

32 - Varenicline

Varenicline

524 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 4 Clinical effectiveness A Cochrane review of NRT suggests combination NRT (i.e. two formulations such as a patch and an oral/nasal product) is associated with higher long-term abstinence rates than using a single NRT product (risk ratio [RR] 1.27).⁵ Higher dose nicotine patches (25mg patches worn for 16 hours, or 21mg patches worn for 24 hours) are more likely to help people stop smoking compared with using lower dose patches (15mg patches worn for 16 hours, or 14mg patches worn for 24 hours).⁵ Studies with smokers from the general population suggest that each cigarette provides a smoker with approximately 1–2.9mg of nicotine, depending on the frequency and intensity of smoking.⁶ Findings from studies in people with schizophrenia who smoke suggest they take more frequent puffs over a shorter period of time and, as a result, extract more nicotine from cigarettes compared with those without a mental health condition.⁷ It is therefore plausible that these smokers may require higher doses of nicotine replacement. However, in general population studies, there is no clear evidence of superiority for higher dose NRT patches (42/44mg) over 21/22mg (24-hour) patches.⁵ The nicotine from oral products has to be absorbed through the cheeks, gums and back of the lips. The correct technique is to chew the gum/suck the lozenge until the taste becomes strong and then rest it between the cheek and gum. When the taste starts to fade, it is advised to repeat this process for about 20–30 minutes. Many gum users press the gum down against the (buccal) gum to increase the surface area of contact and hence the rate of nicotine absorption. Lozenges also allow sublingual absorption of nicotine but their physical size usually precludes this method unless the lozenge is broken into smaller pieces. Sublingual tablets are much smaller in size. Drinking coffee and carbonated drinks may block the absorption of nicotine from oral nicotine products.⁸ Preparations and dose Table 4.20 details preparations and doses of different types of NRT. Adverse effects Adverse effects from using NRT are related to the type of product and include skin irritation from patches and irritation to the inside of the mouth and coughs from oral products. Nausea may occur if the patient is still smoking. Some sleep disturbance can be expected in the early days of treatment, though this is also a symptom of nicotine withdrawal. NRT has no known pharmacokinetic interactions with psychotropic medication. Overdosing on nicotine is very rare (and usually intentional). Initial signs include nausea, vomiting, headache and diarrhoea. It has been estimated that the lower limit for causing a fatal outcome is 0.5–1g of ingested nicotine.⁹ Varenicline Varenicline is a selective nicotinic acetylcholine receptor partial agonist. It mimics the action of nicotine and causes a sustained release of dopamine in the mesolimbic pathway. It also blocks dopamine release resulting from subsequent nicotine intake.

Addictions and substance misuse CHAPTER 4 This means if it is taken as prescribed, any attempt to smoke a cigarette will be less pharmacologically rewarding and feel less satisfying to a smoker.

Varenicline is indicated for smokers over the age of 18 who are motivated to stop smoking. It should be avoided in pregnancy and breastfeeding. In 2021, Pfizer recalled varenicline because it exceeded acceptable intake limits of a nitrosamine impurity (N-nitroso-varenicline). Generic versions of varenicline are available in some countries (e.g. USA). Clinical effectiveness A 2023 Cochrane review¹⁰ found high-certainty evidence that varenicline is more effective than placebo (RR 2.32), bupropion (RR 1.36) and single-product NRT (RR 1.25), and is similarly effective to combination NRT.^{11,12} Varenicline is more effective than placebo among patients with cardiovascular disease, COPD, severe mental illness, depression and HIV.¹⁰ In smokers with serious mental illness, varenicline improved the odds of stopping smoking by 4–5 times compared with placebo.^{13,14} There is inconclusive evidence for its effectiveness compared with placebo among people with asthma, substance use disorder and alcohol dependence.¹⁰

Table 4.20 Nicotine preparations and doses.

Smoking <20 cigarettes/day	Smoking >20 cigarettes/day or people who smoke within 30 minutes of waking up
Topical patch 24-hour formulation (21mg, 14mg, 7mg)	16-hour formulation (25mg, 15mg, 10mg)
If smoking >20 cigarettes/day use 21mg (24-hour) or 25mg (16-hour) patch. There is no difference in efficacy between 16-hour and 24-hour formulations. The 16-hour patch should be removed at bedtime.	
Nasal spray (0.5mg/spray)	One spray in each nostril when craving; no more than twice per hour; maximum 64 sprays/day
Oral spray (1mg/spray)	1–2 sprays when craving; no more than 2 sprays per episode; no more than 4 sprays/h; maximum 64 sprays/day
Lozenge (1mg, 2mg, 4mg)	One 1mg lozenge hourly to prevent craving One 2mg or 4mg lozenge hourly to prevent craving; usually no more than 15 lozenges/day
Gum (2mg, 4mg, 6mg)	One piece of 2mg hourly to prevent craving One piece of 4mg or 6mg hourly to prevent craving; no more than 15 pieces 4mg/day
Inhalator (15mg)	No more than 6 cartridges of 15mg/day
Sublingual tablet	1–2 tablets hourly to prevent craving 2 tablets hourly to prevent craving; no more than 40 tablets/day
Mouth strips (2.5mg)	One strip hourly to prevent craving One strip hourly to prevent craving; no more than 15 strips/day

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