Northamptonshire Healthcare
NHS Foundation Trust

MMG036 Guidance on the use of Smoking Cessation Products

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Why we need this Guideline

Following this guideline will help the Trust:

- Achieve smoke free status across the organisation
- Provide nicotine replacement therapy (NRT) to relieve cravings and withdrawal symptoms in nicotine dependent inpatients
- To encourage the continuation of care between NHFT and Stop Smoking Services (SSS)
- Provide information for staff to ensure that they are aware of the impact of smoking and stopping smoking on medication

What the Guideline is trying to do

To provide assurance to Northamptonshire Healthcare NHS Foundation Trust and its patients that smoking cessation and associated Nicotine Replacement Therapy will be provided according to patient need and choice

This guideline does not cover the use of electronic cigarettes and othe vaping devices. Electronic cigarettes are not classified as a medicinal product and cannot be prescribed as an alternative to nicotine replacement therapy (NRT). They can be used according to the guidelines in the NHFT smoke free policy.

Which stakeholders have been involved in the creation of this Guideline

Medicines Management Committee, NHFT Smoke Free Project Group

Any required definitions/explanations

NHFT - Northamptonshire Healthcare NHS Foundation Trust

NRT - Nicotine Replacement Therapy

SSS - Smoking Cessation Services

Key duties

Medicines Management Committee

Will approve the guideline and is responsible for the implementation and dissemination of this policy

Ward or unit manager

It is the responsibility of the ward/unit manager to ensure:

- All members of staff use these guidelines when assessing a patient or service user under the care of NHFT in smoke free areas

NHFT staff providing clinical care

It is the responsibility of all clinical staff to ensure:

- All patients or service users are treated according to these guidelines
- To enter and update quit dates and NRT used on the Quit Manager web portal.

Guideline detail

To comply with the NHFT Smoke Free Policy and the NICE guidelines for smoking cessation in secondary care (PH 48, Nov 2013); smokers will need to stop smoking whilst in Trust buildings and grounds during an inpatient admission.

During an in-patient admission a smoker has three options:

Option 1 - Patients who do not intend to stop smoking (at discharge) but are suffering acute nicotine withdrawal

- Patients suffering acute nicotine withdrawal can be prescribed NRT to help with withdrawal symptoms (which may include; agitation, headaches, moodiness, irritability, nervousness, fidgeting, anger and cigarette craving). NRT in these cases will be limited to symptomatic management with patches and / or lozenges only.
- All inpatients will be given the opportunity for stop smoking support while in the Trust's care.
- No NRT will be given on discharge to patients who do not intend to stop smoking
- The telephone number of the relevant NHS Stop Smoking Service (SSS) will be given on discharge and if contacted will arrange an appointment as soon as possible

Option 2 - Patients who are motivated to stop smoking and are suffering acute nicotine withdrawal

- Patients will be offered NRT according to formulary and patient preference
- On discharge the patient will be given 7 days supply of NRT and advised on future support
- The SSS will be informed and referral arrangements confirmed
- The GP practice will be informed of NRT provided at discharge and referral arrangements to SSS

Option 3 - Patients abstaining from smoking but not suffering acute nicotine withdrawal

- Support should be offered and withdrawal symptoms monitored
- If withdrawal symptoms occur NRT should be considered

Stop smoking products including NRT

1. Nicotine replacement therapy

Several different forms of NRT can be prescribed for those undergoing an attempt to quit smoking; the preparation chosen should be safe for the patient and most likely to succeed. Refer to current BNF for dosing guidance.

Treatment Choices	Administration	Dose
Patch	Record administration on a Patch Chart to ensure site rotation. Apply on waking to dry non-hairy skin on the hip, trunk or upper arm. Avoid applying to broken, red or irritated skin. Skin sites should not be re-used for at least 7 days. Only one patch should be worn at a time. Exercise may increase absorption of nicotine and therefore side effects. Patients/staff should not try to alter the dose of the patch by cutting it up	Individuals who smoke more than 10 cigarettes a day should apply a high strength patch daily for 6-8 weeks, followed by a medium patch for two weeks, then the low strength patch for the final two weeks. Individuals who smoke fewer than 10 cigarettes a day can start with the medium strength patch for 6-8 weeks followed by a low strength patch for 2 weeks.
Lozenges	One lozenge should be placed in the mouth and allowed to dissolve – suck until taste becomes strong, then 'park' at side of the mouth. It should be moved from one side of the mouth to the other until completely dissolved (approximately 20-30 minutes). Do not chew or swallow whole. Use of coffee, acid drinks and soft drinks at the same time may decrease absorption of nicotine and should be avoided for 15 minutes prior to sucking lozenge.	One lozenge should be used every 1-2 hours when the urge to smoke occurs. Individuals smoking less than 20 cigarettes a day should use the lower strength lozenge and those who smoke more than 20 a day should use the higher strength lozenge Patients should not exceed 15 lozenges a day
Inhalator (each cartridge)	Insert cartridge into the device and draw in air through the mouthpiece. Each session can last for approximately five minutes. The amount of nicotine from one puff of the cartridge is less than a cigarette, so it may be necessary to inhale more often.	To be used when the urge to smoke occurs. Maximum of six 15 mg cartridges daily. A single 15 mg cartridge lasts approximately 40 minutes of use. Record when the inhalator is given to the patient.
Gum	The "chew and rest" technique should be used to absorb the nicotine from the gum. After about 30 minutes of such use, the gum will be exhausted.	To be used when the urge to smoke occurs. Sufficient gums should be used, usually 8-12 per day, up to a maximum of 15.

Cautions with NRT

Risks / benefits must be considered before prescribing NRT in the following circumstances

- Those who are under 18 years old;
- Pregnant or breastfeeding women;
- Stable Cardiovascular Disease;
- Uncontrolled hypertension;
- Those with a previous serious reaction to NRT or any ingredients contained in the product, e.g. glue in the patch;
- Those taking medicines which interact with cigarette smoke
- Diabetes (additional glucose monitoring is required).

Cautions for patches only:

- Those with a chronic generalised skin disease such as psoriasis, chronic dermatitis and urticaria;
- Those who have had a previous reaction to the transdermal patch;
- Occasional smokers.

Cautions for nasal spray only:

- Those with chronic nasal disorders such as polyposis, vasomotor rhinitis and perennial rhinitis

Cautions for inhalation only:

- Bronchospastic disease
- Chronic throat disease
- Obstructive lung disease

Caution with oral use:

- Gastritis (can be aggravated by swallowed nicotine)
- Oesophagitis (can be aggravated by swallowed nicotine)
- Peptic ulcers (can be aggravated by swallowed nicotine)

Cautions for oral topical use:

- Gum may also stick to and damage dentures

Adolescents

Many young smokers show signs of nicotine dependence. Although there is little published data demonstrating the efficacy of NRT in young smokers, there is no logical reason why it should not help as long as it is used correctly and the smoker is determined to give up. Ultimately the decision to use NRT should be based on the smoker's determination to quit, and on their level of dependence (as opposed to age). Given that NRT is less harmful than smoking, safety concerns should not be a barrier to use and harm reduction principles should be applied when considering NRT for young people (12-17 years). The recommendations are to use NRT for three months in this age group. If it is needed for longer it should be reviewed by a health professional. Young people have the right to confidential medical advice and treatment if the provider assesses that the young person is able to understand what is being proposed

and this will apply to the use of NRT products.

Pregnancy

Ideally, pregnant women should stop smoking without using NRT but, if this is not possible, NRT may be recommended to assist a quit attempt as it is considered that the risk to the foetus of continued smoking by the mother outweighs any potential adverse effects of NRT

The decision to use NRT should be made following a risk-benefit assessment as early in pregnancy as possible. The aim should be to discontinue NRT use after 2-3 months. Intermittent forms of NRT are preferable during pregnancy although a patch may be appropriate if nausea and/or vomiting are a problem. If patches are used, they should be removed before going to bed at night.

Breastfeeding

NRT can be used by women who are breastfeeding. The amount of nicotine the infant is exposed to from breast milk is relatively small and less hazardous than the second-hand smoke they would otherwise be exposed to if the mother continued to smoke. If possible, patches should be avoided.

NRT products taken intermittently are preferred as their use can be adjusted to allow the maximum time between their administration and feeding of the baby, to minimise the amount of nicotine in the milk.

Cardiovascular disease

Although nicotine has some acute effects on the cardiovascular system, unlike tobacco smoke it is not a significant risk factor for cardiovascular disease or acute cardiac events. NRT provides less nicotine, less rapidly than cigarette smoking, without substances such as carbon monoxide (which is known to have adverse effects on the cardiovascular system). On this basis, experts agree that smokers with stable cardiovascular disease can safely use all NRT products.

It is recommended that the risks and benefits of using NRT should be assessed for smokers with unstable cardiovascular disease, or who have suffered an acute event in the past four weeks. If the only other option for this group is continued smoking, a risk–benefit assessment invariably leads to recommending NRT. Stopping smoking via non-pharmacological methods should be tried first. When using NRT for smokers with unstable cardiovascular disease, it is advisable to use the shorter-acting oral products, which can be discontinued immediately in the event of any problems. Nicotine patches, even once removed, leave a small reservoir of nicotine under the skin.

Diabetes mellitus

Nicotine releases catecholamines which can affect carbohydrate metabolism. Diabetic patients should be advised to monitor their blood sugar levels more frequently than usual when starting NRT.

Renal or hepatic impairment

NRT should be used with caution in patients with moderate to severe hepatic impairment and/or severe renal impairment, as the clearance of nicotine and/or its metabolites may be decreased, with the potential for increased adverse effects.

Phaeochromocytoma and uncontrolled hyperthyroidism

Use NRT with caution.

2. Bupropion

Bupropion is contraindicated in bipolar affective disorder, epilepsy, CNS tumours, alcohol withdrawal, benzodiazepine withdrawal and eating disorders. It should not be prescribed with other drugs that can cause seizures. This includes tricyclic antidepressants and some antipsychotic medicines. In view of the above bupropion is not approved for smoking cessation within NHFT. Treatment may however be continued if initiated prior to admission

3. Varenicline

Varenicline has been linked to depression, suicidal ideation and exacerbation of underlying psychiatric illness. Other side effects include sleep problems and anxiety. Varenicline has not been approved for use within NHFT. Treatment may however be continued if initiated prior to admission**.**

Access to NRT

Initial management can be undertaken using NRT available as ward stock. For those described in option 1 above they can continue to be symptomatically managed with patches and lozenges from ward stock.

For those described in option 2, a formal assessment must be carried out and a quit date set on the quit manager IT system. Please refer to the flowchart in appendix 1 for details. Appropriate NRT can then be ordered from pharmacy using the proforma in appendix 2 and recorded on quit manager.

Quit status must then be recorded at 4 weeks on quit manager.

Access to NRT in 136 suites

NRT can be administered to service users undergoing acute assessment in section 136 suites in the form of sublingual microtabs to manage acute symptoms of nicotine withdrawal according to the process described in appendix 3.

Smoking and Medication

- Tobacco smoke contains polycyclic aromatic hydrocarbons within the tar that increase the activity of certain hepatic enzymes (CYP1 A2 in particular).
- Many commonly used medicines are substrates for CYP1A2: theophylline, fluvoxamine, caffeine, coumarins including warfarin and the antipsychotics clozapine and olanzapine
- Smokers taking a medication that is metabolised by this enzyme may require higher doses than non-smokers
- When people stop or reduce their smoking, there can be a decrease in enzyme activity with a corresponding increase in drug levels: hence they may require a reduction in the dosage of

the interacting medication. Conversely if non-smokers restart smoking, a dose increase should be anticipated to maintain therapeutic levels.

- Not all possible drug-smoking interactions are clinically significant
- For patients taking clozapine who are intending to stop smoking, advice should be sought from the clozapine clinic staff or consultant psychiatrist who will formulate a plan, to ensure the patient's ongoing safety.
- For a full list of drugs affected by smoking cessation see UKMI guidance in Appendix 4
- Information should be given to service users and carers regarding the likely need to increase the dose of their medication if they start smoking again.

Training requirements associated with this Policy

Mandatory Training

There is no mandatory training associated with this policy.

Specific Training not covered by Mandatory Training

- Training is available for level 2 smoking cessation trainers via the First for Wellbeing Smoking Cessation service

How this Policy will be monitored for compliance and effectiveness

The table below outlines the Trusts' monitoring arrangements for this document. The Trust reserves the right to commission additional work or change the monitoring arrangements to meet organisational needs.

Aspect of compliance or effectiveness being monitored	Method of monitoring	Individual responsible for the monitoring	Monitoring frequency	Group or committee who receive the findings or report	Group or committee or individual responsible for completing any actions
Adherence to guidelines for quit attempts	Review of NRT request forms	Senior Pharmacist Community Services	6 monthly	MMc	MMC

Equality considerations

See MMP001 Control of medicines Policy.

Harvard Reference Guide

UKMi Q&A 136.4 Which medicines need dose adjustment when a patient stops smoking?

BNF 72 September 2016

Document control details

Author:	Senior Pharmacist Community Services
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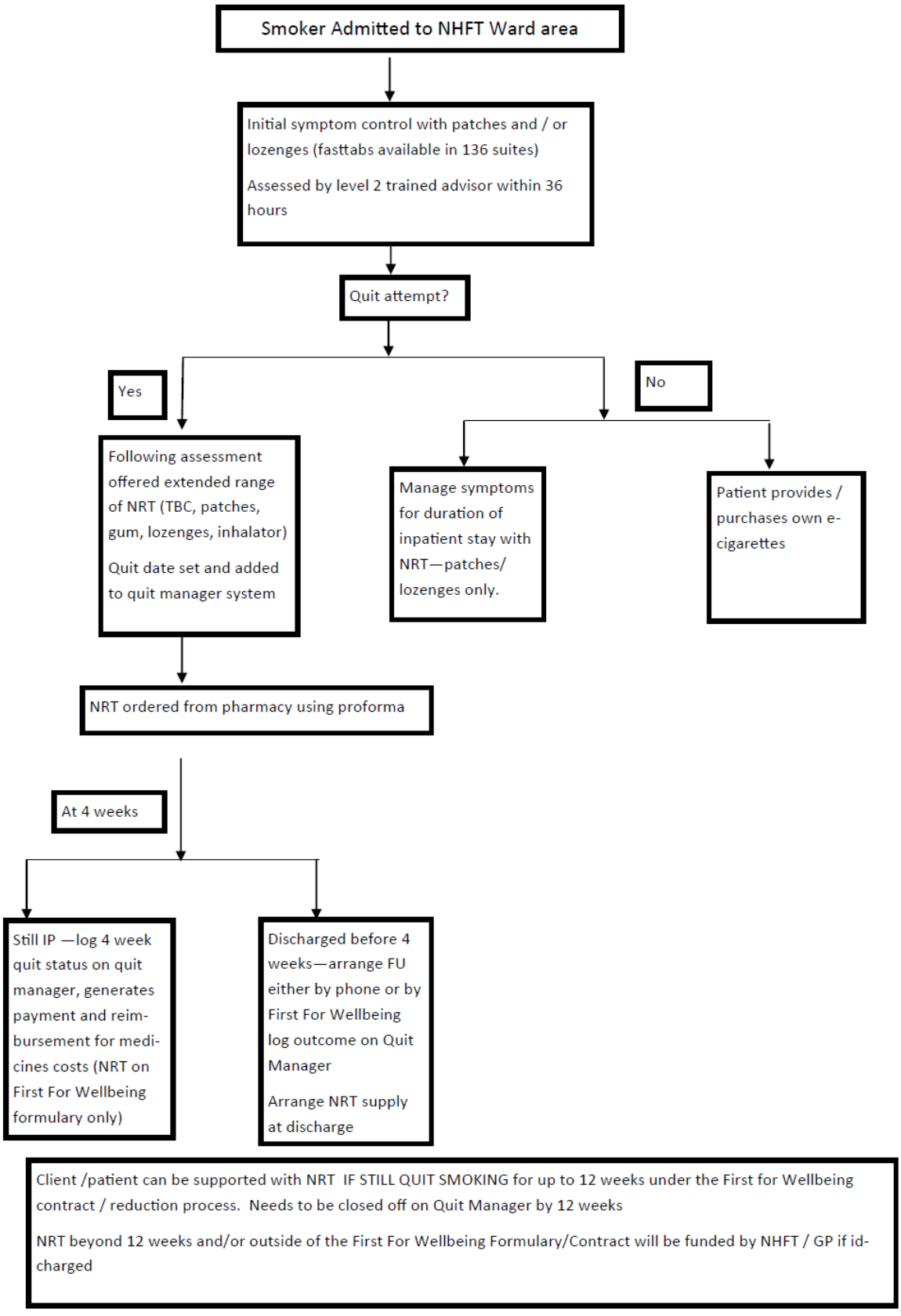
Version No.	Date Ratified/ Amended	Date of Implementation	Next Review Date	Reason for Change (eg. full rewrite, amendment to reflect new legislation, updated flowchart, minor amendments, etc.)
1.0	19.9.17	19.9.17	19.9.19	New Guidance.

Appendix 1 – Flowchart for NRT assessment



Appendix 2 – Order form for NRT

NHFT Smoke Free project
NRT / Medication Request Form

Please circle/delete as appropriate when completing this form

This form to be used for those service users undergoing a quit attempt.
For individuals prevented from smoking who do not want to attempt to quit NRT can be provided in the form of patches and / or lozenges.

Assessor's name

Telephone number:

Job Title:

Advisor / Specialist Signature:

.....

As a trained associate advisor/stop smoking specialist I am supporting the following patient with their quit attempt

Patient's name: _____

D.O.B: _____

Address/postcode: _____

_____

NHFT ward / clinic _____

Patient Signature:

.....

Med Pad Number

1). Please supply the following NRT for inpatient use (circle medicine and strength)

After discussing all NRT products please supply 2 weeks of the patients preferred option of the following:

Single or **Combined** therapy

Patch	24hr	21mg	16hr	25mg	
	Niquitin CQ	14mg	Nicorette Invisi	15mg	
		7mg		10mg	
Niquitin CQ Lozenge	4mg	Original		Mint	
	2mg	Original		Mint	
Nicorette Inhalator	15mg	Starter pack (4)		Spare cartridge pack (20) (36)	
Mouth Spray**		Quickmist 1mg (13.2ml)		Quickmist 1mg (2 x 13.2ml)	
Nicorette Gum	4mg	Fruit	Icy-white	Original	Fresh-Mint
	2mg	Fruit	Icy-white	Original	Fresh-Mint

Quit Date Set: ..... **CO reading today:**.....**ppm** **Date:**.....

Please call the First for Wellbeing Stop Smoking Team on 0300 126 5700 if you have any concerns regarding this request.

** **Specialist Service recommendation only**

Entered on to quit manager ☐ Quit manager client number ☐

NHFT Smoke Free project
NRT / Medication Request Form

Please circle/delete as appropriate when completing this form

This form to be used for those service users undergoing a quit attempt.
For individuals prevented from smoking who do not want to attempt to quit NRT can be provided in the form of patches and / or lozenges.

Assessor's name

Telephone number:

Job Title:

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As a trained associate advisor/stop smoking specialist I am supporting the following patient with their quit attempt

Patient's n: _____

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_____

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After discussing all NRT products please supply 2 weeks of the patients preferred option of the following:

Single or **Combined** therapy

Patch	24hr	21mg	16hr	25mg	
	Niquitin CQ	14mg	Nicorette Invisi	15mg	
		7mg		10mg	
Niquitin CQ Lozenge	4mg	Original		Mint	
	2mg	Original		Mint	
Nicorette Inhalator	15mg	Starter pack (4)		Spare cartridge pack (20) (36)	
Mouth Spray**		Quickmist 1mg (13.2ml)		Quickmist 1mg (2 x 13.2ml)	
Nicorette Gum	4mg	Fruit	Icy-white	Original	Fresh-Mint
	2mg	Fruit	Icy-white	Original	Fresh-Mint

Quit Date Set: ..... **CO reading today:**.....**ppm** **Date:**.....

Please call the First for Wellbeing Stop Smoking Team on 0300 126 5700 if you have any concerns regarding this request.

** **Specialist Service recommendation only**

Entered on to quit manager ☐ Quit manager client number ☐

Appendix 3 – Sublingual tablets in 136 suites

Provided there is no contraindication (refer to guideline and latest BNF) or known hypersensitivity and service users are demonstrating symptoms of nicotine withdrawal these symptoms can be managed by administration of sublingual tablets by registered nurses.

Any doses administered must be recorded below and brought to the attention of all staff providing care. A formal smoking cessation assessment must be made as soon as possible and options considered according to Trust guidelines.

Administration of NRT according to this process is limited to 24 hours and doses must be administered to the service user, rather than being supplied to them for self administration.

For individuals smoking fewer than 20 cigarettes per day 1 sublingual tablet can be administered every hour increased to 2 sublingual tablets every hour if required. For individuals smoking more than 20 cigarettes per day 2 sublingual tablets can be administered every hour as required.

Name and date of birth	Allergies / sensitivities

Date	Time	Dose given	Signature

Continue on second sheet if necessary

Appendix 4 – Medicines Advice on stopping smoking

UKMi Q&A 136.4

Which medicines need dose adjustment when a patient stops smoking?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals
Before using this Q&A, read the disclaimer at www.ukmi.nhs.uk/activities/medicinesQAs/default.asp
Date prepared: August 2012

Summary

- The majority of interactions between medicines and smoking are not clinically significant.
- Healthcare professionals giving smoking cessation advice should be aware of a small number of medicines, and in particular theophylline, clozapine and olanzapine, which may require dose adjustment or increased monitoring when smoking is stopped.

Background

Cigarette smoking can interact with some medicines. This is mainly due to polycyclic aromatic hydrocarbons in cigarette smoke that stimulate cytochrome P450 enzymes, particularly CYP1A2. A number of medicines that are metabolised via CYP1A2, for example theophylline, may consequently be more rapidly metabolised in smokers. There have also been reports of pharmacodynamic interactions with some medicines.

Answer

The majority of interactions are not clinically significant but the potential for interaction should be borne in mind if a patient starts or stops smoking. The table below lists those interactions considered to be of most clinical importance, describes the nature of the interaction and advises on appropriate management when a patient taking an interacting drug stops smoking. Since the majority of interactions are due to components of cigarette smoke other than nicotine, these interactions are not expected to occur with nicotine replacement therapy (NRT). The information in the table applies to patients who stop smoking regardless of whether they use NRT or not.

A full list of interactions (including those that have been investigated but are clinically insignificant) is available in Appendix 1 and may be useful for healthcare professionals giving advice on smoking cessation.

BNF category/ Drug name	Nature of interaction	Clinical relevance	Action to take when stopping smoking
2.8.2 Warfarin	Warfarin is partly metabolised via CYP1A2. An interaction with smoking is not clinically relevant in most patients. The dose of warfarin is adjusted according to a patient's INR (International Normalised Ratio).	Moderate	If a patient taking warfarin stops smoking, their INR might increase so monitor the INR more closely. Advise patients to tell the physician managing their anticoagulant control that they are stopping smoking.

BNF category/ Drug name	Nature of interaction	Clinical relevance	Action to take when stopping smoking
3.1.3 Theophylline	Theophylline is metabolised principally via CYP1A2. Smokers need higher doses of theophylline than non-smokers due to theophylline's shortened half-life and increased elimination. Some reports suggest smokers may need twice the dose of non-smokers.	High	Monitor plasma theophylline concentrations and adjust the dose of theophylline accordingly. The dose of theophylline may need to be reduced by about one quarter to one third one week after withdrawal. However, it may take several weeks for enzyme induction to dissipate. Monitor theophylline concentration periodically. Advise the patient to seek help if they develop signs of theophylline toxicity such as palpitations or nausea.
4.2.1 Chlorpromazine	Chlorpromazine is metabolised principally via CYP1A2. Smokers have lower serum levels of chlorpromazine compared with non-smokers. A case report describes a 25 year old patient with schizophrenia who experienced increased adverse effects of chlorpromazine (sedation and dizziness) and increased plasma chlorpromazine levels after abruptly stopping smoking.	Moderate	Be alert for increased adverse effects of chlorpromazine (e.g. dizziness, sedation, extra-pyramidal symptoms). If adverse effects occur, reduce the dose as necessary.
4.2.1 Clozapine	Clozapine is metabolised principally via CYP1A2 and clearance is increased in smokers. Serum clozapine levels are reduced in smokers compared with non-smokers; smokers may need higher doses. There have been case reports of adverse effects in patients taking clozapine when they have stopped smoking.	High	Monitor serum drug levels before stopping smoking and one or two weeks after stopping smoking. Be alert for increased adverse effects of clozapine. If adverse effects occur, reduce the dose as necessary.
4.2.1 Olanzapine	Olanzapine is metabolised principally via CYP1A2 and clearance is increased in smokers. Serum olanzapine levels are reduced in smokers compared with non-smokers; smokers may need higher doses. There have been case reports of adverse effects in patients taking olanzapine when they have stopped smoking.	High	Be alert for increased adverse effects of olanzapine (e.g. dizziness, sedation, hypotension). If adverse effects occur, reduce the dose as necessary.

BNF category/ Drug name	Nature of interaction	Clinical relevance	Action to take when stopping smoking
4.10 Methadone	Methadone is metabolised via isoenzymes including CYP1A2. There has been a case report of respiratory insufficiency and altered mental status when a patient taking methadone for analgesia stopped smoking.	Moderate	Be alert for signs of opioid toxicity and reduce the methadone dose accordingly.
6.1.1 Insulin	Smoking is associated with poor glycaemic control in patients with diabetes. Smokers may require higher doses of insulin but the mechanism of any interaction is unclear.	Moderate	If a patient with insulin-dependent diabetes stops smoking, their dose of insulin may need to be reduced. Advise the patient to be alert for signs of hypoglycaemia and to test their blood glucose more frequently.

The following criteria have been considered in grading the clinical relevance of interactions:

High: Documented interaction with clinically important effects in a number of patients and/or
Drugs metabolised principally by CYP1A2 and with a narrow therapeutic range.
Moderate: Documented pharmacokinetic interaction with no or minor clinical effects, or isolated reports of clinically important effects and/or
Drugs metabolised partly by CYP1A2 and with a narrow therapeutic range and/or
Drugs metabolised principally by CYP1A2 and with a wide therapeutic range.
Low: Theoretical interaction without documented cases and/or
Drugs metabolised partly by CYP1A2 and with a wide therapeutic range.

Limitations

This table does not consider interactions with pharmacological agents used for smoking cessation (e.g. bupropion, varenicline), or indirect interactions caused by the effects of smoking on, for example, blood pressure and lipid levels.

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Search strategy

- In-house MI Databank [SMOKING] 2/7/2012
- Electronic Medicines Compendium www.medicines.org.uk/emc/ [SMOKING or SMOKER or CIGARETTE] 2/7/2012
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Appendix 4a: Drug interactions with smoking

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
1.3.1	H2 receptor antagonists	Smoking is not considered to have a clinically significant effect on the pharmacokinetics of cimetidine, famotidine or ranitidine. Healing of ulcers is slower in smokers than non-smokers.	Low	None
1.3.3	Sucralfate	Smoking does not appear to reduce the efficacy of sucralfate.	Nil	None
2.2.2	Furosemide	Smoking might reduce the diuretic effect of furosemide but any interaction is not expected to be clinically relevant.	Low	None
2.3.2	Adenosine	Nicotine from nicotine-replacement therapy can enhance the effect of adenosine. Smoking may have a similar effect.	Low	None
2.3.2	Flecainide	Smoking increases the clearance of flecainide. Smokers appear to need higher doses of flecainide, compared with non-smokers.	Low	Be alert for dose-related adverse effects of flecainide such as dizziness and visual disturbances. If adverse effects occur, reduce the dose as necessary.
2.3.2	Lidocaine	Smoking reduces the bioavailability of oral, but not parenteral, lidocaine. Lidocaine is not used orally; this interaction is of no clinical relevance.	Nil	None
2.3.2	Mexiletine	Mexiletine is metabolised partly via CYP1A2 and its half-life may be reduced in smokers compared to non-smokers. The dose of mexiletine is titrated according to response.	Low	Be alert for adverse effects of mexiletine (e.g. nausea, tremor, hypertension) and reduce the dose as necessary.
2.4	Beta-blockers	Smoking opposes the beneficial effects of beta-blockers on blood pressure and heart rate. This is a pharmacodynamic rather than a pharmacokinetic interaction. Serum propranolol levels may be lower in smokers than non-smokers.	Low	None
2.5.2	Clonidine	Historically, an interaction between adrenergic receptor agonists and smoking was listed in the prescribing information for nicotine replacement products.	Nil	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
2.5.4	Alpha-adrenoreceptor blocking drugs	Historically, an interaction between adrenergic receptor blockers and smoking was listed in the prescribing information for nicotine replacement products.	Nil	None
2.5.5	Irbesartan	Smokers may have higher serum irbesartan levels than non-smokers but this is not expected to be clinically relevant.	Low	None
2.6.2	Nifedipine	Historically, an interaction between nifedipine and smoking was listed in the prescribing information for nicotine replacement products. However, smoking appears not to interact with nifedipine.	Nil	None
2.6.2	Verapamil	Verapamil may be metabolised partly via CYP1A2. Smokers may have lower serum concentrations of verapamil than non-smokers but this is not expected to be clinically relevant.	Low	None
2.6.4	Cilostazol	Smokers may have lower serum concentrations of cilostazol than non-smokers but this is not expected to be clinically relevant.	Low	None
2.8.1	Epoprostenol	Smoking does not appear to affect the efficacy of epoprostenol.	Nil	None
2.8.1	Heparin	Heparin and low-molecular weight heparins may be slightly less effective in smokers but the difference is probably too small to be of practical importance.	Low	None
2.8.2	Warfarin	Warfarin is partly metabolised via CYP1A2. An interaction with smoking is not clinically relevant in most patients. The dose of warfarin is adjusted according to a patient's INR (International Normalised Ratio).	Moderate	If a patient taking warfarin stops smoking, their INR might increase so monitor the INR more closely. Advise patients to tell the physician managing their anticoagulant control that they are stopping smoking.
2.9	Clopidogrel	Some studies suggest the antiplatelet effect of clopidogrel is greater in smokers. A clinically relevant interaction is not established.	Low	None
3.1	Beta-adrenoreceptor agonists	Historically, an interaction between adrenergic receptor agonists and smoking was listed in the prescribing information for nicotine replacement products.	Nil	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
3.1.3	Theophylline	Theophylline is metabolised principally via CYP1A2. Smokers require higher doses of theophylline than non-smokers due to theophylline's shortened half-life and increased elimination. Some reports suggest smokers may need twice the dose of non-smokers.	High	Monitor plasma theophylline concentrations and adjust the dose of theophylline accordingly. The dose of theophylline may need to be reduced by about one quarter to one third one week after withdrawal. However, it may take several weeks for enzyme induction to dissipate. Monitor theophylline concentration periodically. Advise the patient to seek help if they develop signs of theophylline toxicity such as palpitations or nausea.
3.3.2	Zafirlukast	Clearance of zafirlukast may be increased in smokers but this is not expected to be clinically relevant.	Low	None
3.5.1	Caffeine	Smoking increases the rate of metabolism of caffeine.	Low	None
4.1.1	Melatonin	Melatonin is metabolised principally via CYP1A2; plasma levels may be lower in smokers than non-smokers.	Low	Be alert for increased effects of melatonin if a patient stops smoking.
4.1.2	Benzodiazepines	Smokers taking benzodiazepines may experience less drowsiness than non-smokers. Results from pharmacokinetic studies have been mixed and the interaction, if any exists, may be due to stimulation of the central nervous system from smoking.	Low	Patients may experience an enhanced effect of benzodiazepines after stopping smoking. If so, consider reducing the dose.
4.2.1	Benperidol	Benperidol is metabolised via liver enzymes, possibly including CYP1A2 but there are no documented cases of an interaction with smoking.	Low	Be alert for increased adverse effects of benperidol. If adverse effects occur, reduce the dose as necessary.
4.2.1	Chlorpromazine	Chlorpromazine is metabolised principally via CYP1A2. Smokers have lower serum levels of chlorpromazine compared with non-smokers. A case report describes a 25 year old patient with schizophrenia who experienced increased adverse effects of chlorpromazine (sedation and dizziness) and increased plasma chlorpromazine levels after abruptly stopping smoking.	Moderate	Be alert for increased adverse effects of chlorpromazine (e.g. dizziness, sedation, extra-pyramidal symptoms). If adverse effects occur, reduce the dose as necessary.

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
4.2.1	Flupentixol	Flupentixol clearance might be increased by smoking but an interaction is not thought to be clinically relevant. There is no simple correlation between plasma levels of flupentixol and clinical effects.	Low	None
4.2.1	Fluphenazine	Studies suggest that smokers have increased fluphenazine clearance compared with non-smokers and may require higher doses, but have not shown any difference in behavioural and adverse effects.	Low	Be alert for increased adverse effects of fluphenazine (e.g. drowsiness, extra-pyramidal symptoms). If adverse effects occur, reduce the dose as necessary.
4.2.1	Haloperidol	Studies suggest that smokers have increased haloperidol clearance compared with non-smokers and may require higher doses, but have not shown any difference in behavioural and adverse effects.	Low	Be alert for increased adverse effects of haloperidol (e.g. drowsiness, extra-pyramidal symptoms). If adverse effects occur, reduce the dose as necessary.
4.2.1	Perphenazine	Perphenazine is metabolised principally via CYP2D6. A clinically relevant interaction is not expected between perphenazine and smoking.	Nil	None
4.2.1	Thioridazine	Thioridazine is metabolised principally via CYP2D6 but it has been suggested that clearance of thioridazine may be higher in smokers than non-smokers and that smokers may require higher doses. NB: Thioridazine is no longer marketed in the UK.	Low	Be alert for increased adverse effects of thioridazine (hypotension, arrhythmias, drowsiness, extra-pyramidal symptoms). If adverse effects occur, reduce the dose as necessary.
4.2.1	Trifluoperazine	Smoking did not have any effect on serum levels of trifluoperazine in a single dose study. There are no reports of an interaction between trifluoperazine and smoking.	Nil	None
4.2.1	Zuclopenthixol	Zuclopenthixol clearance appears not to be increased by smoking. There is no simple correlation between plasma levels of zuclopenthixol and clinical effects.	Nil	None
4.2.1	Amisulpride	Smoking appears to have no effect on amisulpride serum levels.	Nil	None
4.2.1	Aripiprazole	Smoking appears to have no effect on aripiprazole serum levels.	Nil	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
4.2.1	Clozapine	Clozapine is metabolised principally via CYP1A2 and clearance is increased in smokers. Serum clozapine levels are reduced in smokers compared with non-smokers; smokers may need higher doses. There have been case reports of adverse effects in patients taking clozapine when they have stopped smoking.	High	Monitor serum drug levels before stopping smoking and one or two weeks after stopping smoking. Be alert for increased adverse effects of clozapine. If adverse effects occur, reduce the dose as necessary.
4.2 .1	Olanzapine	Olanzapine is metabolised principally via CYP1A2 and clearance is increased in smokers. Serum olanzapine levels are reduced in smokers compared with non-smokers; smokers may need higher doses. There have been case reports of adverse effects in patients taking olanzapine when they have stopped smoking	High	Be alert for increased adverse effects of olanzapine (e.g. dizziness, sedation, hypotension). If adverse reactions occur, reduce the dose as necessary.
4.2.1	Paliperidone	Paliperidone pharmacokinetics should not be affected by smoking.	Nil	None
4.2.1	Quetiapine	Quetiapine is metabolised principally via CYP3A4. Smoking appears to have no effect on quetiapine serum levels.	Nil	None
4.2.1	Risperidone	Risperidone is metabolised principally via CYP2D6. A clinically relevant interaction is not expected between risperidone and smoking.	Nil	None
4.2.1	Sertindole	Sertindole clearance might be increased by smoking but an interaction is not thought to be clinically relevant.	Low	None
4.2.1	Ziprasidone	Ziprasidone is not metabolised via CYP1A2. Smoking appears to have no effect on ziprasidone serum levels. NB: Ziprasidone is not marketed in the UK.	Nil	None
4.2.1	Zotepine	Zotepine is metabolised via CYP1A2 and CYP3A4. Zotepine clearance might be increased by smoking but an interaction is not thought to be clinically relevant.	Low	None
4.2.1	Asenapine	Asenapine is metabolised via CYP1A2 but appears to be unaffected by smoking.	Low	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
4.2.3	Lithium	There is a theoretical indirect interaction between smoking and lithium. Stopping smoking could lead to increased xanthine levels by reducing metabolism of dietary caffeine. Raised xanthine levels could in turn lead to increased lithium excretion. There are no documented cases of an interaction.	Low	None
4.3.1	Tricyclic antidepressants	Serum levels of amitriptyline, clomipramine, imipramine and nortriptyline are lower in smokers than in non-smokers, but the concentration of free drug rises, which appears to offset the effects of this interaction.	Low	Be alert for increased adverse effects of the antidepressant. If adverse effects occur, reduce the dose as necessary.
4.3.1	Trazodone	Smokers may have lower plasma levels of trazodone than non-smokers but a clinically relevant interaction is not expected.	Low	None
4.3.3	Selective serotonin reuptake inhibitors	Fluvoxamine is the only SSRI expected to interact with smoking. Fluvoxamine is metabolised by CYP1A2 and plasma levels may be lower in smokers than non-smokers. Smokers might need higher doses than non-smokers.	Low	Be alert for increased adverse effects of fluvoxamine. If adverse effects occur, reduce the dose as necessary.
4.3.4	Agomelatine	Agomelatine is metabolised via CYP1A2; its bioavailability is reduced by smoking.	Low	None
4.3.4	Duloxetine	Duloxetine is metabolised via CYP2D6 and CYP1A2. Serum levels of duloxetine are lower in smokers, but the difference is not considered to be clinically relevant.	Low	None
4.3.4	Mirtazapine	Mirtazapine is metabolised via CYP2D6 and CYP1A2. Smoking may affect mirtazapine clearance but is not thought to interact to a clinically relevant extent.	Low	None
4.3.4	Venlafaxine	Venlafaxine is metabolised principally via CYP2D6. A clinically relevant interaction is not expected between venlafaxine and smoking.	Nil	None
4.7.1	Paracetamol	Paracetamol is metabolised partly via CYP1A2 but there is no clinically relevant interaction between therapeutic doses of paracetamol and smoking.	Nil	None
4.7.2	Codeine	Smoking appears not to interact with codeine.	Nil	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
4.7.2	Morphine	Smokers who stop smoking prior to surgery appear to use more morphine postoperatively via patient-controlled analgesia than non-smokers.	Low	None
4.7.2	Fentanyl	Smokers who stop smoking prior to surgery appear to use more fentanyl postoperatively via patient-controlled analgesia than non-smokers.	Low	None
4.7.2	Pentazocine	Pentazocine metabolism is increased by smoking. Smokers may need higher doses than non-smokers. NB: Pentazocine is not prescribable under the NHS.	Low	None
4.7.2	Pethidine	Animal data suggest that pethidine metabolism may be increased in smokers but this has not been shown in humans.	Nil	None
4.7.2	Dextropropoxy-phene	The efficacy of dextropropoxyphene may be reduced in smokers; this appears to be a pharmacodynamic rather than a pharmacokinetic interaction. NB: Dextropropoxyphene is not recommended for use in the UK. It is available on a named-patient basis in combination with paracetamol as co-proxamol.	Low	None
4.7.4	Triptans (5HT1 agonists)	The clearance of frovatriptan and naratriptan is increased by smoking, but not to a clinically relevant extent. Clearance of sumatriptan is unaffected by smoking.	Nil	None
4.7.4	Clonidine	Historically, an interaction between adrenergic receptor agonists and smoking was listed in the prescribing information for nicotine replacement products.	Nil	None
4.7.4	Methysergide	The manufacturer of *Deseril* (methysergide) advises against its use in patients who smoke heavily since this may result in enhanced vasoconstriction.	Low	None
4.8.1	Carbamazepine	Smoking appears to have little or no effect on carbamazepine serum levels.	Nil	None
4.8.1	Lamotrigine	Smokers may have reduced lamotrigine levels compared with non-smokers but a clinically relevant interaction has not been documented.	Low	None
4.8.1	Phenobarbital	Smoking appears to have no effect on phenobarbital serum levels.	Nil	None
4.8.1	Phenytoin	Smoking appears to have no effect on phenytoin serum levels.	Nil	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
4.9.1	Amantadine	Smoking appears to have no effect on amantadine serum levels.	Nil	None
4.9.1	Rasagiline	Rasagiline is metabolised principally via CYP1A2 but there are no documented reports of an interaction with smoking.	Low	None
4.9.1	Ropinirole	Ropinirole is metabolised principally via CYP1A2 and smokers may require higher doses than non-smokers. The dose of ropinirole is titrated according to response.	Low	Be alert for increased adverse effects of ropinirole (e.g. nausea, dizziness). If adverse effects occur, reduce the dose as necessary.
4.9.3	Riluzole	Riluzole is metabolised principally via CYP1A2 but there are no documented cases of an interaction with smoking.	Low	Be alert for increased adverse effects of riluzole (e.g. gastrointestinal effects, weakness). If adverse effects occur, reduce the dose as necessary.
4.10	Methadone	Methadone is metabolised via isoenzymes including CYP1A2. There has been a case report of respiratory insufficiency and altered mental status when a patient taking methadone for analgesia stopped smoking.	Moderate	Be alert for signs of opioid toxicity and reduce the methadone dose accordingly.
4.11	Memantine	There is a theoretical interaction between memantine and smoking but it is not expected to be clinically relevant.	Low	None
4.11	Tacrine	Tacrine is metabolised principally via CYP1A2 and smokers may require higher doses than non-smokers. NB: Tacrine is not marketed in the UK; Historically an interaction between smoking and tacrine was included in prescribing information for nicotine replacement products.	Low	Be alert for increased adverse effects of tacrine (e.g. gastrointestinal effects, hepatotoxicity). If adverse effects occur, reduce the dose as necessary.
4.11	Donepezil	Donepezil is not metabolised via CYP1A2. A clinically relevant interaction is not expected between donepezil and smoking.	Nil	None
4.11	Galantamine	Galantamine is not metabolised via CYP1A2. A clinically relevant interaction is not expected between galantamine and smoking.	Nil	None
4.11	Rivastigmine	Rivastigmine is not metabolised via CYP1A2. US prescribing information suggests clearance of rivastigmine may be higher in smokers compared with non-smokers; this is not expected to be clinically relevant.	Low	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
5.1.9	Rifabutin	The volume of distribution of rifabutin might be altered in smokers but any interaction is not expected to be clinically significant.	Low	None
5.4.1	Quinine	The clearance of quinine appears to be increased in healthy smokers. If a patient taking quinine stops smoking, plasma levels of quinine might rise. There is no documented case of an interaction but it should be noted that quinine is highly toxic in overdose. Patients with acute falciparum malaria have reduced clearance of quinine and this effect opposes the effect from smoking.	Low	If a patient taking quinine stops smoking, be alert for signs of quinine toxicity (e.g. nausea, tremor, tinnitus, visual disturbance). If toxic effects occur, stop the drug and monitor the patient closely.
6.1.1	Insulin	Smoking is associated with poor glycaemic control in patients with diabetes. Smokers may require higher doses of insulin but the mechanism of any interaction is unclear. NB: Inhaled insulin (*Exubera*, now discontinued in the UK) is contraindicated in smokers as smoking affects the rate and extent of absorption of inhaled insulin.	Moderate	If a patient with insulin-dependent diabetes stops smoking, their dose of insulin may need to be reduced. Advise the patient to be alert for signs of hypoglycaemia and to test their blood glucose more frequently.
6.1.2	Sulphonylureas	Smoking is associated with poor glycaemic control in patients with diabetes. There is a theoretical interaction between sulphonylureas and smoking but this has not been studied.	Low	If a patient taking a sulphonylurea stops smoking, their dose may need to be altered. Advise the patient to be alert for signs of hypo- and hyperglycaemia.
6.3.2	Prednisolone	Smoking appears to have no effect on prednisolone serum levels.	Nil	None
6.3.2	Dexamethasone	Smoking appears to have no effect on dexamethasone serum levels.	Nil	None
6.4	Raloxifene	Smoking appears to have no effect on the efficacy of raloxifene.	Nil	None
7.3.1	Oestrogen	Smoking might affect the metabolism of oestrogens but there is insufficient information to recommend dose changes in oestrogen therapy. NB: Oestrogen-containing contraceptives are not recommended in heavy smokers or any smokers aged over 35 years of age due to the increased risk of circulatory disorders.	Low	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
7.4.1	Alpha-adrenoreceptor blockers	Historically, an interaction between smoking and adrenergic receptor antagonists was included in the prescribing information for nicotine replacement products.	Nil	None
7.4.2	Duloxetine	Duloxetine is metabolised via CYP2D6 and CYP1A2. Serum levels of duloxetine are lower in smokers, but the difference is not considered to be clinically relevant.	Low	None
7.4.5	Papaverine	Smoking may reduce the response to intercavernosal injection of papaverine. It is thought that this is due to the effect of nicotine.	Low	None
8.1.5	Erlotinib	Plasma levels of erlotinib are decreased in current smokers compared with non-smokers. The clinical effect of reduced plasma levels has not been formally assessed but is likely to be clinically significant. Smokers should be encouraged to stop before erlotinib therapy is initiated. NB: Erlotinib is used in the management of lung cancer.	Moderate	None
8.1.5	Irinotecan	Clearance of irinotecan is increased in smokers compared with non-smokers but the evidence is insufficient to recommend dose adjustments for smokers.	Low	None
9.1.2	Vitamin B12	Historically, an interaction between vitamin B12 and smoking has been included in the prescribing information for nicotine replacement products.	Nil	None
9.5.1	Cinacalcet	Cinacalcet is metabolised partly via CYP1A2. Dose adjustment may be required if a patient starts or stops smoking. There are no documented cases of an interaction.	Low	Advise the patient to inform their nephrologist when they stop smoking. Monitor parathyroid hormone levels and adjust the dose accordingly.
10.1.1	NSAIDs	Historically, an interaction between smoking and the NSAIDs phenazone and phenylbutazone was included in the prescribing information for nicotine replacement products. Phenazone and phenylbutazone are metabolised via CYP1A2. In single-dose studies their half-lives were shorter in smokers compared with non-smokers. Theoretically, smokers may require higher doses than non-smokers, but a clinically relevant interaction has not been reported. NB: Phenazone has been discontinued in the UK. Diflunisal clearance might be increased in smokers but any interaction not expected to be clinically relevant. NB: Diflunisal has been discontinued in the UK.	Low	None

BNF category	Drug name or class	Nature of interaction	Clinical relevance	Action to take when stopping smoking
10.2.2	Quinine	The clearance of quinine appears to be increased in healthy smokers. If a patient taking quinine stops smoking, plasma levels of quinine might rise but there are no documented cases of an interaction. Patients with acute falciparum malaria have reduced clearance of quinine and this effect opposes the effect from smoking.	Low	If a patient taking quinine stops smoking, be alert for increased adverse effects or signs of quinine toxicity (e.g. nausea, tremor, tinnitus, visual disturbance). If adverse or toxic effects occur, reduce the dose or stop the drug as necessary.
11.6	Alpha-adrenoreceptor agonists	Historically, an interaction between adrenergic receptor agonists and smoking was included in the prescribing information for nicotine replacement products.	Nil	None
14.4	Hepatitis B vaccine	Smoking is associated with poor response to hepatitis B vaccination. Other risk factors include age over 40 years and obesity.	Low	None
15.1.1	Propofol	Smokers may require higher doses of propofol to achieve anaesthesia.	Low	Anaesthetists should be aware of their patients' smoking status and past anaesthetic history.
15.1.5	Neuromuscular blockers	Smokers might need smaller doses of atracurium but higher doses of rocuronium and vecuronium compared with non-smokers.	Low	Anaesthetists should be aware of their patients' smoking status and past anaesthetic history.
15.2	Lidocaine	Smoking reduces the bioavailability of oral, but not parenteral, lidocaine. Lidocaine is not used orally so this interaction is of no clinical relevance.	Nil	None
15.2	Ropivacaine	Ropivacaine is metabolised partly via CYP1A2 but is not expected to interact with smoking to a clinically relevant extent.	Low	None