

RESCUE THERAPIES for EPILEPSY

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Disclosures

Consulting/Ownership: Empatica &
Engage

RESCUE THERAPIES

- Rescue therapy is a treatment as needed to:
 - Abort a prolonged seizure or seizure cluster
 - Treat when the risk of a seizure is higher than usual
- Like an “epi-pen” for seizures
- Many people can benefit from rescue therapies
 - An insurance policy
 - Prevents need for ER/Hospital
 - Minimizes post-seizure consequences (eg, headache, confusion)

FDA- APPROVED RESCUE MEDS

- Rectal
 - Diazepam Gel (Diastat)
- Oral
 - Diazepam
 - Lorazepam
 - Clonazepam
- Nasal
 - Midazolam
 - Diazepam
- Sublingual/Buccal/Tongue
 - Lorazepam
 - Midazolam
 - Clobazam



NEW RESCUE THERAPIES

Approved

- Nasal midazolam (Nayzilam)
- Nasal diazepam (Valtoco)

Under development

- Inhaled (Staccato™) Alprazolam
(works < 2 minutes)



Nasal midazolam (Nayzilam)



Nasal diazepam (Valtoco)

Staccato™
Alprazolam



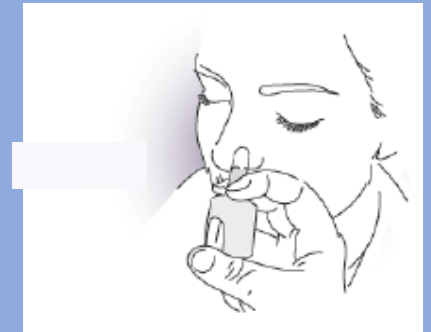
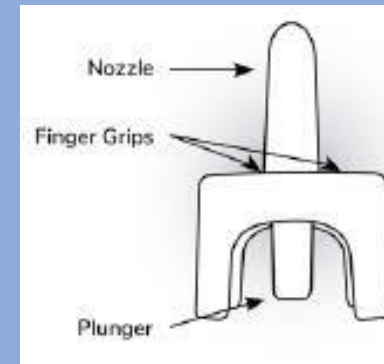
ADVANTAGES OF NASAL DELIVERY

- Easy access with/without patient cooperation
- Rapid & extensive absorption via nasal mucosa
- Convenient and easy administration
- Needle-less
- Rectal-less

NAYZILAM (MIDAZOLAM NASAL SPRAY 5 mg)

Indication: acute treatment seizure clusters & acute repetitive seizures distinct from a patient's usual seizure pattern

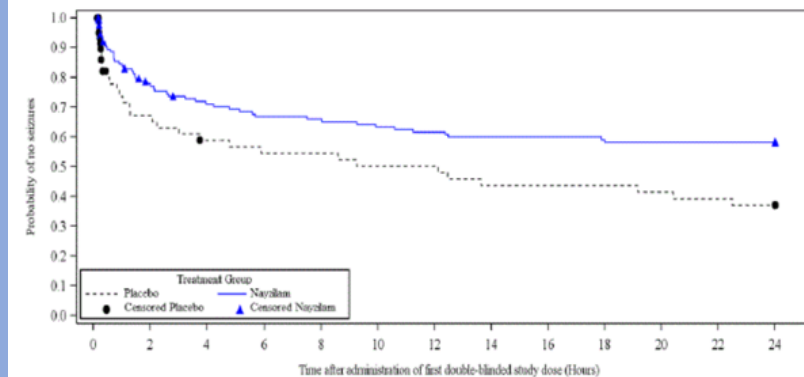
Patients: 12 years of age and older



Primary Endpoint Results: Treatment Success (cessation within 10 minutes)

	NAYZILAM (N=134)	Placebo (N=67)
Treatment success (%)	53.7	34.3
95% CI	(45.3, 62.2)	(23.0, 45.7)
p-value	0.011	

FIGURE 1: Kaplan-Meier Analysis of Time-to-Next-Seizure (Study 1)



Detyniecki K, Van Ess PJ, Sequeira DJ, Wheless JW, Meng TC, Pullman WE. Safety and efficacy of midazolam nasal spray in the outpatient treatment of patients with seizure clusters-a randomized, double-blind, placebo-controlled trial. *Epilepsia*. 2019 Sep;60(9):1797-1808.

VALTOCO (DIAZEPAM NASAL SPRAY 5, 10, 15 & 20 mg)

Indication: acute treatment seizure clusters & acute repetitive seizures distinct from a patient's usual seizure pattern

Patients ≥ 6 yo

Peak levels – 1.5 hrs

Mean $\frac{1}{2}$ life – 49 hrs

Main metabolism: CYP2C19 & CYP3A4



USING RESCUE MEDS

General principles

- Limit use (tolerance)

- Use when needed

- Consider higher doses if on clobazam/chronic benzos

Which one to use?

- Dissolvable clonazepam – C_{max} 1-4 hrs; $\frac{1}{2}$ life 35 hrs

 - Slow onset, long duration

- Rectal – great for babies...

- Intranasal – rapid onset, shorter duration