

Pharmacotherapy



START

After completing the Course you will be familiar with:

01

Be familiar with first line quit smoking pharmacotherapies including their appropriate use to maximize cessation outcomes

- Nicotine replacement therapy, Bupropion, Varenicline

02

Be knowledgeable about other smoking cessation medications.



"Clinicians should encourage all patients attempting to quit to use effective medications for tobacco dependence treatment, except where contraindicated or for specific populations for which there is insufficient evidence of effectiveness."

**Can double or triple
the chance of long-
term cessation**



Individualizing therapy

Prolonging therapy

Adjusting Dosages

Combining Medications





How they work?

What forms are available?

How effective are they?

Who can use them?

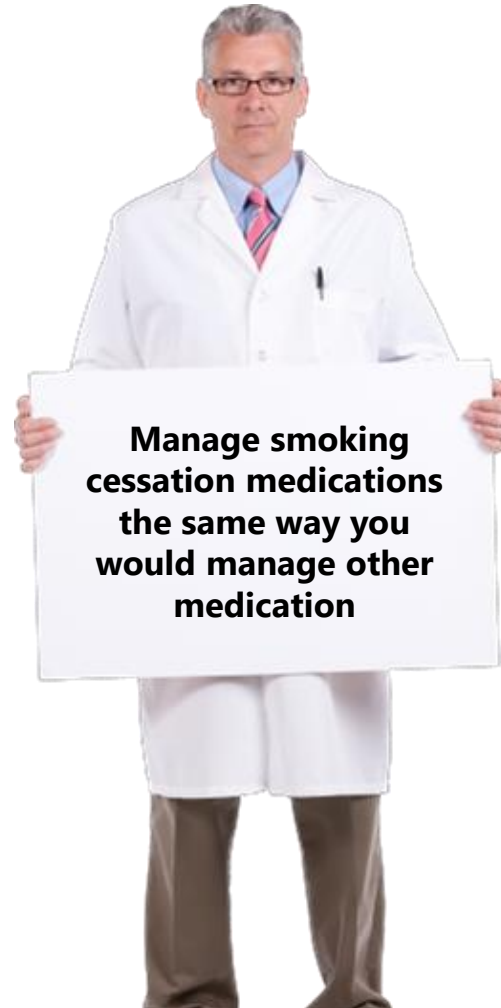
What are their side effects?

What instructions should be given to smokers?

**Nicotine
replacement
therapy
(NRT)**

Varenicline

Bupropion



**Manage smoking
cessation medications
the same way you
would manage other
medication**



**Nicotine
Replacement
Therapy (NRT)**

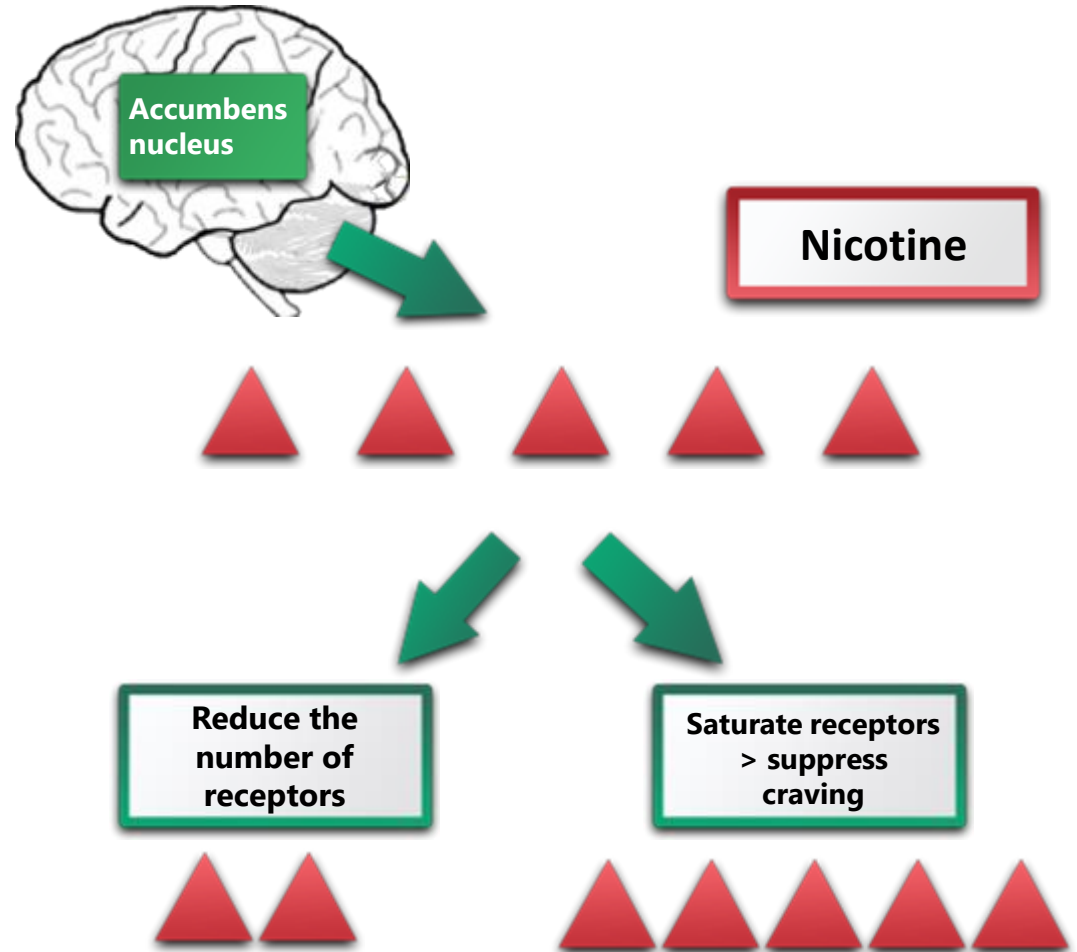
The ENSP European Tobacco Treatment Guideline Recommends:

Nicotine replacement therapy (NRT) is recommended as an effective pharmacotherapy for smoking cessation (level of evidence A).



Nicotine replacement therapies have been on the market for more than 40 years and there is very strong, Level A, evidence of their efficacy in supporting cessation. The goals of nicotine replacement therapy are:

- to stimulate the nicotine receptors and reduce cravings and withdrawal symptoms
- reduce the number of nicotinic receptors over the course of several weeks or months.






Patch

16h (25mg, 15mg, 10mg, 5mg)
24h (21mg, 14mg, 7mg)




Inhaler

10mg (per cartridge)
2mg (absorbed)



Mouth Spray

1mg per spray/dose



Gum

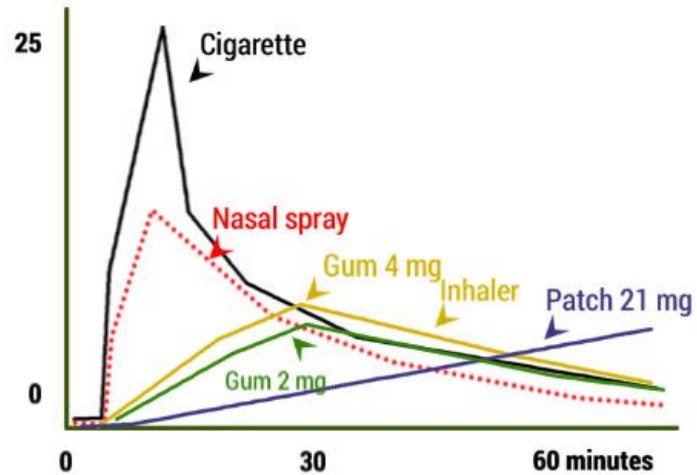
2mg, 4mg



**Lozenge &
Sublingual
tablets**

1 to 4 mg

Kinetics of nicotine arterial blood after smoking a cigarette or NRTs



- The **16 hour** formulation comes in 4 strengths (5mg, 10mg, 15mg, 25 mg)
- The **24 hour** patch comes in 3 strengths (7, 14, 21 mg)



	0.3 mg/h	0.6 mg/h	0.9 mg/h	1.6 mg/h
16 hours	5mg	10mg	15mg	25mg
24 hours	7mg	14mg	21mg	

Instructions

- Apply the patch to a clean, dry, non hairy area on the upper part of your body (arms, chest, back).
- Replace the patch with a new one every 24 hours.
- Remove the patch at bedtime, if you have difficulty sleeping





Gum

2mg, 4mg



Inhaler

10mg (per cartridge)
2mg (absorbed)



Mouth Spray

1mg per spray/dose



**Lozenge &
Sublingual tablets**

1 to 4 mg

- Use gum once or twice at approximately the same frequency you would take a drag on a cigarette.
- Chew slowly until you can taste the nicotine or feel a slight tingling in your mouth, then stop chewing.
- Place the gum between your cheek and gum.
- After one minute, repeat the process until cravings are resolved.
- Avoid eating or drinking 15 minutes before or during use.



- ❑ **Fast Acting to address urges or cravings**
- ❑ **Provides hand to mouth motion of smoking**
- ❑ **10 mg nicotine per cartridge**
 - 4 mg can be extracted per cartridge
 - Only 2mg systemically absorbed



- Upon first use, prime the spray pump
- Point spray nozzle as close to open mouth as possible and release
- Refrain from swallowing for a few seconds



- **Lozenges** (1 to 4 mg)
 - sucked slowly without chewing.
- **Sublingual tablets (2mg)**
 - placed under the tongue.
 - melt in the mouth in 15-30 minutes



Tailoring NRT dose

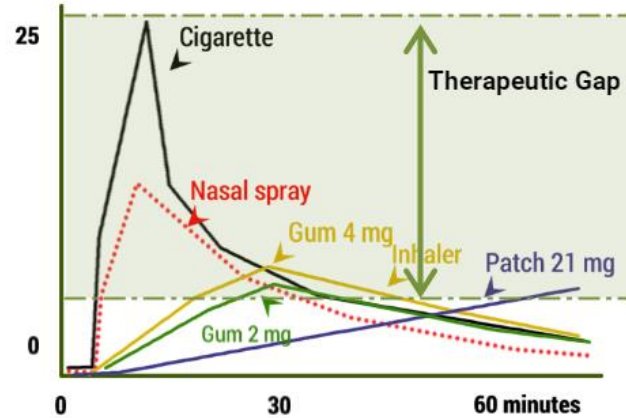


As with most medications, different doses work for different people.

50-65% of tobacco users will need increased dosing of NRT



Kinetics of nicotine arterial blood after smoking a cigarette or NRTs



The initial dose of nicotine replacement products can be easily determined by **three pieces** of information

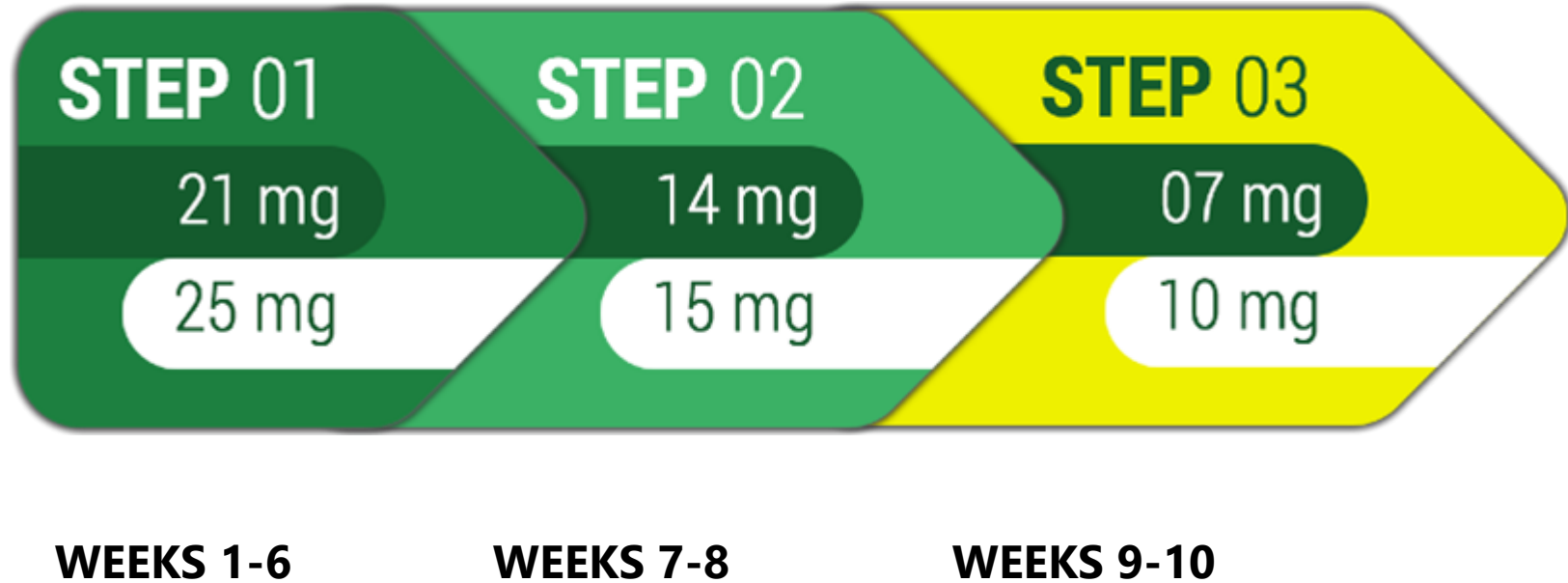
- ❑ the amount smoked per day
- ❑ time to first cigarette in the morning
- ❑ past experience with quitting





1-1.5 mg nicotine = 1 cigarette

Smokes \geq 30 minutes of waking	Smokes \leq 30 minutes of waking	16 hour patch	24 hour patch
<10		10mg daily fOR; Use short acting NRT	7mg daily fOR; Use short acting NRT
10 - 19	<10	15mg daily	14mg daily
20 - 29	10 – 19	25mg daily	21mg daily
30 - 39	20 – 29	25mg daily (25mg + 10mg) daily	28mg daily (21mg + 7mg) daily
	30 - 40	35mg daily (25mg + 15mg) daily	35mg daily (21mg + 14mg) daily
40+		40mg daily (25mg X 2) daily	40mg daily (21mg X 2) daily



NRT Patch



Flexible, short acting format:

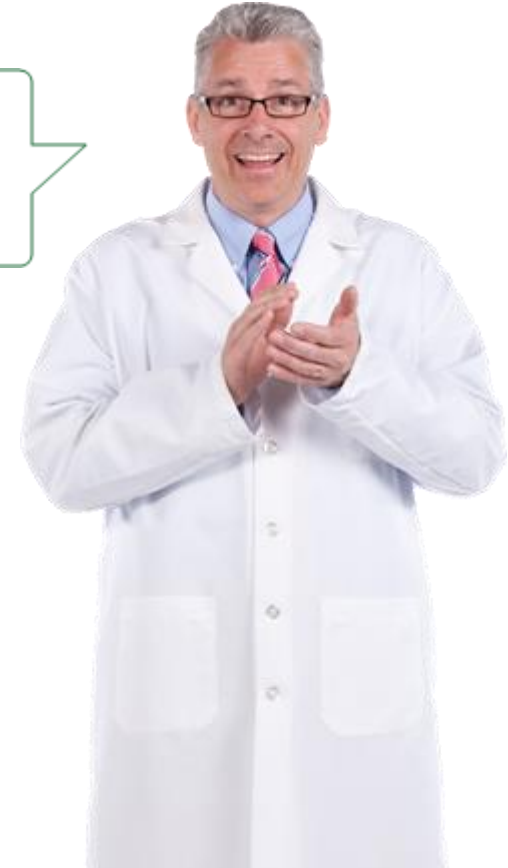


The ENSP European Tobacco Treatment Guideline Recommends:

A combination of oral NRT and the NRT patch, which is titrated to approximate the daily nicotine intake of the individual when smoking will increase the success with quitting (level of evidence A).

- Smokes 1.5 packs (35 cigs/day)
- Smokes within 30 mins of waking
- Experienced significant withdrawal on previous quit attempts
- Partial denture
- Commercial driver

-30 cigs/day = 30 – 37 mg of nicotine from NRTs
-25 mg patch + oral NRT





If after initial application of Nicotine patch, withdrawal or cravings persist, add other forms of Nicotine Replacement Therapy (gum or inhaler to address cravings as necessary).

If after 24 hours, cravings continue to persist, you may add 7mg Nicotine patch (increase by 7mg increments only)



***The ENSP European Tobacco Treatment
Guideline Recommends:***

Extended use of NRT beyond 14 weeks has been shown to increase success with quitting (level of evidence A).

- Good safety profile
- Skin irritation to patch adhesive
- No evidence that NRT is associated with worsening of CVD symptoms
- Very low risk of addiction to NRTs



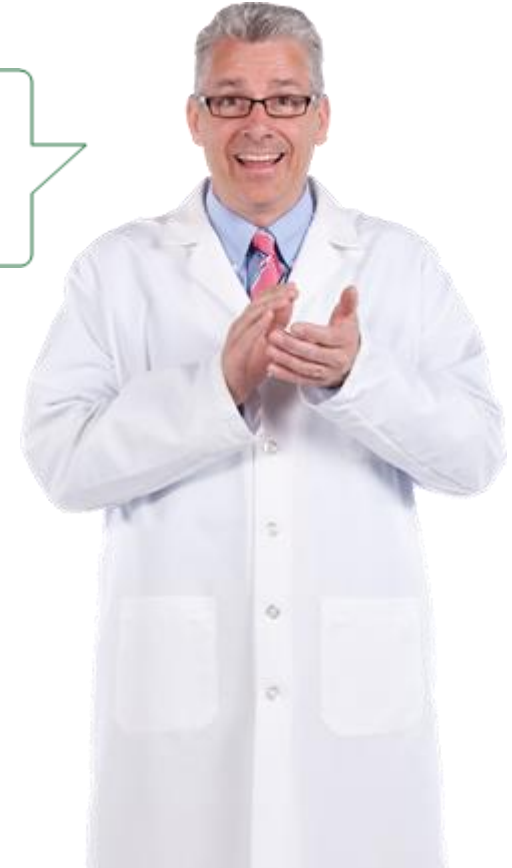


Is it safe to smoke when using the patch or another form of NRT ?

Patients are far safer receiving NRT than smoking cigarettes.



**Bupropion SR is the second
first line quit smoking
medication**



- An anti-depressant that reduces urges to smoke and rewarding effect of nicotine
- First line quit smoking pharmacotherapy
- Doubles rates of smoking abstinence
- Decreases cravings



**7 Days before
Quit Date**



**Begin taking
at least 7
days before
quit date**

Day 1 - 3



150 mg Daily

**Day 4 to
Week 12**

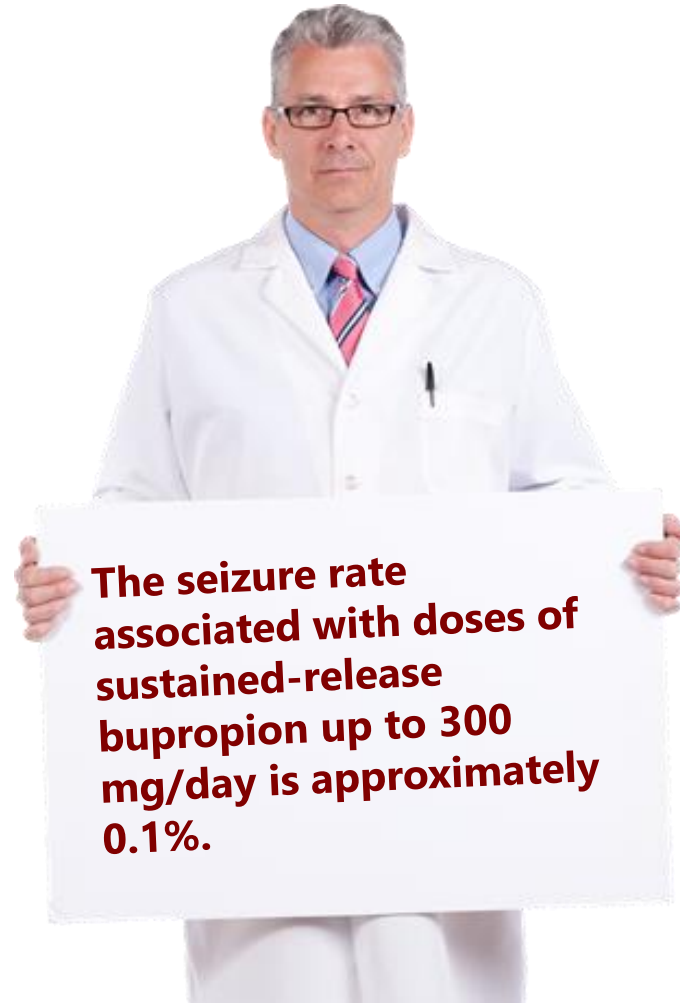


**150 mg at
breakfast and
dinner**

or at least 8 hours
between doses

- Dry mouth
- Insomnia
- Dizziness
- Difficulty concentrating
- Nausea
- Anxiety
- Constipation
- Shakiness
- Skin rash
- *"I don't feel right"*





Addressing Side Effects

- Ensure it is being taken properly with a full glass of water.
- May use OTC anti-nausea medication if symptoms persist.
- Consider reducing dose by half (going back to 150mg twice a day) if symptoms are severe or intolerable.



Side Effects and Contraindications

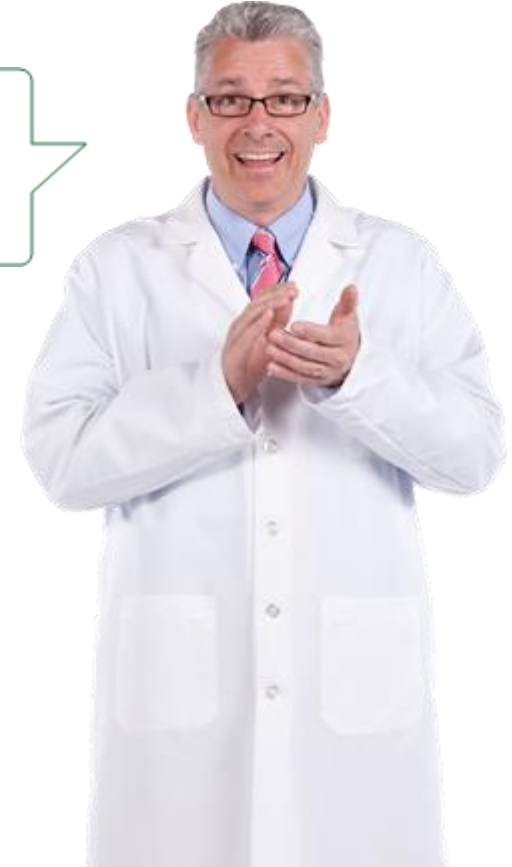
- 18 years of age or less
- Pregnant; breastfeeding; planning pregnancy
- History of seizure disorders or head trauma
- Use of oral hypoglycemics; insulin
- History of or existing eating disorder; alcohol or substance abuse
- CNS tumour; severe hepatic impairment
- Presently taking or previous reaction to bupropion or Wellbutrin
- Use of MAO inhibitors
- Concomitant medications that lower seizure threshold, including but not limited to
 - Antipsychotics, antidepressants, lithium
 - Amantadine, theophylline
 - Systemic steroids; quinolone antibiotics
 - Anti-malarials



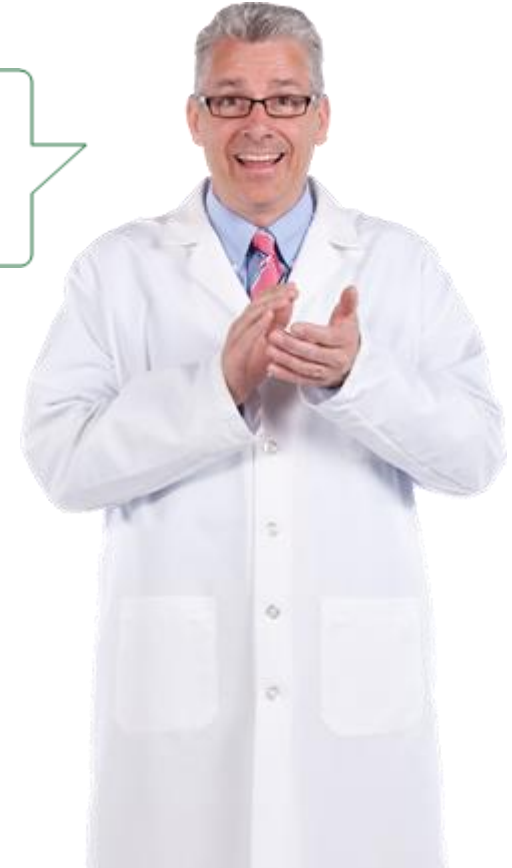
- Smokes 15 cig/day
- Slim build / low weight
- Used bupropion successfully on previous quit attempt
- Free of contraindications
- Reports nausea when dosed increased to 150 BID



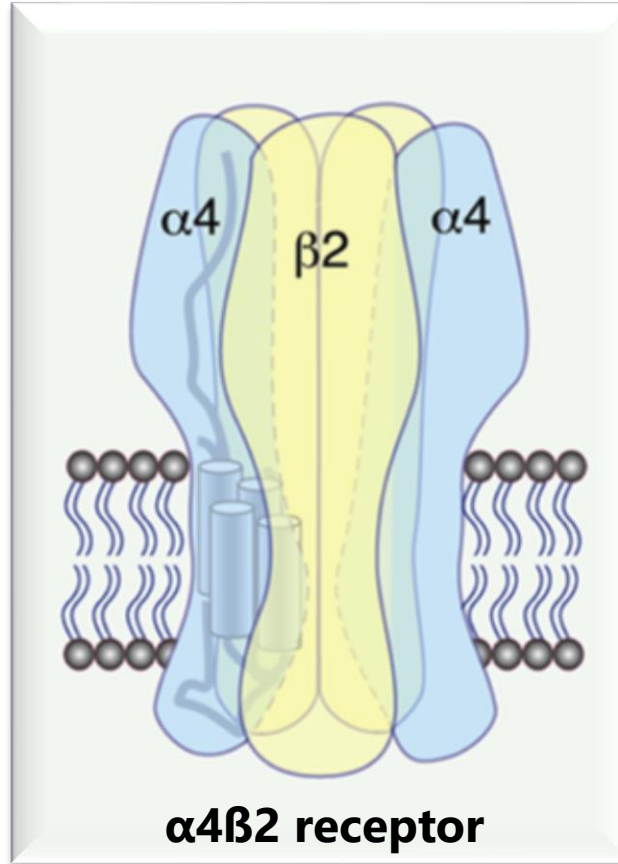
Reduce Dose to **150 mg**
once per day



**Varenicline is the third first
line quit smoking
medication**



Cell Membrane



Varenicline ...*a selective partial agonist of the $\alpha 4 \beta 2$ nicotinic ACh receptor*

Provides relief from craving and withdrawal – agonist effect

Blocks satisfaction and rewarding effects of nicotine – antagonist effect



Smoking No Partial Ag

No Smoking Partial Ag

Smoking + Partial Ag

$\alpha 4\beta 2$ nAChR

Nicotine

Partial Ag

Part Ag

Agonist

Partial Agonist

Antagonist

Response

100%

50%

50%

Dual action of a partial agonist

Potential to relieve craving and withdrawal when quitting

Potential to block reinforcing effects when smoking

Dosage and Duration

1-2 Weeks before
Quite Date



Begin taking 1-2
weeks before
quitting

Day 1 - 3



0.5 mg Daily

Day 4 - 7



**0.5 mg at
breakfast and
dinner**

Week 2 to
Week 12



**1 mg at
breakfast and
dinner**

OPTION TO

Remain at 0.5 mg at
breakfast and dinner



Common Side Effects

- Most common: nausea (30%)
 - Generally mild to moderate (only 3% severe); usually transient

To address Nausea/Headache

- Take with full Glass of Water and meal
- Dimenhydrinate
- If nausea persists, consider dose reduction



Patient Selection Considerations

Contraindications of varenicline are few, namely:

- Pregnant or breast feeding
- Under 18 years of age
- Presently taking bupropion
- Previous reaction to varenicline
- History of renal failure and taking climetidine

Special Considerations

- History of renal failure



Renal Impairment Category	Varenicline Dosing
<p>Mild (creatinine > 50 and < 80ml/min.)</p>	no dose adjustment is necessary
<p>Moderate (creatinine \geq 50 and \leq 80ml/min.)</p>	no dose adjustment is necessary
<p>Severe (creatinine clearance < 30 ml/min.)</p>	The recommended dose is 0.5 mg twice daily. Dosing should begin at 0.5 mg once daily for the first 3 days then increased to 0.5 mg twice daily
<p>End stage Renal Disease</p>	Based on insufficient, treatment with Varenicline is not recommended in patients with end stage renal disease

Varenicline 1 mg BID: Common Side Effects

- Other common side effects:
 - Insomnia (18%)
 - Headache (15%)
 - Abnormal dreams (13%)
- Side effects can be dose related; manage by titrating dose



Several recent well-designed trials have found no evidence to suggest an increase in neuropsychiatric events attributable to these medications.





- Smokes 30 cig/day
- Motivated to quit
- Prescribed Varenicline
- Smoke free at 2 weeks follow-up
- No desire to smoke
- Reports
 - Nausea
 - Vivid dreams
- Would like to discontinue medication due to side effects

So how would you address this patient?



- Smokes 40 cig/day (2 packs)
- Prescribed Varenicline
- Able to reduce to 5 cigs per day
- Unable to achieve full cessation after 3 weeks

So how would we address this particular patient?

The ENSP European Tobacco Treatment Guideline Recommends:

Varenicline is an evidenced-based first line therapy for smoking cessation which has been shown to increase abstinence from smoker to a greater degree than either NRT monotherapy or bupropion (level of evidence A)

Extending treatment for up to 6-months will reduce risk of relapse.

Side effects dissipate over time & can be managed





Cytisine is considered a **second** line smoking cessation medication.

Cytisine is a **natural** alkaloid extracted from the plant seeds.



- **Partial agonist of $\alpha 4\beta 2$ nicotinic ACh receptor**
- **Reducing:**
 - **withdrawal symptoms and cravings**
 - **Satisfaction related to tobacco use**



- Very cheap
- Safe
- Not licensed in many EU countries

Days 1 - 3



**1 Tablet every
2 Hours**

*Smoking must be
reduced

Days 4 - 12



**1 Tablet every
2 -5 Hours**

*Smoking must be
discontinued on the
5th day

Days 13 - 16



**1 Tablet every
3 Hours**

Days 17 - 21

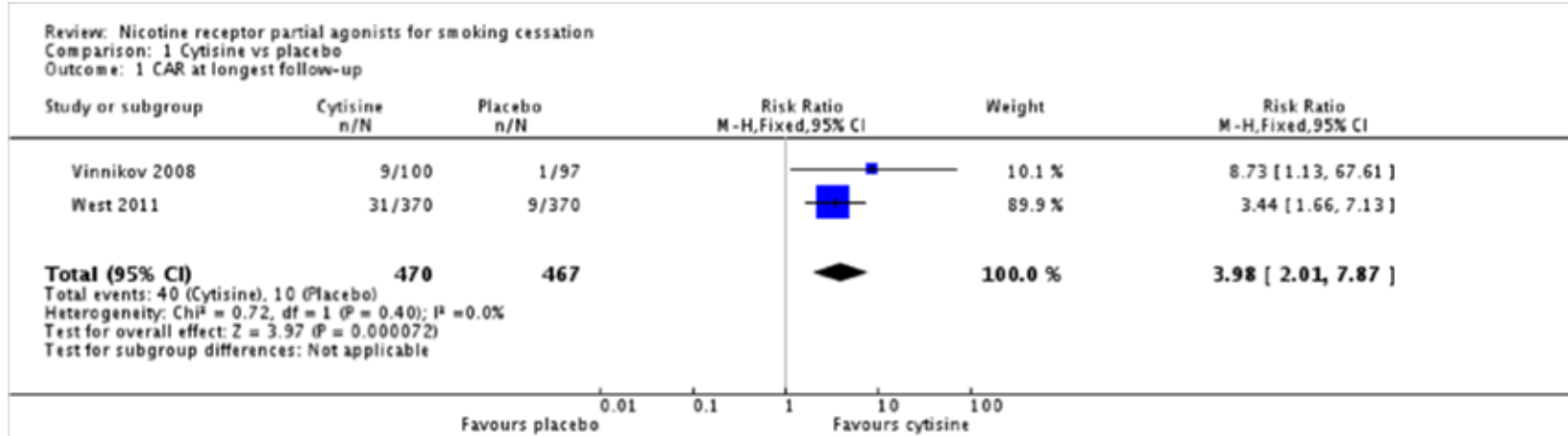


**1 Tablet every
5 Hours**

Days 22 - 25



**1 Tablet every
6 -8 Hours**



Cochrane Database of Systematic Reviews

9 MAY 2016 DOI: 10.1002/14651858.CD006103.pub7

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006103.pub7/full#CD006103-fig-00101>

The ENSP European Tobacco Treatment Guideline Recommends:

Cytisine appears to increase quit rates however evidence is limited to three trials.

(Level of evidence B).

There is a need for further research to examine the efficacy of this promising cessation intervention.



Monotherapy and Combination Therapies

Monotherapies	Est OR (95% CI)	Est Abstinent Rate (95% CI)
Placebo	1.0	13.8
Nicotine patch	1.9 (1.7-2.2)	23.4 (21.3-25.8)
High dose patch	2.3 (1.7-3.0)	26.5 (21.3-32.5)
Nicotine inhaler	2.1 (1.5-2.9)	24.8 (19.1-31.6)
Nicotine gum	1.5 (1.2-1.7)	19.0 (16.5-21.9)
Bupropion	2.0 (1.8-2.2)	24.2 (22.2-26.4)
Varenicline	3.1 (2.5-3.8)	33.2 (28.9-37.8)
Combination therapies	Est OR (95% CI)	Est Abstinent Rate (95% CI)
Patch + inhaler	2.2 (1.3-2.6)	25.8 (17.3-36.5)
Patch + gum	2.6 (2.5-5.2)	26.5 (28.6-45.3)
Patch (LT; > wks) + ad lib NRT (gum or spray)	3.6 (2.5-5.2)	36.5 (28.6-45.3)
Patch + bupropion	2.5 (1.9-3.4)	28.9 (23.5-25.1)

- Patients often express a reluctance to use quit smoking medications
- Encourage all patients to use medications
- Assist them with resolving any concerns



1

Compliance

2

Full course of therapy → Increased cessation



1

The best chance of success is Champix or a combination of nicotine patch plus a faster acting form

2

These drugs are not a magic cure and you will still need a lot of determination to succeed

3

They work by reducing the urge to smoke but they do not eliminate it

4

They work best if you use them as directed. That means taking the full dose and using it for the full length of the course, even if you think you do not need to

5

If you experience unwanted symptoms, let me know and we can discuss what to do about them



Congratulations! You have now completed the Course **Pharmacotherapy**. We hope this module has provided you with a comfort with the use of available quit smoking medications. All clinicians should be prepared to offer these evidence-based medications to their clients who smoke. As you gain experience and comfort in using these medications to help your patients quit, you will be able to see personally their value.

We encourage you to reference the 2017 European Tobacco Treatment Guidelines for any additional information you may need on quit smoking pharmacotherapies.

