

### Key Features:

- Tobalief contains **cytisine - a natural nicotine receptor partial agonist (NRPA)**
- Clinically shown to yield **higher success rate in smoking cessation** than other agents, such as **NRT**, **varenicline**, and **bupropion**
- **Higher Compliance** - short treatment course (25 days) & well-tolerated
- **Cost-Effective** compared to other smoking cessation medications

### Description:

Tobacco smoking is highly addictive, with more than 95% of unaided attempts at cessation failing to last 6 months.<sup>1</sup>

There are a number of pharmacological interventions to aid smoking cessation, including nicotine replacement therapy (NRT), antidepressant medications (eg. Bupropion), and **nicotinic receptor partial agonists** (eg. **Cytisine**, **Varenicline**, and **Danicline**). Nicotinic receptor partial agonists (NRPA) provide the best outcome with the mildest side effects due to its partial binding property. However, the success rates of most smoking cessation aids only range ~25% on average with counselling support.<sup>2</sup>

### Clinical Efficacy of Cytisine

Cytisine is the only naturally occurring NRPA, extracted from the seeds of the plant *Cytisus laborinum* L. (golden rain acacia). It has been widely used as a smoking cessation aid in Europe for more than 40 years. Cytisine has also demonstrated potential anti-depressant and anxiolytic effects via its actions on nicotinic receptors.<sup>3</sup>

**Cytisine acts by relieving craving and withdrawal symptoms, while blocking the reinforcing effects of nicotine from cigarettes.**<sup>4</sup>

In a double-blind RCT<sup>5</sup> involving 1310 smokers, the researchers compared the efficacy of cytisine against NRT head-to-head. Participants were randomized to go on either the **standard protocol\* of cytisine** (9 mg - 3 mg daily for 25 days) or the NRT (patch/gum/lozenges for 8 weeks).

Results showed 42% continuous abstinence from cytisine compared to 33% from NRT at 1 month. Cytisine continued to demonstrate its superior effect than NRT at 2 months (38% vs. 32%).

### Quantity: 101 Vegetarian Capsules

#### Ingredients (per capsule):

Cytisine (isolate from *Cytisus laborinum* L.).....1.5 mg

**Non-medicinal Ingredients:** Microcrystalline cellulose, silicon dioxide, L-Leucine, hypromellose (capsule)

#### \*Standard Protocol:

Day 1-3: 1 capsule every 2 hours; 6 capsules (9 mg) daily.

Day 4-12: 1 capsule every 2.5 hours; 5 capsules (7.5 mg) daily.

Day 13-16: 1 capsule every 3 hours; 4 capsules (6 mg) daily.

Day 17-20: 1 capsule every 4 hours; 3 capsules (4.5 mg) daily.

Day 21-25: 1 capsule every 6 hours; 2 capsules (3 mg) daily.

In other clinical studies involving smaller numbers of subjects, **the success rates of cytisine are even more promising, ranging from 37% to 74%.**<sup>8</sup>

In an RCT conducted in Germany, 1214 subjects were randomised to receive either the standard cytisine protocol or placebo. The result showed a **continuous abstinence rate of 66% after 2 years.**<sup>9</sup>

Another German RCT (n=520) demonstrated a **74% success rate** in cytisine group (n=250) at 3 months.<sup>10</sup>

According to a systematic review comparing cytisine with other smoking cessation aids<sup>6</sup>, **cytisine is able to yield 0.449 absolute probability (ie. 44.9% success rate) of 1-year continuous cessation.** In fact, cytisine is the best among the common agents in terms of continuous abstinence rate (Table 1).

Moreover, the update of Cochrane's 2012 review on smoking cessation aids concludes that cytisine yields **almost twice the success rate** [risk ratio (RR)] compared to low-dose varenicline. **(RR 3.98 vs. 2.09).**<sup>11</sup>



Intervention	HR*
NRT	1.89
<b>Cytisine 1.5 - 9 mg (*standard protocol)</b>	<b>4.27</b>
Varenicline 0.3 mg QD	1.58
Varenicline 1.0 mg QD	1.08
Varenicline 0.5 mg BID	2.16
Varenicline 1.0 mg BID	2.58
Bupropion 150 mg BID	1.59

Table 1. Efficacy of Cytisine Compared to Other Smoking Cessation Agents in Terms of Continuous Abstinence Rate.<sup>6</sup>

\*Hazard ratio (HR): the ratio of abstinence between intervention & placebo.

### Less Side Effects, High Compliance & Cost-Effective

Unlike its counterparts, **cytisine** is generally well-tolerated. In fact, according to the systemic review, it **did NOT significantly increase the incidence of side effects, such as headache, nausea, and other severe adverse effects, compared to placebo.**<sup>6</sup>

**Varenicline** on the other hand, though it yields the second best abstinence ratio, has been shown to cause more severe side effects, such as headache, nausea, and **increased risk of suicide** in patients with pre-existing neuropsychiatric conditions.<sup>6,7</sup>

Cytisine's short treatment course also makes it easier to comply for patients.

In addition, cytisine is the most cost-effective compared to other agents (Table 2).

Medication	Cost per treatment course	Average Duration of Treatment
Nicotine patch	\$180-270	8-12 weeks
Cytisine 1.5 mg (standard protocol)	\$40-50	25 days
Varenicline	\$325-700	12 weeks
Bupropion 150 mg BID	\$80-100	8-10 weeks

Table 2. Costs of smoking cessation aids & the average durations of treatment.

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### Caution:

Consult a health care practitioner prior to use if you have hyperthyroidism, active peptic ulcer, or diabetes mellitus. Do not use if you have arterial hypertension and advanced atherosclerosis; or if you are pregnant or breastfeeding. Simultaneous administration of cytisine and smoking may lead to nicotine intoxication. Some people may experience changes in both taste and appetite, dryness in the mouth, headache, irritability, nausea, constipation, tachycardia, light elevation of the arterial pressure. The majority of the adverse effects can abate during course of the treatment.

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