not licenced or recommended for use in those under 18 years of age due to unknown safety and efficacy in this patient group[1].

Therapeutic Summary

Bupropion is a selective inhibitor of noradrenaline and dopamine re-uptake and also influences re-uptake of serotonin, though this is minimal[1]. It does not inhibit monoamine oxidase enzymes[1].

There is evidence for the off-label use of bupropion as an antidepressant, particularly in the following scenarios:

- For treatment-resistant depression, defined as failure to respond to 2 or more adequate antidepressant trials[5].
- In combination with other antidepressants (e.g. SSRIs) where monotherapy has failed[2,5].
- As an option for patients who have experienced significant sexual dysfunction with SSRI or SNRI antidepressants[2,5].

Medicines Initiation

Bupropion (for depression) can be prescribed in primary care following specialist initiation or recommendation.

Products Available

Bupropion hydrochloride 150mg modified-release tablets. Cost x 60 tablets = £41.76[3].

Dosages and Route of Administration

- The starting dose is 150mg once daily in the morning. The dose can be increased after a week to 150mg twice a day. Successive doses should be taken at least 8 hours apart[1].
- Bupropion can cause insomnia so is best taken morning and afternoon/early evening[1].
- The maximum licensed dose of bupropion in the UK is 300mg daily[1]. However, in the US where bupropion is licenced for the treatment of major depressive disorder the dose can be further increased to 450mg per day if no clinical improvement is seen after several weeks of treatment with 300mg per day[7]. Increasing the dose above 300mg/day should only be undertaken by the specialist.
- Tablets should not be crushed, chewed or cut but should be swallowed whole, to avoid increased risk of adverse effects such as seizures[1].
- Tablets can be taken with or without food[1].
- In the elderly, patients with renal impairment (GFR <50mL/min)[10] and patients with mild to moderate hepatic impairment, the recommended maximum dose is 150mg daily[1].

Ratified by APC July 2024 *Accessibility Checked*
Review date July 2027

Duration of Treatment
NICE depression guidelines (NG222) advise supporting and encouraging persons who have benefited from taking an antidepressant to continue medication for at least 6 months after remission to reduce the risk of relapse[4]. Review the need for continued antidepressant treatment beyond 6 months after remission considering the likelihood of relapse and the potential risks of continuing with antidepressants long term. For people who have been assessed as being at higher risk of relapse, consider continuing with antidepressant medication maintaining the dose that led to full or partial remission, unless there is good reason to reduce it. Review treatment with antidepressant medication at least every 6 months thereafter. When patients are discharged from secondary care the specialist should provide advice to primary care on the expected duration of prescribing and when to review.

Treatment Discontinuation
Discontinuation reactions are a potential risk with all antidepressants following prolonged use and a gradual tapering-off period should be considered[1]. For more information on treatment discontinuation of antidepressants, see our NAPC Primary Care Guide to Antidepressants – Prescribing, Swapping and Stopping[9], NICE Guideline 215[6] and Royal College of Psychiatrists website[8].

Monitoring
- Hypertension has been noted in some patients prescribed bupropion. A baseline blood pressure should be obtained before initiating treatment and checked again after 1-2 weeks, and again 1-2 weeks after any dose changes, especially in patients with pre-existing hypertension. Clinically significant hypertension should result in review with consideration given to bupropion discontinuation[1]. The specialist should include the BP monitoring recommendations with any request to prescribe bupropion. Some patients may be able to check their own BP at home if they have a BP monitor and report the results to the prescriber.

Side effects
- The most common side effects include rash, pruritis, urticaria, agitation, anxiety, insomnia, headache, dizziness, gastrointestinal disturbance, dry mouth and sweating[1].
- Hypertension has been noted in patients prescribed bupropion (see Monitoring section)[1].
- Bupropion is associated with a dose-related risk of seizures (see below)[1,5].
- Refer to the product literature for a comprehensive list of side effects[1].

Contraindications
- Hypersensitivity to the active ingredient or any excipients[1].
- History of seizures or a current seizure disorder, as well as in those who are undergoing withdrawal from any product that has a known risk of seizures on withdrawal (including alcohol, benzodiazepines and benzodiazepine-like substances)[1,2].
- Known tumour of the central nervous system[1].
- Current diagnosis or history of eating disorders such as bulimia or anorexia nervosa[1].
- Patients with severe hepatic cirrhosis[1].
- Patients with a diagnosis of bipolar disorder (risk of precipitation of a manic episode[1].
- Concomitant use with a monoamine oxidase inhibitor (MAOI)[1].

Precautions
- Use with caution in the elderly (due to greater sensitivity), in mild or moderate hepatic impairment (because of pharmacokinetic variability) and in renal impairment (due to increased risk of seizures)[1,2]. The maximum dose should be limited to 150mg daily in these patient groups and they should be monitored for possible undesirable effects, which could indicate high active metabolite or drug levels[1].

- Bupropion may unmask Brugada syndrome and may lead to cardiac arrest or sudden death in these patients. Prescribe with caution in patients with known Brugada syndrome or with risk factors for or family history of cardiac arrest/sudden death[1].
- Bupropion treatment can lead to false-positive results on some rapid urine drug screens for amphetamines, due to their similar chemical structures[1].
- Specialist advice from the perinatal mental health team should be sought if a patient taking bupropion becomes pregnant or wants to breast-feed. Studies suggest exposure to bupropion during the first trimester could be associated with increased risk of congenital cardiovascular malformations, such as ventricular septal defects and left outflow tract heart defects, however animal studies indicated no harmful reproductive toxicity[1]. Bupropion is excreted in breast milk[1].

Clinically Relevant Medicine Interactions and Their Management

- Bupropion is known to inhibit cP450 2D6 and caution should be taken when prescribed with medications that are metabolised by this enzyme[1,5]. Specifically, tamoxifen and bupropion use should be avoided whenever possible due to reduced plasma levels of the active metabolite of tamoxifen[1]. Other examples include imipramine, paroxetine, risperidone, metoprolol, propafenone and flecainide[1].
- Bupropion is known to be metabolised by cP450 2B6 and caution should be taken when prescribing with medications that inhibit or induce this enzyme, including clopidogrel and orphenadrine, the clinical consequences being unknown[1]. Other medicinal products known to affect bupropion metabolism include carbamazepine, phenytoin, ritonavir and efavirenz (which induce metabolism) and valproate (which inhibits metabolism)[1].
- Concomitant bupropion and monoamine oxidase inhibitor (MAOI) use is contraindicated[1]. For irreversible MAOIs (e.g. phenelzine), allow at least 14 days between MAOI discontinuation and bupropion initiation[1]. For reversible MAOIs (e.g. moclobemide) allow 24 hours between MAOI discontinuation and bupropion initiation[1].
- Serotonin syndrome has been reported in patients prescribed bupropion with other serotonergic agents (e.g. SSRIs, SNRIs). Prescribe with caution[1].
- Bupropion should be used with caution alongside medications that lower the seizure threshold and only where the benefit outweighs the risk of seizures[1].
- Concomitant use of bupropion and digoxin may reduce digoxin levels[1].
- Concomitant use of bupropion with levodopa or amantadine may increase the incidence of dopaminergic adverse effects (e.g. nausea and vomiting)[1].
- Alcohol intake during bupropion treatment can cause neuropsychiatric events or reduced alcohol tolerance and should be minimised or avoided[1].
- Please refer to the product literature and BNF for a comprehensive list of drug-interactions[1].

Patient Information

- Patients should be informed of the effects on driving and performing skilled tasks, especially when starting treatment or changing dose[1].
- Patients should be made aware that consuming alcohol during bupropion treatment should be avoided or minimised due to possible neuropsychiatric events or reduced alcohol tolerance[1].
- Patient information leaflets for bupropion, other mental health medicines and mental health conditions can be requested from here:

Pharmacy Contacts - Nottinghamshire Healthcare NHS Foundation Trust
Mental Health Medicines Pharmacist Advice Line: 0300 3035808
Wells Road Centre Pharmacy 01159 555 357
Email MI@nottshc.nhs.uk

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Version Control- Bupropion (in Depression) Information Sheet			
Version	Author(s)	Date	Changes
1.0	**Philippa Cheesman** (Senior Clinical Pharmacist) and **John Lawton** (Lead Pharmacist Clinical Services), Nottinghamshire Healthcare NHS Foundation Trust	July 2024	New document