

**DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
(JAPC)**

Requesting prescriptions for and managing patients using Varenicline

Green Traffic Light status

Varenicline is available as a first line option for smoking cessation, with behavioural support, in discussion with client and clinician. Working in partnership with the GP, varenicline should only be prescribed on the direct advice of the Derby or Derbyshire Public Health Stop Smoking Services and trained smoking cessation advisors. The duration of treatment is for a **maximum of 12 weeks**. The following information will enable confident prescribing and provide the clinician with ongoing reassurance of the patient's concordance and progress.

Patients accessing support from the relevant Derby or Derbyshire Public Health Smoking Cessation Service in either a group session, a one-to-one or telephone support and requesting the use of varenicline will be supported by an assigned advisor following an assessment for suitability according to the following criteria and clinical judgement:

- Stop Smoking Advisors may recommend the prescribing of varenicline. **However the clinical responsibility will lie with the prescriber with access to complete medical notes.**
- Varenicline has been licensed for use with all smokers except those under 18 or pregnant. It is not advised for breast-feeding smokers and cautioned in severe renal impairment. To date there are no known drug interactions that need to be considered.
- Treatment with varenicline begins 1-2 weeks before the quit date. The dose is titrated until it reaches the treatment dose of 1mg twice daily for a total of 12 weeks treatment. Days 1 – 3: 0.5mg once a day, days 4 – 7: 0.5mg twice daily, and day 8 onwards: 1mg twice daily. There is a starter pack containing 11 x 0.5mg tablets and 14 x 1mg tablets.
- In the trials, at the end of the treatment period, discontinuation of varenicline was associated with irritability, an urge to smoke, depression and/or insomnia in up to 3% of patients. Because of this the SPC recommends that patients need to be informed and dose tapering considered.
- The SPC suggests that varenicline be taken with a glass of water to help reduce nausea and experience in the US has indicated that taking the second tablet at dinner or supper time rather than bedtime may help reduce insomnia and disturbed dreams.
- There has been no suggestion in the published studies or case reports that smokers with pre-existing mental health problems are more vulnerable to neuropsychiatric side effects than other patients. In a studyⁱ of over 5000 patients, followed up for 12 months, varenicline increased smoking cessation in smokers with stably treated current or past depression without exacerbating depression or anxiety. A reviewⁱⁱ of the use of varenicline in patients with mental health problems states:

“Although the risk of potential neuropsychiatric events is evident through voluntary reporting systems and reported cases in the literature, multiple studies and case reports support the use of Varenicline in the mental health population”
- When varenicline is prescribed to this patient group, it is recommended that the prescribing physician is cautious with treatment initiation and ensures close surveillance and follow-up including the monitoring of mood and behaviour changes during treatment. More recent studies have also looked at the use of varenicline in patients with stable schizophrenia or schizoaffective disorders

and found it not to be associated with changes in psychiatric symptoms^{iii iv v}. Varenicline has not been studied in people who have epilepsy, so safety data is still not available in this population.

- Clinical trials have demonstrated efficacy in those receiving weekly support, so as far as possible varenicline should be prescribed to those receiving such support, either through the Derbyshire smoking cessation service or from a health professional. This will also enable prescribing to be contingent on continuing effort to quit smoking and remaining completely smoke-free.
- Varenicline was first marketed in the UK in December 2006 and since then its safety has been monitored closely by the Medicines Healthcare products Regulatory Agency (MHRA) in conjunction with the European Medicines Agency (EMA).

Suicidal behaviour and varenicline

Concerns have arisen about reports of suicidal thoughts and behaviour reported in association with the use of varenicline. The SPC states:

‘Changes in behaviour or thinking, anxiety, psychosis, mood swings, aggressive behaviour, depression, suicidal ideation and behaviour and suicide attempts have been reported in patients attempting to quit smoking with varenicline in the post-marketing experience’.

Clinicians should be aware of the possible emergence of any of the above symptoms in patients undergoing a smoking cessation attempt using varenicline and should advise patients accordingly.

Depressed mood, rarely including suicidal ideation and suicide attempt, may be a symptom of nicotine withdrawal. In addition, smoking cessation, with or without pharmacotherapy, has been associated with exacerbation of underlying psychiatric illness (e.g. depression).

MHRA/ CHM advice – BNF online

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 while taking varenicline.

Cardiovascular symptoms

Given the enormous benefits of smoking cessation in smokers with CVD, varenicline has been trialled in this population and shown to be effective.^{vi} However, given that a number of studies have reported cardiovascular serious adverse events in participants using varenicline, there have been calls for systematic reviews to estimate the potential for Varenicline to increase cardiovascular risk.^{vii} The two published reviews reported contradictory findings.^{viii ix} Two more recent studies conclude that the risk of cardiovascular events with varenicline was small.^{x xi} Taking the findings of the reviews and the two most recent studies together, there is little reason to avoid this medication on the grounds that the use of varenicline increases the risk of cardiovascular events. This view is in line with the European Medicines Agency that confirmed a positive benefit-risk balance for varenicline and concluded that its benefits as a smoking cessation medicine outweigh any potential slight increase in cardiovascular events.^{xii} (See [here](#) for EMA press release) Patients taking Varenicline should be instructed to notify their doctor of new or worsening cardiovascular symptoms and seek immediate medical attention if they experience signs and symptoms of myocardial infarction or stroke.

Prescribing details:

Use of varenicline with patients as part of a smoking cessation intervention

FIRST REQUEST (week 1 of course) – 0.5mg and 1mg STARTER PACK (2 week supply)

- Comprehensive assessment undertaken and motivation is established.
- All issues around use of varenicline discussed including; slow titration dosing in week one, setting quit date for stopping smoking in week two, and full awareness of common unwanted effects including nausea (29% in clinical trials), headaches, sleep disturbance, abnormal dreams, dry mouth and changed taste. List not exhaustive.
- Patient provided with suitable patient information leaflet covering all issues discussed on use and management of varenicline. Aware to inform assigned advisor of any symptoms that may require further intervention (e.g. if reduced dose of 0.5mg twice daily does not help with intolerable nausea).
- Patient will be reviewed weekly for at least up to week 6 with appropriate subsequent request for continuing treatment.
- Request documentation completed and sent to GP. Where appropriate a request to measure serum drug levels may be made (physiological changes resulting from smoking cessation may alter the pharmacokinetics of certain drugs e.g. theophylline and clozapine).
- Patient aware to contact their assigned advisor or GP if symptomatic or other difficulties arise - contact numbers provided.

SECOND REQUEST (usually week 3 of course) – 1mg MAINTENANCE PACK (2 week supply - 28 tablets)

- Assessment of progress in first two weeks – review accordingly.
- Record date quit smoking and CO monitoring.
- Any symptoms discussed whether resolving, resolved or asymptomatic – discuss ongoing programme.
- Request documentation completed and sent to GP for second request, which includes a progress summary. Review patient in 2 weeks.

THIRD REQUEST (usually week 5 of course) – 1mg MAINTENANCE PACK (4 week supply - 56 tablets)

- Assessment of progress – discuss ongoing programme.
- Request documentation completed and sent to GP for third request, which includes a progress summary.

FOURTH REQUEST (week 7 of course, at the earliest but usually later than week 7. Client is asked to phone in to the relevant Derby or Derbyshire Public Health Smoking Cessation Service to request last prescription if no longer attending for weekly support) – 1mg MAINTENANCE PACK (4 week supply - 56 tablets)

- Assessment of progress – discuss ongoing programme.
- Preparation for completion – there is evidence in the clinical trials that abrupt completion of the treatment may result in withdrawal symptoms with a possible return to smoking – discuss the possibility of tapering the dose.

References

- ⁱ Anthenelli, RM, Morris, C, Ramey, T, Dubrava, S, Tsilkos, K, Russ, C, et al. Effects of Varenicline on Smoking Cessation in Adults with Stably Treated Current or Past Major Depression; *Annals of Internal Medicine*; (2013); 159:390-400
- ⁱⁱ Purvis TL, Nelson LA, Mambourg SE. Varenicline use in patients with mental illness: an update of the evidence. *Expert Opin Drug Saf* 2010;9(3):471-82.
- ⁱⁱⁱ Pachas GN, Cather C, Pratt SA, Hoepfner B, Nino J, Carlini SV, et al. Varenicline for Smoking Cessation in Schizophrenia: Safety and Effectiveness in a 12 week, Open- Label Trial. *J Dual Diagn* 2012;8(2):117-25
- ^{iv} Williams JM, Anthenelli, RM, Morris CD, Treradow J, Thompson JR, Yuris C, et al. A randomised, double-blind, placebo-controlled study evaluating the safety and efficacy of Varenicline for smoking cessation in patients with schizophrenia or schizoaffective disorder. *J Clin Psychiatry* 2012;73(5);654-60
- ^v Cerimele JM, Durango A. Does Varenicline worsen psychiatric symptoms in patients with schizophrenia or schizoaffective disorder? A review of published studies. *J Clin Psychiatry* 2012;73(8):e1039-47
- ^{vi} Rigotti NA, Pipe AL, Benowitz NL, Argenta C, Garza D, Tonstad S. Efficacy and safety of varenicline for smoking cessation in patients with cardiovascular disease: a randomised trial. *Circulation* 2010; 121(2):221-9
- ^{vii} Food and Drug Administration. FDA drug safety communication. Chantix (Varenicline) may increase the risk of certain cardiovascular adverse events in patients with cardiovascular disease. Silver Spring:FDA, 2001.
- ^{viii} Prochaska JJ, Hilton JF. Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis. *BMJ (clinical research ed)* 2012;344:e2856
- ^{ix} Singh S, Loke YK, Spangler JG, Furberg CD. Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis. *CMAJ* 2011.
- ^x Ware JH, Vetrovec GW, Miller AB, Van Tosh A, Gaffney M, Yunis C et al. Cardiovascular safety of varenicline: patient-level meta-analysis of randomised, blinded, placebo-controlled trials. *Am J Ther* 2013;20(3):235-46
- ^{xi} Svanstrom H, Pastenak B, Hviid A. Use of varenicline for smoking cessation and risk of serious cardiovascular events: nationwide cohort study. *BMJ Clinical Research ed* 2012;345:e7176
- ^{xii} European medicines Agency. Press Release: European Medicines Agency confirms positive benefit-risk for Champix. 21/07/2011