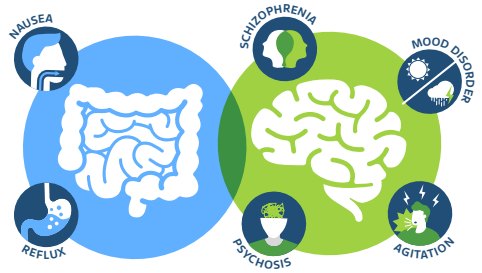
Tardive dyskinesia (TD):
a hyperkinetic movement disorder resulting from long-term use of dopamine receptor-blocking agents (DRAs)

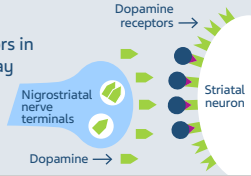
1 TD typically emerges after long-term exposure to DRAs[1–3]

Including:[1]
- Typical and atypical antipsychotics for psychiatric conditions
- Certain drugs used to treat gastrointestinal conditions

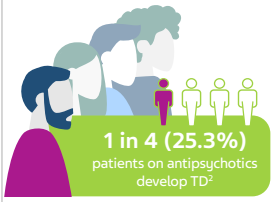


May emerge after **≥3 MONTHS** of continuous use[2,3]

Resulting from:[4]
- Long-term blockade of D2 receptors in the nigrostriatal dopamine pathway
  - D2 receptor upregulation
  - Net striatal output of "Go" in motor pathways



2 All patients receiving DRAs are at risk for TD[5,6]

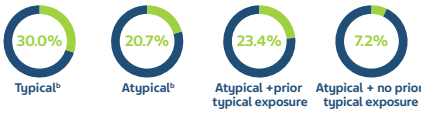


1 in 4 (25.3%) patients on antipsychotics develop TD[2]

In the United States, TD affects **>500,000** patients[a,5]

Risk factors include:[7]
- Older age
- Diagnosis of schizophrenia
- Higher antipsychotic dose
- History of extrapyramidal symptoms or other movement disorders

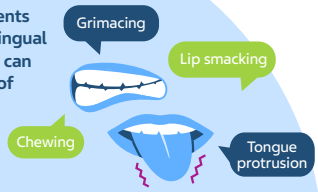
Prevalence is higher among:[5]
- Patients using typical vs atypical antipsychotics
- Typical-treated vs typical-naïve patients using atypical antipsychotics



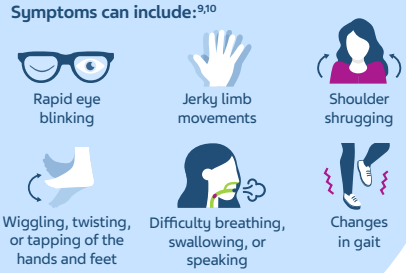
- Most patients with serious psychiatric conditions are exposed to a broad variety of antipsychotics during their lifetime[5]
- Rising antipsychotic drug use is exposing more patients to the risk of developing TD[6,8]

3 TD can affect the face, mouth, tongue, trunk and extremities[9,10]

Classically presents as oral-buccal-lingual movements but can affect any part of the body[9,10]



Symptoms can include:[9,10]



Movements can:
- Range from mild to severe[10,11]
- Worsen with stress, anxiety or different activities[10,11]
- Cause embarrassment and social withdrawal[12,13]
- Negatively impact daily functioning[12,13]
- Affect patient's quality of life regardless of severity[12]

4 Differential diagnosis of TD can be challenging[14,18]

Key Steps

1 Diagnosis according to DSM-5™,3
- DRA use for at least a few months
- Involuntary athetoid and choreiform movements lasting >4–8 weeks

2 Differential diagnosis
- Symptoms are easily mistaken for other movement disorders[14,15]
  - Rabbit syndrome
  - Drug-induced Parkinsonism
  - Lithium-induced tremor
  - Spontaneous dyskinesia
- Misdiagnosis may lead to improper treatment, e.g. anticholinergic treatments (benztropine) for drug-induced Parkinsonism can exacerbate TD

3 Screening of all patients using DRAs at every clinical encounter[16,17]
- Assessment with a structured instrument, such as AIMS[16–18]

5 Withdrawal of DRAs often does not resolve TD[19]

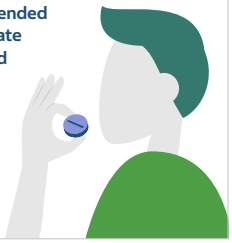
- Can lead to a relapse of the underlying condition[19]
- Can exacerbate or trigger onset of TD[19]
- Dose should be tapered slowly if withdrawal is necessary[19]

~2% spontaneous remission rate[20]

6 VMAT2 inhibitors can be administered without requirement for DRA withdrawal[21,22]

FDA-approved treatments recommended by the APA for patients with moderate to severe or disabling TD, associated with antipsychotic therapy:[c,d,17,21,22]

- **Deutetrabenazine**
- **Valbenazine**



AIMS, Abnormal Involuntary Movement Scale; APA, American Psychiatric Association; FDA, Food and Drug Administration; VMAT2, vesicular monoamine transporter 2

[a]In 2016 data. [b]Current treatment strategies; [c]Strength of guideline statement and supporting evidence = 1B; 1 indicates confidence that the benefits of the intervention clearly outweigh harms (recommendation); B indicates moderate confidence that the evidence reflects the true effect; [d]Deutetrabenazine is contraindicated in patients with hepatic impairment, and those taking reserpine, monoamine oxidase inhibitors, tetrabenazine or valbenazine. Use in pregnancy may cause fetal harm (based on animal data). Please consult full prescribing information before use.

References

1. Arya D, et al. Curr Neurol Neurosci Rep 2019;19:69. **2.** Savitt D, Jankovic J. J Neurol Sci 2018;389:35–42. **3.** American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th ed. Washington, DC: American Psychiatric Association; 2013. **4.** Stahl SM. CNS Spectr. 2017;22:427–34. **5.** Carbon M, et al. J Clin Psychiatry 2017;78:e264–e278. **6.** Dhir A, et al. Poster presented at the American Academy of Neurology 2017 Annual Meeting. April 22–28, Boston, Massachusetts, USA. **7.** Patterson-Lomba O, et al. BMC Neurol 2019;19:174. **8.** Stagnitti MD. Agency for Healthcare Research and Quality. Statistical Brief No. 275. 2010. **9.** Caroff SN, et al. Neurol Clin 2011;29:127–48. **10.** Waln O, Jankovic J Tremor Other Hyperkinet Mov (NY) 2013;3. **11.** Caroff SN. Neuropsychiat Dis Treat 2019;15:785–94. **12.** McEvoy J, el al. Qual Life Res 2019;28:3303–3312. **13.** Caroff SN, et al. J Clin Psychopharmacol 2020;40:259–68. **14.** Ward KM, Citrome L. Neurol Ther 2018;7:233–48. **15.** Citrome L. CNS Spectr 2014; Suppl 1:4–11. **16.** Caroff SN, et al. J Clin Psychiatry 2020;81:19cs12983. **17.** American Psychiatric Association. The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia. 3rd ed. https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841. Accessed February 2021. **18.** Guy W, ed. ECDEU Assessment Manual for Psychopharmacology, revised ed. DHEW Publ No ADM 76–338. Washington, DC: US Department of Health, Education, and Welfare, 1976. **19.** Bhidayasiri R, et al. J Neurol Sci 2018;389:67–75. **20.** Zutshi D, et al. Tremor Other Hyperkinet Mov (NY) 2014;4:266. **21.** Teva Pharmaceuticals. Austedo® (deutetrabenazine) tablets for oral use. Prescribing information, 2021. **22.** Neurocrine Biosciences. Ingrezza® (valbenazine) capsules for oral use. Prescribing information, 2017.

NPS-US-NP-00799. April 2021