All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan

All Wales Guide:

Pharmacotherapy for Smoking Cessation

July 2014

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1.0 INTRODUCTION

Both behavioural support and pharmacotherapies are effective in helping people to stop smoking. Combining both treatment approaches is recommended where possible[1]. Pharmacotherapy should normally be prescribed/supplied as part of an abstinent-contingent treatment, in which the smoker makes a commitment to stop smoking on or before a particular date (target quit date)[2].

Nicotine replacement therapy (NRT), varenicline and bupropion are the three forms of pharmacotherapy that are licensed for use in the UK to assist with smoking cessation. A Cochrane network meta-analysis concluded that each of these improves the chances of quitting. Combination NRT (the use of an immediate-release formulation plus patches) is as effective as varenicline, and more effective than single types of NRT[3].

Clinical suitability and patient preference are important in guiding the choice of pharmacotherapy[4]. NRT, bupropion or varenicline should not be prescribed/supplied together in any combination.

The ultimate responsibility for the prescribing of pharmacotherapy lies with the prescriber who signs the prescription. Where patients are supplied smoking cessation pharmacotherapy as part of a community pharmacy enhanced stop smoking service, the ultimate responsibility for supply lies with the community pharmacist making that supply.

The supply of NRT, varenicline or bupropion should be sufficient to last no more than two weeks after the target quit date[2]. Subsequent supplies should be given only to people who have demonstrated, on re-assessment (e.g. by carbon monoxide testing), that their quit attempt is continuing[2].

Phased prescribing/supply enables ongoing review of the suitability of the formulation and dosage in order to more closely target the individual's needs during their quit attempts and reduce the potential for wastage.

Locally commissioned NHS community pharmacy stop smoking services supply pharmacotherapy at weekly intervals during the first few weeks of a quit attempt followed by two-weekly intervals thereafter. This is in accordance with local arrangements with their health board.

The Stop Smoking Wales communications to healthcare practitioners have been revised so that they are consistent with the supply intervals for pharmacotherapy recommended in this guide. Stop Smoking Wales advisors do not assess patients' clinical suitability for pharmacotherapy.

Tobacco smoking increases the metabolism of some medicines by stimulating the hepatic enzyme CYP1A2. When smoking is discontinued, the dose of these medicines, in particular theophylline, cinacalcet, ropinirole, and some antipsychotics (including clozapine, olanzapine, chlorpromazine and haloperidol), may need to be reduced[5]. Regular monitoring for adverse effects is advised.

A **Summary of cautions in the use of pharmacotherapy in special populations** is provided in Appendix I.

A **Summary dosage and supply guide for smoking cessation pharmacotherapy** is provided in Appendix II.

Healthcare practitioners should refer to the latest edition of the BNF and manufacturers' Summaries of Product Characteristics (SPCs) for further guidance and prescribing information.

1.1 Assessing nicotine dependence

The Fagerström test is widely used to assess nicotine dependence. How soon a person smokes after waking seems to be the most important indicator of dependence[6]. Smoking within 30 minutes of waking is a reliable indicator of nicotine dependence. Smoking within 5 minutes of waking indicates a higher level of dependence.

The number of cigarettes smoked per day is less predictive. Dependence is more likely if more than 10 cigarettes are smoked per day.

The level of nicotine dependence is a predictor of withdrawal symptoms and the intensity of treatment required. Cravings and withdrawal symptoms experienced in previous quit attempts can also be a useful guide.

2.0 NICOTINE REPLACEMENT THERAPY

In the context of this guide, the term NRT refers to its use in place of cigarettes after abrupt cessation of smoking.

The aim of using NRT is to reduce withdrawal symptoms by providing some of the nicotine that would be obtained from cigarettes, without providing the harmful chemicals present in tobacco smoke. NRT delivers nicotine to the body but at a lower dose and slower rate compared with smoking.

2.1 Choice of NRT formulation

There are eight different types of NRT formulations available (patches, gum, lozenges, sublingual tablets, inhalator, oral spray, oral films, and nasal spray) and a variety of strengths. This offers a variety of approaches to best match individual smokers' needs and preferences.

Patches provide slower, sustained-release delivery of nicotine, while oral and nasal formulations provide faster release of nicotine as intermittent doses.

All formulations of NRT have similar effectiveness. Therefore, the choice of NRT depends largely on:

- Patient preference
- Previous patient experience of the type of formulation(s), if any, tried before
- Contraindications, cautions and the potential for adverse effects

Patients with a high level of nicotine dependence, or those who have failed with NRT previously, may benefit from using combination NRT through use of an immediate-release preparation and patches to achieve abstinence.

Table 1. Some advantages and disadvantages of different NRT formulations

Formulation	Advantages/disadvantages
Patch	Discreet and easy to use. Long-acting. Doesn't mimic the highs and lows associated with smoking.
Gum	Allows good control of nicotine dose. Unsuitable for people who use dentures.
Lozenge	Discreet, flexible, good dose control.
Sublingual tablet	Discreet, flexible, good dose control.
Inhalator	May be useful for people who miss the hand-to-mouth movements of smoking.
Oral spray	Rapid delivery of nicotine.
Oral film	Rapid delivery of nicotine, discreet.
Nasal spray	Rapid delivery of nicotine similar to smoking cigarettes.

2.2 Clinical suitability

Most of the health warnings associated with NRT also apply to continued smoking, but the risks of continued tobacco smoking outweigh any risks of using NRT preparations in virtually all situations[5].

NRT can be considered for all people attempting to quit smoking, including pregnant and breast-feeding women, and young people aged 12 to 18 years old[2]. All forms of NRT can be used by patients with stable cardiovascular disease, but should be used with caution in those in hospital for acute cardiovascular events.

The use of NRT in pregnancy is considered preferable to the continuation of smoking, but should be used only if smoking cessation without NRT fails[5,7]. Intermittent therapy is preferable to patches, but avoid liquorice-flavoured products. Patches may be appropriate if pregnancy-related nausea and vomiting is a problem. If patches are used they should be removed at night before going to bed[5,7]. Intermittent therapy is preferable for breast-feeding women[5].

Specific cautions for individual preparations are usually related to the local effect of nicotine. Examples are provided in Table 2.

2.3 Adverse effects

Most adverse effects experienced with NRT are not serious and are similar to the effects experienced from nicotine obtained by smoking[8].

Minor adverse effects are common with NRT use, particularly in patients using high-strength formulations. They usually improve with time but treatment may need to be reviewed if they continue or become troublesome.

However, patients may confuse the side effects of NRT with nicotine withdrawal symptoms. Common symptoms of nicotine withdrawal include malaise, headache, dizziness, sleep disturbance, coughing, influenza-like symptoms, depression, irritability, increased appetite, weight gain, restlessness, anxiety, drowsiness, mouth ulcers, decreased heart rate, and impaired concentration.

Common adverse effects of NRT include headache, dizziness, coughing, and gastrointestinal disturbances. Palpitations may occur and, rarely, allergic reactions (including angioedema) and (very rarely) reversible atrial fibrillation.

Mild local reactions are common on initiation of NRT because of the irritant effect of nicotine. Mouth ulcers have also been reported. Examples of cautions and adverse effects which may be related to formulation type are provided in Table 2.

Table 2. Examples of cautions and adverse effects which may be related to formulation type

NRT formulation	Cautions	Adverse effects
Patch	Nicotine patches should not be placed on broken skin and should be used with caution in patients with skin disorders.	Minor skin irritation at the application site(s). If the skin reaction becomes more severe or more widespread, treatment with patches should be discontinued. Dry mouth, sleep disturbances including abnormal dreams. Chest pain, sweating, myalgia and arthralgia have been reported.
Oral NRT in general	Caution in use with oesophagitis, oral or pharyngeal inflammation, gastritis, or gastric/peptic ulcers. Due to the potential for reduced absorption of nicotine through buccal mucosa, patients should generally avoid: • Acidic beverages for 15 minutes before using oral NRT • Eating or drinking while using oral NRT	Gastrointestinal disturbances are common and may be caused by swallowed nicotine; nausea, vomiting, dyspepsia, and hiccupping occur most frequently.
Gum	The gum may stick to and damage dentures.	Increased salivation, and sore mouth or throat.
Lozenge		Dry mouth, increased salivation, mouth ulcers, and sore mouth or throat. Less commonly: thirst, taste disturbance, gingival bleeding, and halitosis.
Sublingual tablet		Dry mouth, sore mouth or throat, burning sensation in the mouth, rhinitis, coughing.
Inhalator	Care should be taken with the inhalation cartridges in patients with obstructive lung disease, chronic throat disease, or bronchospastic disease.	Mild local reactions such as irritation of the throat and mouth, and coughing occur in about 40% of people using a nicotine inhalator.
Oral spray		Dry mouth, increased salivation, mouth ulcers, burning lips, taste disturbance, toothache, oral soft tissue pain and paraesthesia. Less commonly: watery eyes. Sweating and myalgia have been reported.
Oral film		Pharyngitis, coughing, pharyngolaryngeal pain, dry mouth, mouth ulcers, oral discomfort.
Nasal spray	The nasal spray can cause worsening of bronchial asthma. Use of the spray in patients with hyperreactive airways is not recommended.	Nasal irritation as sneezing, running nose, watering eyes, and cough occur in nearly all (94%) of people using a nicotine nasal spray during the first 2 days of therapy. Both the frequency and severity are likely to decline with continued use. Nose bleeds, gastrointestinal disorders.

2.4 Prescribing/supply notes for NRT

- Prescribing/supply of NRT should not commence until the patient has decided on a target quit date.
- The initial prescription/supply should be sufficient to last a maximum of 2 weeks after the target quit date. (Quantity guide in Table 3.)
- Emphasise the importance of using NRT regularly at first, and at an adequate dose to reduce the symptoms of nicotine withdrawal sufficiently. (Dosage guide in Table 4.)
- Further prescriptions/supplies should only be issued if the quit attempt is continued.
- Prescribing/supplying for a maximum of 14-day intervals can help to tailor the NRT formulation and dosage to the individual patient's needs and to avoid potential waste. (Quantity guide in Table 3 and dosage guide in Table 4.)
- Treatment is recommended for 8 to 12 weeks, unless otherwise stated in the product information.
- If continued longer and abstinence is not achieved after 6 to 9 months, treatment should be reviewed.
- Where NRT is added to repeat prescribing systems this should be for short-term use only.

Table 3. Quantity of NRT: First and further prescription(s)

Formulation	First prescription	Further prescription(s)
Single NRT	1 or 2-week supply at maximum daily dose.	Appropriate quantity to last 2 weeks based on actual usage and any remaining NRT from previous prescription.
Combination NRT	1 or 2-week supply (7 or 14) patches **plus** half the suggested maximum daily dose quantity of one immediate-release NRT.	2-week supply (14) patches **plus** an appropriate quantity of one immediate-release NRT, to last 2 weeks based on actual usage and any remaining NRT from previous prescription.
Patch (single or combination NRT)	1 or 2-week supply (7 or 14 patches).	2-week supply (14 patches).

Table 4. Dosage guide for NRT formulations

Patch (transdermal patches)	Strength	More than 10 cigarettes daily	Fewer than 10 cigarettes daily	Relative cost	2-week supply (max dose)
25 mg/16 hours	High	• Specify the patch strength (mg) and duration (16 or 24 hours). • Start with a high-strength patch daily for the first 6 to 8 weeks. • Follow with a medium-strength patch for 2 weeks. • Then a low-strength patch for the final 2 weeks.	• Specify the patch strength (mg) and duration (16 or 24 hours). • Start with a medium-strength patch daily for the first 6 to 8 weeks. • Follow with a low-strength patch for the final 2 to 4 weeks.	£	14 patches
15 mg/16 hours	Medium				
10 mg/16 hours	Low				
21 mg/24 hours	High				
14 mg/24 hours	Medium				
7 mg/24 hours	Low				
Additional information	• 24-hour patches may be more suitable if patients have strong cravings for cigarettes on waking. • Sleep disturbances may be helped by removing the patches before bed (changing from a 24-hour patch to a 16-hour patch). • If abstinence is not achieved, or if withdrawal symptoms are experienced, maintain or increase the strength of the patch until the patient is stabilised. If patients using a high-strength patch experience excessive side effects that do not resolve within a few days, change to a medium-strength patch for the remainder of the initial period, and then a low-strength patch for 2 to 4 weeks.				
Gum (medicated chewing gum sugar-free)	**Strength**	**More than 20 cigarettes daily**	**Fewer than 20 cigarettes daily**		
4 mg	Higher	• Start with higher-strength gum (4 mg). • Maximum 15 pieces of gum daily. • *Consider starting with higher strength if the first cigarette of the day is smoked within 30 minutes of waking up.*	• Start with lower-strength gum (2 mg). • Up to 15 pieces of gum daily. • If patient uses more than 15 pieces of 2 mg gum daily, change to the higher-strength (4 mg) gum • *Consider starting with lower strength if the first cigarette of the day is smoked more than 30 minutes after waking up.*	£	210 pieces of gum
2 mg	Lower				
Lozenge (sugar-free)	**Strength**	**More than 20 cigarettes daily**	**Fewer than 20 cigarettes daily**		
4 mg (mini or standard), 2 mg	Higher	• Start with higher-strength (2 mg or 4 mg) standard or (4 mg) mini lozenge. • Maximum 15 higher-strength standard or mini lozenges daily. • *Consider starting with a higher strength if the first cigarette of the day is smoked within 30 minutes of waking up.*	• Start with lower-strength (1 mg) standard or (1.5 mg) mini lozenge. • Up to 30 standard (1 mg) or 15 mini (1.5 mg) lozenges daily. • Change to higher-strength (2 mg) standard or (4 mg) mini lozenges if insufficient effect at maximum dose of lower strength. • *Consider starting with a lower strength if the first cigarette of the day is smoked more than 30 minutes after waking up.*	£	210 lozenges
1 mg (standard) 1.5 mg (mini)	Lower				

Table 4. Dosage guide for NRT formulations (continued)

Sublingual tablets (sugar-free)	More than 20 cigarettes daily	Fewer than 20 cigarettes daily	Relative cost	2-week supply (max dose)
2 mg (cyclodextrin complex)	• Start with higher dosage: 2 tablets each hour. • Maximum 40 tablets daily.	• Start with lower dosage: 1 tablet each hour. • Increase to 2 tablets each hour if necessary. • Maximum 40 tablets daily.	££	280 tablets (lower dose) 560 tablets (higher dose)
Inhalator (inhalation cartridges)	**All dependency levels**			
15 mg	• Maximum 6 cartridges of the 15 mg strength daily.		£££	84 cartridges
Oral spray (oromucosal spray sugar-free)	**All dependency levels**			
1 mg per spray (150 sprays per 13.2 ml)	• Maximum 2 sprays per episode (up to 4 sprays every hour). • Maximum of 64 sprays daily.		£££	5 packs (150 sprays per 13.2ml)
Oral film (orodispersible film sugar-free)	**First cigarette of the day smoked more than 30 minutes after waking up**			
2.5 mg	• Maximum 15 films daily.		££	210 films
Nasal spray	**All dependency levels**			
500 micrograms per dose (200 sprays per 10 ml)	• Use one spray in each nostril, up to twice every hour for 16 hours daily. • Maximum 64 sprays daily.		£££	4 packs (200 sprays per 10ml)

3.0 VARENICLINE

Varenicline is a selective nicotine-receptor partial agonist. It reduces the severity of cravings and withdrawal symptoms, while simultaneously reducing the rewarding effects of nicotine[9]. It should normally be prescribed/supplied only as part of a programme of behavioural support.

3.1 Clinical suitability

Varenicline is licensed for use with all smokers except those under 18 or pregnant women. It should be avoided in breast-feeding women due to a lack of safety data and is contraindicated in those with hypersensitivity to varenicline or any of the excipients in the formulation[10].

Care should be taken when considering prescribing varenicline to patients with a history of psychiatric illness. Where a decision is taken to prescribe varenicline to such patients, they should be closely monitored.

Caution is recommended for use in patients with cardiovascular disease, or predisposition to seizures (including conditions that lower seizure threshold). Dosage may need to be adjusted in moderate or severe renal impairment. Treatment with varenicline is not recommended for use in patients with end-stage renal disease.

To date, there are no known clinically meaningful drug interactions with varenicline.

3.2 Adverse effects

Varenicline is a black triangle medicine (▼) subject to intensive monitoring and all suspected adverse reactions should be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA) through the Yellow Card Scheme.

Nausea is the most common adverse effect of varenicline (almost 30% of patients). Very commonly reported adverse effects include headache, insomnia, abnormal dreams and nasopharyngitis.

Whilst these side effects are generally not serious, there have been reports of more serious suspected side effects associated with the use of varenicline.

Changes in behaviour or thinking, anxiety, psychosis, mood swings, aggressive behaviour, depression, suicidal thoughts, suicide attempts and completed suicides have been reported in patients attempting to quit smoking with varenicline. Some of the patients had no known pre-existing psychiatric condition and some continued to smoke.

The BNF highlighted MHRA/Commission on Human Medicines (CHM) advice on the risk of suicidal thoughts and behaviour with varenicline[5]:

MHRA/CHM advice
Suicidal behaviour and varenicline

Patients should be advised to discontinue treatment and seek prompt medical advice if they develop agitation, depressed mood or suicidal thoughts.

Patients with a history of psychiatric illness should be monitored closely whilst taking varenicline.

Varenicline may also affect a patient's ability to drive or use machines: patients should not drive or operate complex machinery, or take part in potentially hazardous activities until they know how varenicline affects them.

3.3 Dose and duration of treatment

The recommended duration of treatment with varenicline is 12 weeks. Review every 2 weeks.

The 12-week course can be repeated in abstinent individuals to reduce the risk of relapse.

Table 5. Dosage guide for varenicline

Dose	Relative cost = £££
Adults over 18 years	Start 1 to 2 weeks before target quit date (up to maximum of 5 weeks before target quit date). 500 micrograms once daily for 3 days, increase to 500 micrograms twice daily for 4 days, then 1 mg twice daily for 11 weeks. Reduce dose to 500 micrograms twice daily if not tolerated.
Severe renal impairment (eGFR < 30 ml/min/1.73 m^2). Avoid in end-stage renal disease	500 micrograms once a day for the first 3 days, then increase to 1 mg once a day.

Stopping varenicline is associated with an increase in irritability, urge to smoke, depression and/or insomnia in up to 3% of patients. Dose tapering should be considered at the end of a 12-week course to prevent symptoms and reduce the risk of relapse.

Table 6. Prescribing/supply intervals and quantities for varenicline

Varenicline prescription/supply	Duration	Quantity
1st	2 weeks (starter pack)	11 x 500 microgram tablets and 14 x 1 mg tablets (starter pack)
2nd, 3rd, 4th, 5th & 6th	2 weeks	1 mg x 28 tablets (500 microgram x 28 tablets if using lower dose)

4.0 BUPROPION

Bupropion is a non-nicotine aid to smoking cessation that reduces the urge to smoke and withdrawal symptoms. It has dopaminergic and noradrenergic effects that can aid smoking cessation. Bupropion was originally developed as an antidepressant.

4.1 Clinical suitability

Bupropion is licensed for use with all smokers except those under 18 or pregnant women. It should be avoided in breast-feeding women due to a lack of safety data and is contraindicated in those with hypersensitivity to bupropion or any of the excipients in the formulation[11].

Bupropion is associated with a dose-related risk of seizure. The incidence of seizures is approximately 1 in 1,000 at doses up to 150 mg twice daily.

Bupropion is contraindicated in patients with: a current seizure disorder or any history of seizures, central nervous system (CNS) tumour, acute alcohol or benzodiazepine withdrawal, eating disorders, severe hepatic cirrhosis, bipolar disorder, or use of monoamine oxidase inhibitors (MAOIs).

The risk of seizures is increased in the presence of predisposing factors. Prescribe bupropion only if the potential benefit clearly outweighs risks. Risk factors for seizures include: alcohol misuse, history of head trauma, diabetes, and concomitant use of any medicine known to lower seizure threshold. Reduced dosage should be considered if prescribing for patients with risk factors for seizures.

Bupropion may be used with caution in patients with hepatic impairment and in the elderly. Reduced dosage is recommended for these patients.

Bupropion inhibits the CYP2D6 pathway. Medicines predominantly metabolised by CYP2D6 (including certain antidepressants, antipsychotics, beta-blockers, and anti-arrhythmics) should be started at the lower end of the dose range in patients taking bupropion. If bupropion is prescribed to a patient already taking such a medicine, the need to decrease the dose of that medicine should be considered. The expected benefits of treatment with bupropion should be weighed against the potential risks.

Bupropion is metabolised primarily by CYP2B6, and medicines which affect this enzyme such as substrates (e.g. cyclophosphamide) or inhibitors (e.g. orphenadrine or clopidogrel) may alter levels of bupropion and its metabolites. The clinical effect of this is unknown.

Since bupropion is extensively metabolised, medicines that inhibit its metabolism (e.g. valproate) or induce metabolism (e.g. carbamazepine and phenytoin), may affect its clinical effects.

4.2 Adverse effects

Bupropion causes insomnia very commonly. This can be reduced by avoiding bedtime doses, provided there is at least 8 hours between doses. Common adverse effects include: hypersensitivity reactions (e.g. urticaria), dry mouth, gastrointestinal disorders, taste disturbance, agitation, anxiety, tremor, dizziness, depression, headache, impaired concentration, rash, pruritus, sweating, and fever.

Seizures are a rare but clinically important adverse effect of bupropion. At doses up to 150 mg twice daily, the incidence of seizures is approximately 0.1% (1 in 1,000). Treatment with bupropion should be stopped if a patient has a seizure while taking it.

Hypertension, in some cases severe, has been reported in patients taking bupropion. This has been observed in patients with and without pre-existing hypertension. Blood pressure should be measured at the start of treatment and monitoring undertaken.

Depression and, very rarely, suicide attempts have been reported during treatment with bupropion.

Patients should exercise caution before driving or using machinery until they are reasonably certain bupropion does not adversely affect their performance.

4.3 Dose and duration of treatment

The recommended duration of treatment with bupropion is 7 to 9 weeks. Review every 2 weeks.

Table 7. Dosage guide for bupropion

Dose	Relative cost = £££
Adults over 18 years	Start 1 to 2 weeks before target quit date. 150 mg daily for 6 days then 150 mg twice daily (max. single dose 150 mg, max. daily dose 300 mg; minimum 8 hours between doses). Period of treatment 7–9 weeks; discontinue if abstinence not achieved at 7 weeks.
Elderly	Max.150 mg once a day.
Hepatic impairment. (Avoid in severe hepatic cirrhosis.)	Reduce dose to 150 mg once a day.
Renal impairment	Reduce dose to 150 mg once a day.
Predisposition to seizures	Consider a maximum dose of 150 mg daily.

Although discontinuation reactions are unlikely on stopping bupropion, a tapering off period may be considered 1 to 2 weeks before stopping if the patient prefers.

Table 8. Prescribing/supply intervals and quantities for bupropion

Bupropion prescription/supply	Duration	Quantity
1st	2 weeks	22 x 150 mg tablets (provides 2-week supply at standard initiation dose)
2nd & 3rd	2 weeks	28 x 150 mg tablets (14 x 150 mg tablets if using lower dose)
4th	Up to 3 weeks (to complete the course of treatment)	Up to 42 x 150 mg tablets (Up to 21 x 150 mg tablets if using lower dose)

APPENDIX I: SUMMARY OF CAUTIONS IN THE USE OF PHARMACOTHERAPY IN SPECIAL POPULATIONS

Special population	NRT	Varenicline	Bupropion
Pregnant women	NRT use in pregnancy is preferable to the continuation of smoking, but should only be used if smoking cessation without NRT fails. Intermittent therapy is preferable to patches. Avoid liquorice-flavoured NRT. Patches are useful, however, if the patient is experiencing pregnancy-related nausea and vomiting. If patches are used, they should be removed before bed.	Avoid – lack of safety data.	Avoid – lack of safety data.
Breast-feeding women	Nicotine from NRT is present in breast milk; however, the amount to which the infant is exposed is small and less hazardous than second-hand smoke. Intermittent therapy is preferred.	Avoid – lack of safety data.	Avoid – lack of safety data. Present in breast milk.
Cardiovascular disease	Caution in use with haemodynamically unstable patients hospitalised with severe arrhythmias, myocardial infarction, or cerebrovascular accident. Initiation should only be under medical supervision. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the dose should be reduced or discontinued.	Caution in use with history of cardiovascular disease.	Measure blood pressure before and during treatment, especially with pre-existing hypertension.
Diabetes mellitus	Care in use in patients with diabetes mellitus. Blood glucose concentration should be monitored closely while using NRT.	No specific cautions. However, blood glucose concentrations may be more variable when stopping smoking and should be monitored closely.	
Hepatic impairment	Caution in use with moderate to severe hepatic impairment.		Reduce dose to 150 mg daily. Avoid in severe hepatic cirrhosis.
Renal impairment	Caution in use with severe renal impairment.	If eGFR less than 30 ml/minute/1.73 m^2, initial dose 500 micrograms once daily, increased after 3 days to 1 mg once daily. Avoid in end-stage renal disease.	Caution in use with renal insufficiency. Reduce dose to 150 mg daily.
Psychiatric illness		Care should be taken with patients with a history of psychiatric illness.	
Predisposition to seizures	Potential risks and benefits of NRT should be considered before use in patients taking anti-convulsant therapy or with a history of epilepsy as cases of convulsions have been reported in association with nicotine.	Caution in use, including conditions that may lower seizure threshold.	Prescribe only if benefit clearly outweighs risks. Risks include the concomitant use of medicines and/or presence of other conditions that may lower seizure threshold. Consider a maximum dose of 150 mg daily.
Phaeochromocytoma	Caution in use.		
Uncontrolled hyperthyroidism	Caution in use.		
Children and adolescents (12 to 18 years)	All NRT preparations are licensed for adolescents over 12 years old (with the exception of Nicotinell™ lozenges which are licensed for those under 18 years old only when recommended by a doctor).	Not licensed for use in those under 18 years old.	Not licensed for use in those under 18 years old.
Elderly			Maximum dose of 150 mg once a day.

APPENDIX II: SUMMARY DOSAGE AND SUPPLY GUIDE FOR SMOKING CESSATION PHARMACOTHERAPY

NRT		More than 10 cigarettes daily	Fewer than 10 cigarettes daily	Relative cost	2-week supply (max. dose)
Patch	**Strength**				
25 mg/16 hours	High	• Specify the patch strength (mg) and duration (16 or 24 hours). • Start with a high-strength patch daily for the first 6 to 8 weeks. • Follow with a medium-strength patch for 2 weeks. • Then a low-strength patch for the final 2 weeks.	• Specify the patch strength (mg) and duration (16 or 24 hours). • Start with a medium-strength patch daily for the first 6 to 8 weeks. • Follow with a low-strength patch for the final 2 to 4 weeks.	£	14 patches
15 mg/16 hours	Medium				
10 mg/16 hours	Low				
21 mg/24 hours	High				
14 mg/24 hours	Medium				
7 mg/24 hours	Low				
Gum	**Strength**	**More than 20 cigarettes daily**	**Fewer than 20 cigarettes daily**		
4 mg	Higher	• Start with higher-strength gum (4 mg). • Maximum 15 pieces of gum daily. • *Consider starting with higher strength if the first cigarette of the day smoked within 30 minutes of waking up.*	• Start with lower-strength gum (2 mg). • Up to 15 pieces of gum daily. • If patient uses more than 15 pieces of 2 mg gum daily, change to the higher-strength (4 mg) gum. • *Consider starting with lower strength if the first cigarette of the day smoked more than 30 minutes after waking up.*	£	210 pieces of gum
2 mg	Lower				
Lozenge	**Strength**	**More than 20 cigarettes daily**	**Fewer than 20 cigarettes daily**		
4 mg (mini or standard), 2 mg	Higher	• Start with higher-strength (2 mg or 4 mg) standard or (4 mg) mini lozenge. • Maximum 15 higher-strength standard or mini lozenges daily. • *Consider starting with a higher strength if the first cigarette of the day is smoked within 30 minutes of waking up.*	• Start with lower-strength (1 mg) standard or (1.5 mg) mini lozenge. • Up to 30 standard (1 mg) or 15 mini (1.5 mg) lozenges daily. • Change to higher-strength (2 mg) standard or (4 mg) mini lozenges if insufficient effect at maximum dose of lower strength. • *Consider starting with a lower strength if the first cigarette of the day is smoked more than 30 minutes after waking up.*	£	210 lozenges
1 mg (standard) 1.5 mg (mini)	Lower				
Sublingual tablets		**More than 20 cigarettes daily**	**Fewer than 20 cigarettes daily**		
2 mg (cyclodextrin complex)		• Start with higher dosage: 2 tablets each hour. • Maximum 40 tablets daily.	• Start with lower dosage: 1 tablet each hour. • Increase to 2 tablets each hour if necessary. • Maximum 40 tablets daily.	££	280 tablets Lower dose 560 tablets Higher dose
Inhalator		**All dependency levels**			
15 mg		• Maximum 6 cartridges of the 15 mg strength daily.		£££	84 cartridges
Oral spray		**All dependency levels**			
1 mg per spray (150 sprays per 13.2 ml)		• Maximum 2 sprays per episode (up to 4 sprays every hour). • Maximum of 64 sprays daily.		£££	5 packs
Oral film		**First cigarette of the day smoked more than 30 minutes after waking up**			
2.5 mg		• Maximum 15 films daily.		££	210 films
Nasal spray		**All dependency levels**			
500 micrograms per dose (200 sprays per 10 ml)		• Use one spray in each nostril, up to twice every hour for 16 hours daily. • Maximum 64 sprays daily.		£££	4 packs

ADDITIONAL INFORMATION

NRT

Formulation	First prescription	Further prescription(s)
Single NRT	1 or 2-week supply at maximum daily dose.	Appropriate quantity to last 2 weeks based on actual usage and any remaining NRT from previous prescription.
Combination NRT	1 or 2-week supply (7 or 14) patches **plus** half the suggested maximum daily dose quantity of one immediate-release NRT.	2-week supply (14) patches **plus** an appropriate quantity of one immediate-release NRT, to last 2 weeks based on actual usage and any remaining NRT from previous prescription.
Patch (single or combination NRT)	1 or 2-week supply (7 or 14 patches)	2-week supply (14 patches)

NRT patches

- 24-hour patches may be more suitable if patients have strong cravings for cigarettes on waking.
- Sleep disturbances may be helped by removing the patches before bed (changing from a 24-hour patch to a 16-hour patch).
- If abstinence is not achieved, or if withdrawal symptoms are experienced, maintain or increase the strength of the patch until the patient is stabilised.
- If patients using a high-strength patch experience excessive side effects that do not resolve within a few days, change to a medium-strength patch for the remainder of the initial period, then a low-strength patch for 2 to 4 weeks.

Varenicline

Dose		Relative cost = £££
Adults over 18 years		Start 1 to 2 weeks before target quit date (up to maximum of 5 weeks before target quit date). 500 micrograms once daily for 3 days, increase to 500 micrograms twice daily for 4 days, then 1 mg twice daily for 11 weeks.
Severe renal impairment (eGFR < 30 ml/min/1.73 m^2). Avoid in end-stage renal disease		Reduce dose to 500 micrograms twice daily if not tolerated. 500 micrograms once a day for the first 3 days, then increase to 1 mg once a day.
Varenicline prescription/supply	**Duration**	**Quantity**
1st	2 weeks (starter pack)	11 x 500 microgram tablets and 14 x 1 mg tablets (starter pack)
2nd, 3rd, 4th, 5th & 6th	2 weeks	1 mg x 28 tablets (500 microgram x 28 tablets if using lower dose)

Bupropion

Dose		Relative cost = £££
Adults over 18 years		Start 1 to 2 weeks before target quit date. 150 mg daily for 6 days then 150 mg twice daily (max. single dose 150 mg, max. daily dose 300 mg; minimum 8 hours between doses). Period of treatment 7–9 weeks; discontinue if abstinence not achieved at 7 weeks.
Elderly		Max.150 mg once a day.
Hepatic impairment. (Avoid in severe hepatic cirrhosis.)		Reduce dose to 150 mg once a day.
Renal impairment		Reduce dose to 150 mg once a day.
Predisposition to seizures		Consider a maximum dose of 150 mg daily.
Bupropion prescription/supply	**Duration**	**Quantity**
1st	2 weeks	22 x 150 mg tablets (provides 2-week supply at standard initiation dose)
2nd & 3rd	2 weeks	28 x 150 mg tablets (14 x 150 mg tablets if using lower dose)
4th	Up to 3 weeks (to complete the course of treatment)	Up to 42 x 150 mg tablets (Up to 21 x 150 mg tablets if using lower dose)

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