

Supplemental materials

Supplemental Figure 1: Syqe inhaler titration plans

Tailoring a Treatment Plan

Patient	Total dosage per day	Number of cartridges per month
Naive* Patient at the beginning of treatment without comorbidities	Up to 2,000mcg	1-2 cartridges
Naive* Patient at the beginning of treatment Having underlying comorbidities **** Under 80 years old	Up to 2,000mcg	1-2 cartridges
Naive* Patient at the beginning of treatment Having underlying comorbidities **** Over 80 years old	Up to 1,500mcg	1-2 cartridges
Experienced Patient** at the beginning of treatment With a previous license	Up to 2,000mcg Up to 3,000mcg Up to 4,000mcg Up to 6,000mcg	2 cartridges 3 cartridges 4 cartridges 6 cartridges

* Naive Patient - includes patients who used cannabis in any method other than inhalation (flower)

** Experienced Patient - a patient who has been using cannabis (flower) via inhalation under a license, before switching to the Syqe inhaler

**** Comorbidities - see the "Comorbidity" section on the back of this leaflet

Treatment Plan Instructions

- A patient that has reached a sufficient dose, should not exceed it without consulting the treating physician.
- Titration plans for a naive patient - on the first day of treatment up to 2 doses of 250mcg may be inhaled one during a training meeting (if held), and one before sleep. From the second day onwards, use should be according to Dosage A, and thereafter according to the Plan's instructions.
- Titration plan for an experienced patient - on the first day of treatment up to 3 doses of 500mcg each may be inhaled. From the second day onwards, use should be according to Dosage A, and thereafter according to the Plan's instructions. Patients with a licence preceeding 30 grams or more, may start with Dosage A on the first day.

Naive Patient at the Beginning of Treatment No underlying comorbidities

	Daily Dosage	Sufficient?	How to act?
A	250mcg X 2	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage B.
B	250mcg X 3	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage C.
C	250mcg X 3	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage D.
D	250mcg X 5 600mcg X 1 (before sleep)	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage E.
E	500mcg X 3 500 - 600mcg X 1 Or spreading inhalations and doses in any effective pattern, up to 2,000 mcg per 24 hour period.	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient, please consult your treating physician/nurse.

Naive Patient at the Beginning of Treatment, Having Underlying Comorbidities Under 80 Years Old

	Daily Dosage	Sufficient?	How to act?
A	250mcg X 2	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage B.
B	250mcg X 3	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage C.
C	250mcg X 3 500 - 550mcg X 1	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage D.
D	250mcg X 4 500 - 550mcg X 1	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage E.
E	250mcg X 5 500mcg X 1 (before sleep)	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage F.
F	Up to 2,000 mcg per 24 hours (spreading inhalations and doses in any effective pattern)	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage is insufficient, please consult your treating physician/nurse.

Naive Patient at the Beginning of Treatment, Having Underlying comorbidities Over 80 years old

	Daily Dosage	Sufficient?	How to act?
A	250mcg X 1	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage B.
B	250mcg X 2	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage C.
C	250mcg X 3 600mcg X 1 (before sleep)	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage D.
D	Up to 1,000 mcg per 24 hours (spreading inhalations and doses in any effective pattern)	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage E.
E	Up to 1,500 mcg per 24 hours (spreading inhalations and doses in any effective pattern)	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage is insufficient, please consult your treating physician/nurse.

Experienced Patient at the Beginning of treatment With a previous license

	Daily Dosage	Sufficient?	How to act?
A	500mcg X 4	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage B.
B	500mcg X 4 500 - 600mcg X 2	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage C.
C	500mcg X 3 1000mcg X 1 (before sleep) 500 - 550mcg X 3	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage D.
D	1000mcg X 4 500 - 600mcg X 2	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage was insufficient and there were no side effects, you may proceed to Dosage E.
E	Up to 5,000 mcg per 24 hours (spreading inhalations and doses in any effective pattern)	✓	You reached the right dosage.
		✗	If for at least 3 consecutive days this dosage is insufficient, please consult your treating physician/nurse.

Please note: 1,000 mcg = 2 consecutive inhalations of 500mcg; no need to wait between inhalations.

Supplemental Table 1: Specific sample etiologies

Pain diagnosis etiology	Study population N=143 n (%)
Neuropathic pain	103 (72)
Lumbar radicular pain	44 (27)
Complex regional pain syndrome	12 (8)
Painful diabetic peripheral pain	9 (6)
Phantom limb pain	8 (6)
Nerve injury	8 (6)
Cervical radicular pain	7 (5)
Post herpetic neuralgia	3 (2)
Berger's disease	2 (1)
Chemotherapy induced neuropathic pain	1 (<1)
Chronic inflammatory demyelinating polyradiculoneuropathy	1 (<1)
Facial nerve injury	1 (<1)
Idiopathic peripheral neuropathy	1 (<1)
Myasthenia Gravis related peripheral neuropathy	1 (<1)
Neurofibromatosis	1 (<1)
Post mastectomy pain	1 (<1)
Post thoracotomy pain	1 (<1)
Spinal cord injury	1 (<1)
Unknown	1 (<1)
Musculoskeletal pain	14 (10)
Rheumatic arthritis	4 (3)
Osteoarthritis	3 (2)
Arthropathy	1 (<1)
Gout, Palindromic rheumatism	1 (<1)
Post hip replacement pain	1 (<1)
Post knee replacement pain	1 (<1)
Widespread muscle pain	1 (<1)
Reiter's Syndrome	1 (<1)
Ischemic pain	1 (<1)
Nociplastic pain	4 (3)
Fibromyalgia	4 (3)
Visceral pain	2 (1)
Chronic post abdominal surgery pain	1 (<1)
Endometriosis	1 (<1)
Cancer pain etiologies	9 (6)
Prostate	2 (1)
Lungs	1 (<1)
Myelodysplastic syndrome	1 (<1)
Ovarian	1 (<1)
Colon	1 (<1)
Renal	1 (<1)
Thyroid	1 (<1)
Unknown origin- metastatic	1 (<1)
Conditions with co-existing chronic pain	6 (4)
Crohn's disease	2 (1)
Post-traumatic stress disorder	2 (1)
Amyotrophic lateral sclerosis	1 (<1)
None painful etiologies	5 (3)

Essential tremor	1 (<1)
Obsessive compulsive disorder	1 (<1)
Parkinson's disease	1 (<1)
Symptomatic cancer	1 (<1)
Multiple sclerosis	1 (<1)