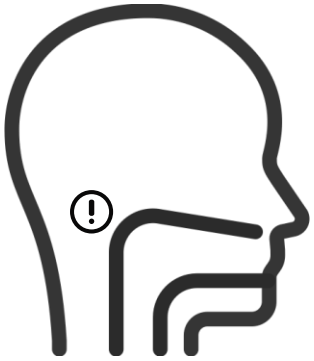


# Dysphagia



# What is Dysphagia?



Dysphagia is a swallowing impairment that may result in penetration or aspiration of food contents into the airways.<sup>1</sup> Patients with tardive dyskinesia and Huntington's Disease may experience dysphagia.<sup>2,3</sup>

Dysphagia is typically subclassified by location (**oropharyngeal** or **esophageal**), mechanism (**structural** or **propulsive**), and timing of symptoms (**intermittent** or **progressive**).<sup>1</sup>



Patients with dysphagia may have a **higher risk of medication errors** when they cannot easily swallow a prescribed dosage form.<sup>4</sup>

Additionally, patients with dysphagia may require alternative formulations of medications that may be unavailable, unacceptable to the patient, or cost prohibitive.<sup>4</sup>

Penetration = passage of material into the larynx, but not beyond true vocal cords; Aspiration = passage of material below the true vocal cords and into trachea

1. McCarty EB, et al. *Med Clin North Am.* 2021;105(5):939-954.
2. Aldridge KJ, et al. *Dysphagia.* 2012;27(1):124-137.
3. Schindler A, et al. *Sci Rep.* 2020;10(1):15242
4. Blaszczyk A, et al. *Drugs Aging.* 2023;40(10):895-907.

# Dysphagia Prevalence

9-  
42%

## Mental Illness

of patients with a mental illness (including schizophrenia) across six studies in a systematic review reported having dysphagia.<sup>1</sup>

7-  
40%

## LTC

Of individuals living in LTC were reported to have dysphagia in a literature review of 14 studies on malnutrition and dysphagia in LTC facilities.<sup>2</sup>

35-  
100%

## HD

Of 61 HD patients were found to have dysphagia, with prevalence correlating with disease progression in a FEES study.<sup>3</sup>  
- Early: 35%; Moderate: 94%; Advanced: 100%



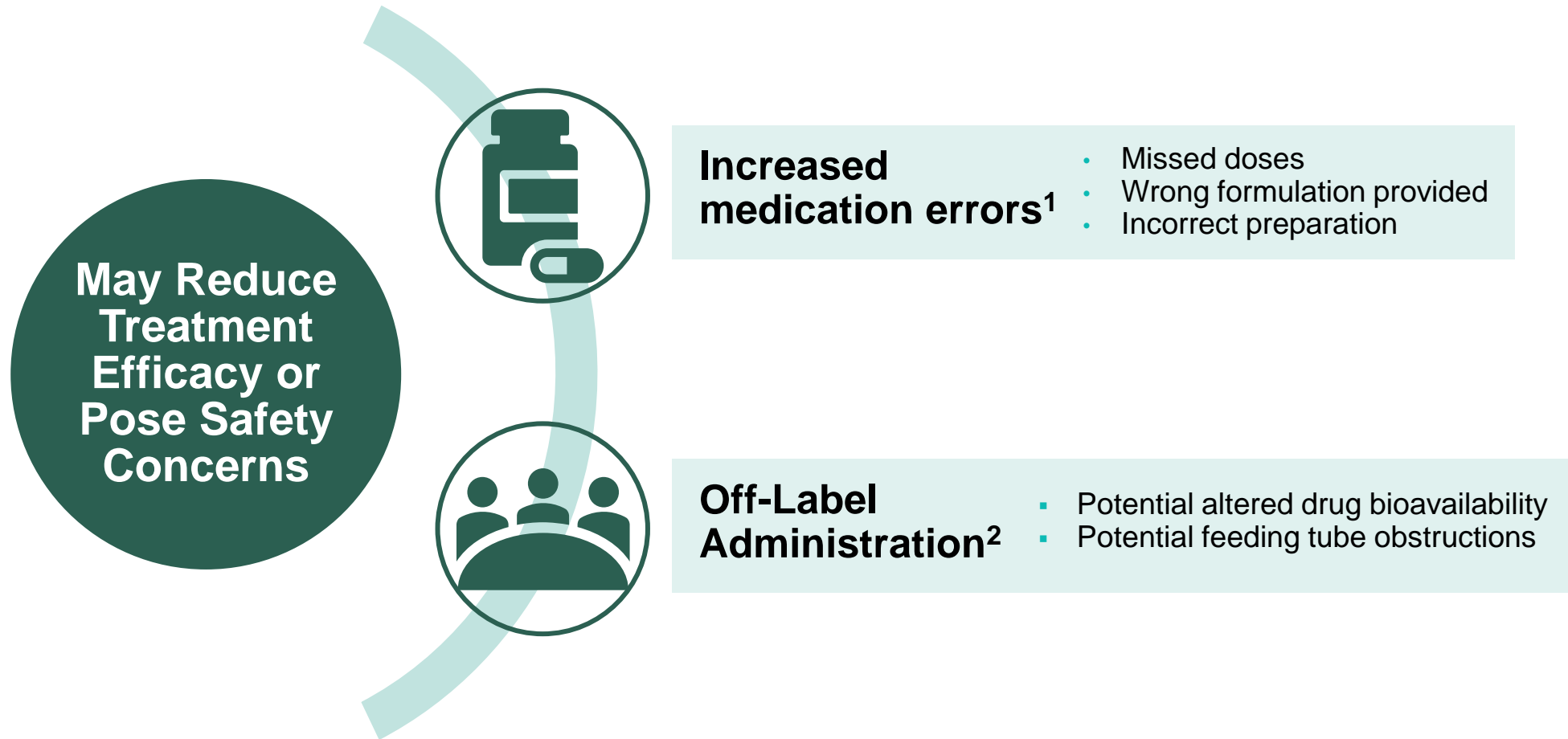
LTC, Long-Term Care; HD, Huntington's Disease; FEES, Fiberoptic Endoscopic Evaluation of Swallowing

1. Aldridge KJ, et al. *Dysphagia*. 2012;27(1):124-137.

2. Namasivayam AM, et al. *J Nutr Gerontol Geriatr*. 2015;34(1):1-21.

3. Schindler A, et al. *Sci Rep*. 2020;10(1):15242

# Dysphagia's Impact on Medication Administration



1. Wright DJ, et al. *Geriatrics (Basel)*. 2020;5(1):9.  
2. Blaszczyk A, et al. *Drugs Aging*. 2023;40(10):895-907

# INGREZZA<sup>®</sup> SPRINKLE (valbenazine) capsules



# INGREZZA SPRINKLE (valbenazine) Overview

- INGREZZA and INGREZZA SPRINKLE is FDA approved for the treatment of adults with **tardive dyskinesia** and **chorea associated with Huntington’s Disease**.
- INGREZZA SPRINKLE is a formulation that provides an alternative administration option for those who experience difficulty swallowing or prefer not to swallow whole capsules.



<b>Available Dose Strengths</b>	40, 60 and 80 mg
<b>Dosing</b>	1 capsule once daily, sprinkled on soft food
<b>Administration</b>	Administer INGREZZA SPRINKLE capsules orally with or without food. Do not sprinkle the contents of the capsule into milk or drinking water. INGREZZA SPRINKLE capsules may be swallowed whole with water. Do not crush or chew.
<b>G-tube Compatibility</b>	Do not administer INGREZZA SPRINKLE via nasogastric, gastrostomy, or other enteral tubes because it may cause obstruction of enteral tubes.



## Administration Information for INGREZZA SPRINKLE

- Administer INGREZZA SPRINKLE capsules orally with or without food.
- Open INGREZZA SPRINKLE and sprinkle the entire contents of the capsule over a bowl containing a small amount (1 tablespoonful) of soft food such as applesauce, yogurt, or pudding.
- Stir the contents of the capsule into the soft food with the tablespoon and swallow the drug/food mixture immediately. If necessary, the mixture can be stored for up to 2 hours at room temperature.
- Discard of any unused portion after 2 hours.
- Following administration of the drug/food mixture, drink a glass (e.g., 240 mL) of water.



Applesauce  
Yogurt  
Pudding



Discard after  
2 hours

# INGREZZA and INGREZZA SPRINKLE Important Safety Information

**Depression and Suicidality in Patients with Huntington's Disease:** VMAT2 inhibitors, including INGREZZA and INGREZZA SPRINKLE, can increase the risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease. Balance the risks of depression and suicidality with the clinical need for treatment of chorea. Closely monitor patients for the emergence or worsening of depression, suicidal ideation, or unusual changes in behavior. Inform patients, their caregivers, and families of the risk of depression and suicidal ideation and behavior and instruct them to report behaviors of concern promptly to the treating physician. Exercise caution when treating patients with a history of depression or prior suicide attempts or ideation, which are increased in frequency in patients with Huntington's disease.

## CONTRAINDICATIONS

INGREZZA and INGREZZA SPRINKLE are contraindicated in patients with a history of hypersensitivity to valbenazine or any components of INGREZZA or INGREZZA SPRINKLE.

## WARNINGS & PRECAUTIONS

### Hypersensitivity Reactions

Hypersensitivity reactions, including cases of angioedema involving the larynx, glottis, lips, and eyelids, have been reported in patients after taking the first or subsequent doses of INGREZZA. Angioedema associated with laryngeal edema can be fatal. If any of these reactions occur, discontinue INGREZZA or INGREZZA SPRINKLE.

**Somnolence and Sedation:** INGREZZA and INGREZZA SPRINKLE can cause somnolence and sedation. Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by INGREZZA or INGREZZA SPRINKLE.



# INGREZZA and INGREZZA SPRINKLE Important Safety Information

## QT Prolongation

INGREZZA and INGREZZA SPRINKLE may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. INGREZZA and INGREZZA SPRINKLE should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval. For patients at increased risk of a prolonged QT interval, assess the QT interval before increasing the dosage.

## Neuroleptic Malignant Syndrome

A potentially fatal symptom complex referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with drugs that reduce dopaminergic transmission, including INGREZZA. The management of NMS should include immediate discontinuation of INGREZZA or INGREZZA SPRINKLE, intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems. If treatment with INGREZZA or INGREZZA SPRINKLE is needed after recovery from NMS, patients should be monitored for signs of recurrence.

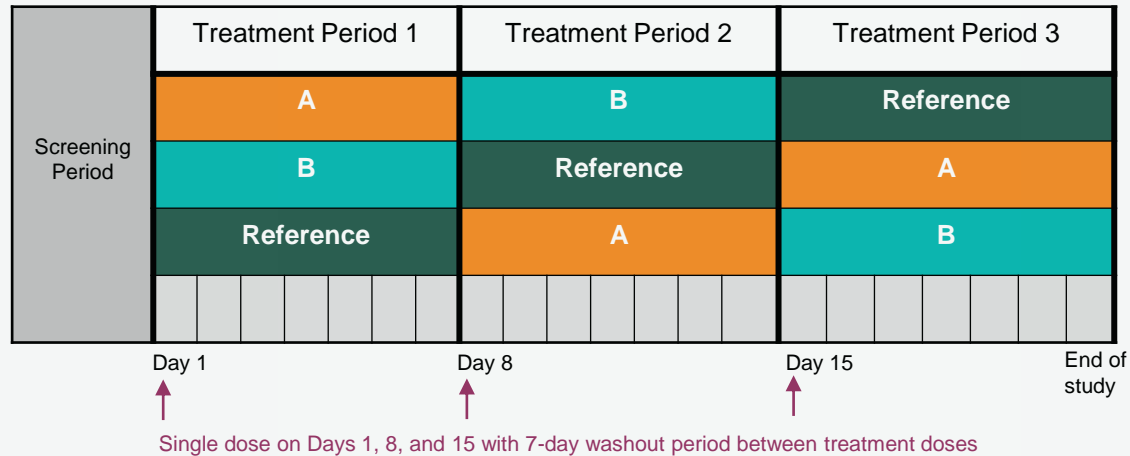
## Parkinsonism

INGREZZA and INGREZZA SPRINKLE may cause parkinsonism. Parkinsonism has also been observed with other VMAT2 inhibitors. Reduce the dose or discontinue INGREZZA or INGREZZA SPRINKLE treatment in patients who develop clinically significant parkinson-like signs or symptoms.

## ADVERSE REACTIONS

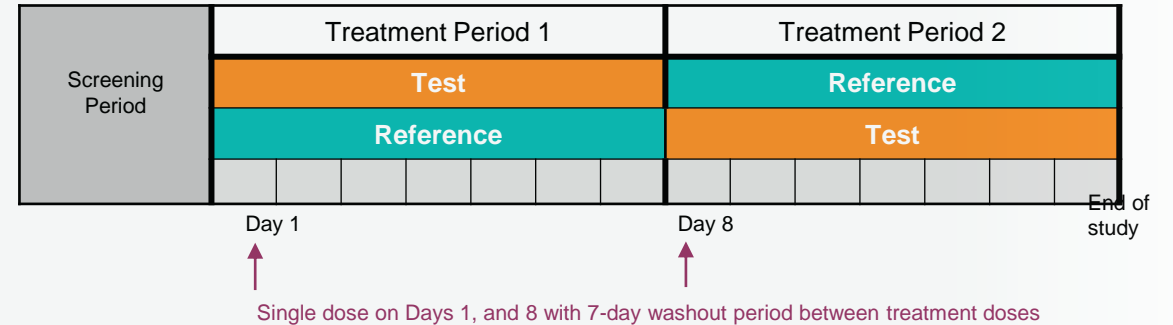
The most common adverse reaction in patients with tardive dyskinesia ( $\geq 5\%$  and twice the rate of placebo) is somnolence. The most common adverse reactions in patients with chorea associated with Huntington's disease ( $\geq 5\%$  and twice the rate of placebo) are somnolence/lethargy/sedation, urticaria, and insomnia.

# The Bioequivalence of INGREZZA SPRINKLE Was Studied in a Phase 1, Randomized, Open-Label, Crossover Design, Two-Cohort Study



**Treatment A** = VBZ oral granules 80 mg sprinkled on applesauce  
**Treatment B** = VBZ oral granules 80 mg swallowed whole  
**Reference** = VBZ commercial capsule 80mg

**Cohort 1**



**Test Meal** = VBZ oral granules 80 mg sprinkled on applesauce after a standard high fat meal  
**Reference Meal** = VBZ oral granules 80 mg sprinkled on applesauce after fasting

**Cohort 2**

# INGREZZA SPRINKLE Swallowed Whole or Sprinkled on Applesauce is Bioequivalent to the INGREZZA capsule

		$C_{max}$ (ng/mL)	$AUC_{inf}$ (ng*hr/mL)	$T_{max}$ (hour)
INGREZZA SPRINKLE as <u>sprinkled on applesauce</u>	VBZ	512	5600	1.5
	[+]- $\alpha$ -HTBZ	23	739	6
INGREZZA SPRINKLE capsule <u>swallowed whole</u>	VBZ	685	5981	1
	[+]- $\alpha$ -HTBZ	23	772	6
INGREZZA capsule	VBZ	744	6419	0.5
	[+]- $\alpha$ -HTBZ	26	859	6

The lower  $C_{max}$  of oral granules sprinkled on applesauce without impact on AUC indicates a slight reduction in the **rate** of absorption but similar **extent** of absorption relative to the capsule formulation

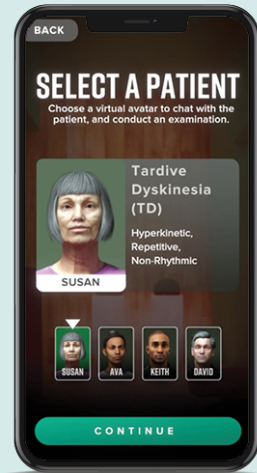


# FREE EDUCATIONAL RESOURCES on Tardive Dyskinesia and Other Drug-Induced Movement Disorders

These educational resources were sponsored and developed by Neurocrine Biosciences, Inc.

## Discover TD®

**Discover TD®** is an interactive experience designed to inform health care providers about tardive dyskinesia and other drug-induced movement disorders. By interacting with hypothetical virtual patients, you can diagnose and determine an appropriate management plan.<sup>a</sup>



<sup>a</sup>For educational purposes only. Should not be interpreted as medical advice for any particular patient. Individual results may vary.

Experience  
Discover TD®

[mind-td.com/discover-td](http://mind-td.com/discover-td)



## DIMD Course

The **DIMD Course** is a free, virtual learning resource for health care providers that delves into various clinical aspects of the most common DRBA-induced movement disorders.



Join the  
DIMD Course

[dimdcourse.getlearnworlds.com](http://dimdcourse.getlearnworlds.com)



## Neurocrine Medical Website

The **Neurocrine Medical Website** houses a variety of resources, such as educational podcasts and videos, to assist healthcare providers in the recognition and appropriate differentiation of DRBA-induced movement disorders.



Visit the  
Neurocrine Medical Website

[neurocrinemedical.com](http://neurocrinemedical.com)



DIMD, drug-induced movement disorder; DRBA, dopamine receptor-blocking agent; TD, tardive dyskinesia.

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# Appendix







# Oropharyngeal v. Esophageal Dysphagia

	Oropharyngeal Dysphagia	Esophageal Dysphagia
<b>TIMING</b>	Within 1 second of swallow initiation	After swallow passes through back of throat
<b>LOCATION</b>	High neck of throat	Retrosternal area or sternal notch
<b>ASSOCIATED SYMPTOMS</b>	Coughing, aspiration Nasal regurgitation Drooling Hoarseness Nasal tone of voice	Heartburn Chest Pain Bland regurgitation of food
<b>COMMON DISORDERS</b>	Stroke Parkinson's disease Muscular dystrophy Brain stem disorders	GERD Benign strictures Eosinophilic esophagitis
<b>DIFFERENTIAL DIAGNOSIS</b>	Xerostomia Globus Food aversion	Odynophagia Rumination Globus Food aversion
<b>TEST OF CHOICE</b>	Videofluoroscopy Modified barium swallow	Upper endoscopy

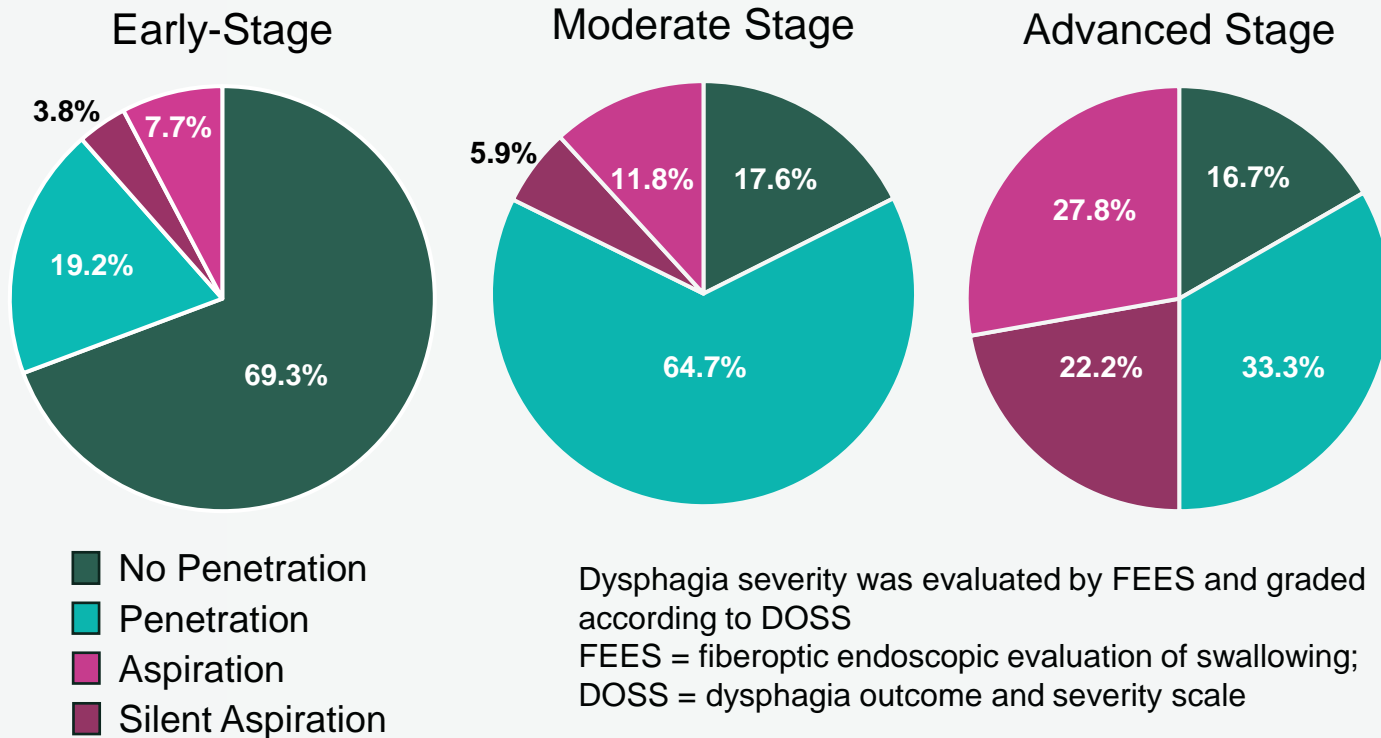
# Oropharyngeal Dysphagia Etiology

Progressive Chronic Disease	Neuromuscular Disease	Structural Causes	Oral Causes
<ul style="list-style-type: none"> <li>• Stroke</li> <li>• Parkinson Disease</li> <li>• Alzheimer and other dementias</li> <li>• Sarcopenia</li> </ul>	<ul style="list-style-type: none"> <li>• Amyotrophic Lateral Sclerosis</li> <li>• Myasthenia Gravis</li> <li>• Multiple Sclerosis</li> <li>• Dermatomyositis / polymyositis (myopathies)</li> <li>• <b>Antipsychotic medications</b></li> </ul>	<ul style="list-style-type: none"> <li>• Head and neck cancers</li> <li>• Recent surgery of radiation for head and neck cancers (altered anatomy)</li> <li>• Chemoradiation-induced mucositis and edema (short term)</li> <li>• Cervical osteophytes</li> <li>• Lymphadenopathy</li> <li>• Goiter</li> <li>• Cricopharyngeal bar</li> </ul>	<ul style="list-style-type: none"> <li>• Poor dentition or dentures</li> <li>• Dry mouth</li> <li>• Medications causing dry mouth               <ul style="list-style-type: none"> <li>- alpha and beta blockers</li> <li>- angiotensin-converting enzyme inhibitors</li> <li>- anticholinergics</li> <li>- antihistamines</li> <li>- anxiolytics</li> <li>- calcium channel blockers</li> <li>- diuretics</li> <li>- muscle relaxants</li> <li>- tricyclic antidepressants</li> </ul> </li> <li>• <b>Antipsychotic medications</b></li> </ul>

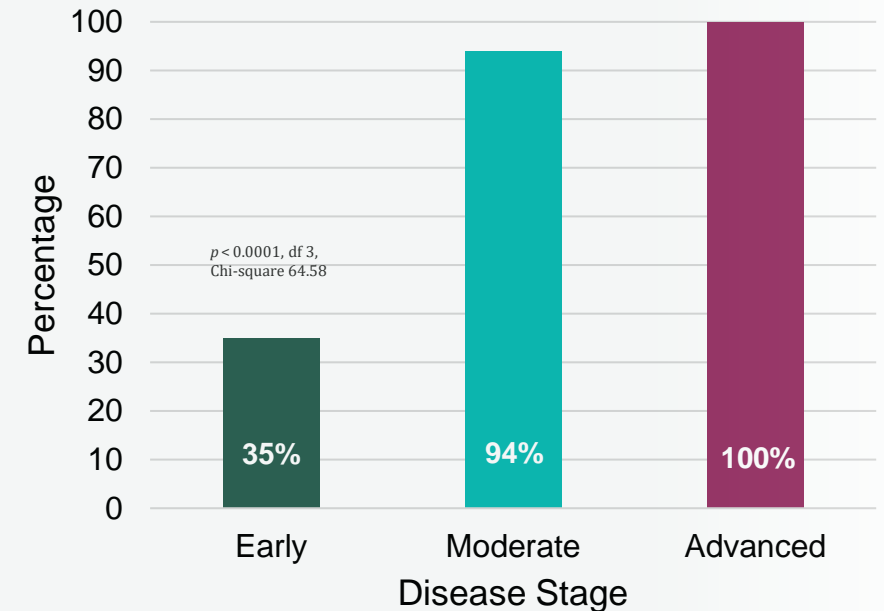


# Dysphagia Prevalence in Huntington's Disease Correlates with Disease Progression<sup>1,2</sup>

## Percentage of Silent Aspiration, Aspiration, and Penetration in HD Patients<sup>3</sup>



## Percentage of HD Patients with Dysphagia<sup>3</sup>



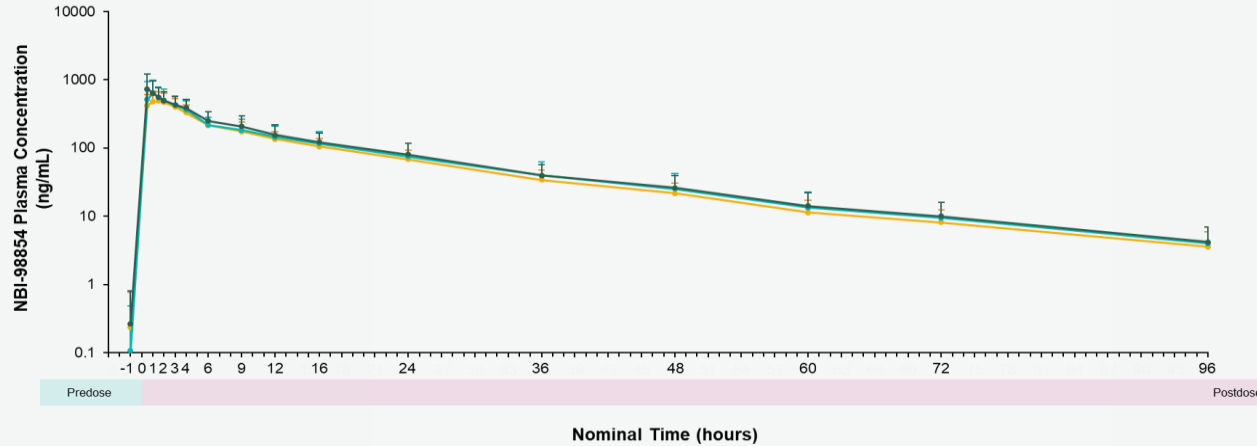
Silent Aspiration, Failure of subglottic penetration in eliciting the cough reflex; Penetration, Passage of material into the larynx but not beyond true vocal cords; Aspiration, Passage of material below the true vocal cords and into trachea; HD, Huntington's Disease

1. Aldaz T, et al. *J Neurol*. 2019;266(6):1340-1350.
2. Munhoz L, et al. *Oral Dis*. 2023;29(1):62-74.
3. Schindler A, et al. *Sci Rep*. 2020;10(1):15242.

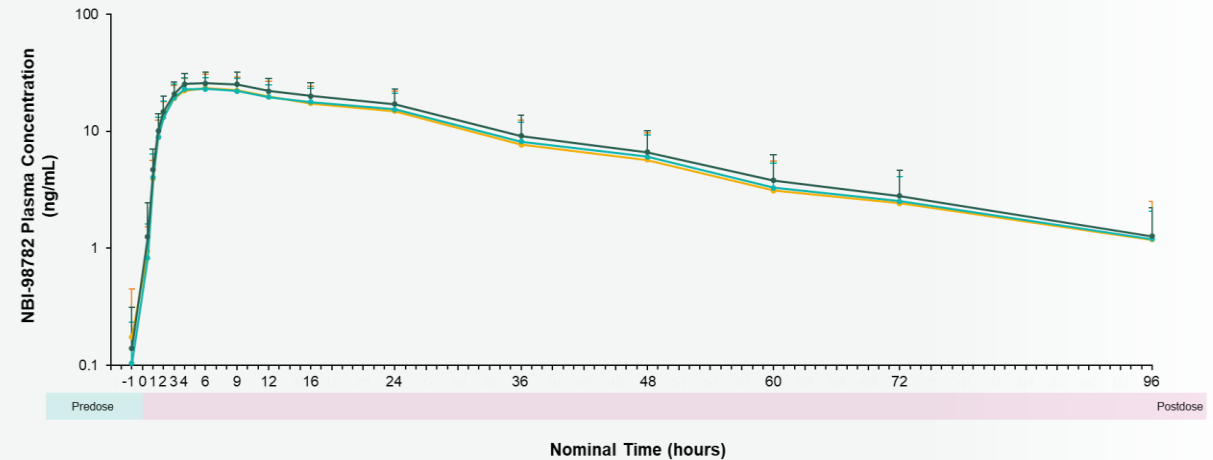


# Plasma Concentrations Over Time for Valbenazine and $[+]$ -alpha-HTBZ

Mean (+SD) Plasma Valbenazine Concentrations vs Time (Log Scale) (Bioequivalence Cohort: PK Analysis Set)



Mean (+SD) Plasma  $[+]$ -alpha-HTBZ Concentrations versus Time (Log Scale) (Bioequivalence Cohort: PK Analysis Set)



**Treatment A** = VBZ oral granules 80 mg sprinkled on applesauce  
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**Reference** = VBZ commercial capsule 80mg