Did You Know?

HEALTHDIRECT PHARMACY SERVICES

Recognizing and Managing Tardive Dyskinesia (TD)

May 2024

What is Tardive Dyskinesia (TD)?

Tardive Dyskinesia (TD) is a drug-induced involuntary movement disorder (DIMD) generally of the tongue, lower face, jaw, and extremities (but sometimes also pharyngeal, diaphragmatic, and trunk muscles) that can persist even after the discontinuation or alteration of neuroleptic medication regimens.

Movements may be stereotypic (repetitive, purposeless), choreoathetotic (irregular, dance-like), or athetotic (slow, writhing).

TD usually presents after at least 3 months of antipsychotic use and can lead to chronic dyskinesias if not detected early and managed appropriately.

Who is at Risk for Developing Tardive Dyskinesia (TD)?

Antipsychotic Use (and other dopamine receptor blocking agents - DRBAs) is the Primary Risk Factor for Developing Tardive Dyskinesia (TD)

- Overall antipsychotic medication use has increased across the general population, including children, adolescents, adults and geriatrics.
  - —Antipsychotic medications are FDA approved for bipolar disorder, schizophrenia, and adjunct therapy in major depressive disorder.
  - —Some antipsychotic medications and dosage forms are approved for acute management of mania and paranoia.
  - —They are often used off-label for mood disorders, agitation and behavioral symptoms of dementia, despite black box warnings in this population.
  - —Increased broader antipsychotic usage in the general population has increased the incidence rate of TD, although many patients have yet to be diagnosed and treated.
- Longer duration of therapy on an antipsychotic medication increases the risk of developing TD.
  - —45-60% of antipsychotic regimens are prescribed for long-term use.
- Other dopamine receptor blocking agents (DRBAs), such as metoclopramide, can also precipitate development of TD, especially when used for longer durations, and in older adults that may have altered or delayed metabolism of the medication(s).
- Higher incidence with first generation antipsychotics vs. second generation antipsychotics.

PATIENT RISK FACTORS	TREATMENT RISK FACTORS
Age ≥ 50 years	Cumulative exposure to antipsychotics
Diagnosis of mood disorder	Treatment with anticholinergics
Postmenopausal status	History of acute drug-induced movement disorders
Substance abuse	Antidopaminergic (D2) potency of antipsychotic

** adapted from American Diabetes Association 2024 Standards of Care in Diabetes*

CONTINUED

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HEALTHDIRECT PHARMACY SERVICES

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May 2024

MEDICATIONS THAT REQUIRE MONITORING FOR TD

FIRST-GENERATION ANTIPSYCHOTICS		
Chlorpromazine **(Thorazine)**	Loxapine **(Loxitane)**	Thioridazine **(Mellaril)**
Molindone **(Moban)**	Haloperidol **(Haldol)**	Thiothixene **(Navane)**
Fluphenazine **(Prolixin)**	Perphenazine **(Trilafon)**	Trifluoperazine **(Stelazine)**

SECOND-GENERATION ANTIPSYCHOTICS		
Aripiprazole **(Abilify)**	Loxapine **(Loxitane)**	Quetiapine **(Seroquel, Seroquel XR)**
Asenapine **(Saphris)**	Lumateperone **(Caplyta)**	Risperidone **(Risperdal)**
Brexpiprazole **(Rexulti)**	Lurasidone **(Latuda)**	Ziprasidone **(Geodon)**
Cariprazine **(Vraylar)**	Olanzapine **(Zyprexa)**	
Clozapine **(Clozaril)**	Paliperidone **(Invega)**	
Iloperidone **(Fanapt)**	Pimavanserin **(Nuplazid)**	

OTHER DRBA's		
Prochlorperazine **(Compazine, Compro)**	Trimethobenzamide **(Tebamide, Tigan)**	Metoclopramide **(Reglan)**
Promethazine **(Phenergan, Promethegan, Phenadoz)**	Thiethylperazine **(Torecan)**	

The American Psychiatric Association (APA) recommends:

1. Screen for TD before starting or changing DRBA treatment.
2. Monitor for signs of TD at every clinical encounter.
3. Conduct a structured TD assessment every 6 to 12 months, depending on patient's risk, and if new or worsening movements are detected at any clinical encounter.

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SELECT CMS REGULATIONS & GUIDANCE

CMS Regulations also state that adverse effects related to DRBA therapies (i.e. antipsychotics), such as movement disorders and tardive dyskinesia, must be screened for and monitored while residents receive these medications in the Skilled Nursing Facility (SNF).

Recognize and Report Symptoms of TD

From CMS - Each resident's medication regimen must be managed and monitored to promote or maintain the resident's highest practicable mental, physical, and psychosocial well-being.

Select CMS Regulations & Guidance	
F757 – §483.45(D) UNNECESSARY DRUGS AND F758 – §483.45(C)(3) AND (E) PSYCHOTROPIC DRUGS	The use of a medication without adequate monitoring may increase the risk of adverse consequences
MEDICATION MANAGEMENT MONITORING FOR EFFICACY AND ADVERSE CONSEQUENCES	Monitoring and accurate documentation of the resident's response to any medication(s) is essential to evaluate the ongoing benefits as well as risks of various medications
PSYCHOTROPIC MEDICATIONS AND ANTIPSYCHOTIC MEDICATIONS (F758 ONLY GUIDANCE)	Residents who take these medications must be monitored for any adverse consequences. TD is considered a potential adverse consequence
MONITORING OF PSYCHOTROPIC MEDICATIONS	If psychotropic medication is identified as possibly causing or contributing to an adverse consequence, the facility and prescriber must document it in the medical record. TD is considered a potential adverse consequence.

* Select guidance is provided for education and information purposes. See full CMS State Operations Manual for long-term facilities for complete information.

** adapted from Centers for Medicare & Medicaid Services - State Operations Manual Pub. 100-07. Appendix PP – Guidance to Surveyors for Long Term Care Facilities. Baltimore, MD: US Dept of Health and Human Services; 2017.

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HEALTHDIRECT PHARMACY SERVICES

Recognizing and Managing Tardive Dyskinesia (TD)

May 2024

The AIMS Assessment:

The **Abnormal Involuntary Movement Scale (AIMS)** is the standard structured assessment for the **initial screening and the routine monitoring of TD symptoms**.

This 10-minute subjective patient assessment uses a 5 point (0-4) rating scale for recording movement scores for 7 body areas: face, lips, jaw, tongue, upper extremities, lower extremities, and trunk.

Items 1 to 7 rate the severity of movements in different body areas

0 - No dyskinesia

1 - Minimal or slight dyskinesia
(Low amplitude, present during some but not most of the exam)

2 - Mild dyskinesia
(Low amplitude and present during most of the exam, or moderate amplitude and present during some of the exam)

3 - Moderate dyskinesia
(Moderate amplitude and present during most of the exam)

4 - Severe dyskinesia
(Maximal amplitude and present during most of the exam)

Item **8** rates the global severity of abnormal movements

Item **9** measures incapacitation and item **10** measures awareness

Items **11** and **12** rate dental status

Download: Abnormal Involuntary Movement Scale (AIMS) Worksheet

Tips for performing an AIMS Assessment:

BEFORE THE EXAM

- Always observe the patient. The exam starts from the moment the examiner lays eyes on the patient and must start observing their movements immediately.
- Abnormal movements can fluctuate and can change in amplitude when stressors are introduced. It is important to observe the patient at all times during the exam in order to get a wholistic picture of their symptoms.
- Ask the patient to remove their shoes and socks and anything in their mouth. This will be able to help clearly identify movements.
- Seat the patient in a firm chair with no arms. Have them rest their arms in front of their body.

CONTINUED

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May 2024

DURING THE EXAM

Mouth observation: Observe the tongue at rest and identify any changes in tongue movement

- — Have the patient open their mouth for 15 seconds, close, and then repeat for a total of 2 times.
- — Have the patient protrude their tongue for 15 seconds, stop, and repeat for a total of 2 times.

Finger tapping: Observe the face and legs

- — Have patient tap each finger rapidly to their thumb for 15 seconds per hand.
- — While looking at finger movements, it is also important to observe facial, leg, and other body movements.

Nonphysical activation maneuver

- — Have patient do a mental task (recite the names of months backwards, count backward from 100, etc.) and observe any movements.

Arm elevation: Observe the trunk, legs, and mouth

- — Have patient hold arms out flat, palms down for multiple seconds and observe any movements.

FOLLOW-UP EXAMS

- Even those with already diagnosed tardive dyskinesia should receive AIMS exams at a minimum of every 6 months for high-risk patients and 12 months for stable patients. This is necessary to measure the progression of TD over time.

SELF-REPORTING

- Most patients are aware of their abnormal movements and can communicate onset, characterization and severity to their healthcare provider.
- Patients may not recognize some involuntary movements they are experiencing to self report, physical examination should be achieved on all patients suspected of developing tardive dyskinesia or other DIMDs (i.e. AIMS)

To watch the AIMS in practice, scan the QR code to view expert-led videos demonstrating the use of the AIMS with real patients.

Differentiating Drug-Induced Movement Disorders

	When did onset of movements occur?	What does it look like	How might it change?
Acute Movement Disorders	Acute: hours to months	Akathisia (ex. restlessness), dystonia (ex. muscle contractions), parkinsonism (ex. tremors)	May resolve after discontinuation of antipsychotics
Tardive Dyskinesia	Delayed: months to years	Stereotypic (ex. repetitive, purposeless), athetoid (ex. slow, writhing), choreiform (repetitive, jerky) movements	Symptoms may be masked or revealed by changes in antipsychotic medication regimen

MIND-TD®

Scan the QR code or visit MIND-TD.com for more information on recognizing and screening for tardive dyskinesia in clinical practice.

CONTINUED

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HEALTHDIRECT PHARMACY SERVICES

Recognizing and Managing Tardive Dyskinesia (TD)

May 2024

Impacts of TD on Patients' Wellness and Self-Esteem

Tardive dyskinesia often causes people to become embarrassed about their abnormal movements. Among a sample of 204 patients with tardive dyskinesia, 76% of them were noted to be embarrassed by or self-conscious about their involuntary movements.

Abnormal movements associated with TD can also decrease physical functioning of a patient. These can present as respiratory, orofacial, and truncal dystonia which can interfere with activities of daily life and add unneeded stress to the patient's life.

These movements have had reported moderately to extremely negative effects on confidence, self-esteem, self-worth, and overall quality of life.

Pharmacological Management of Tardive Dyskinesia:

In previous years, there was no evidence-based treatment for tardive dyskinesia and patients who developed it had no answer for their symptoms. They could be taken off their antipsychotic medications but since TD symptoms are commonly non-reversible, often symptoms persisted despite removal of the DRBA. Recent studies have found strong evidence for the efficacy and tolerability of VMAT2 inhibitors in the treatment of tardive dyskinesia and the use of them as part of a patient and symptom management plan.

American Psychiatric Association (APA) recommends that patients who have moderate to severe antipsychotic-induced TD be treated with a VMAT2 inhibitor:

- Treatment with a VMAT2 inhibitor can also be considered in mild TD based on factors like patient preference, other impairments, and psychosocial functioning.
- New generation VMAT2 inhibitors are preferred because there is greater evidence supporting their use and tolerability profile.
- **Anticholinergic medications should not be used in TD**
  —They do not alleviate symptoms and can even aggravate them in some instances

Options for treatment based on the Modified Delphi Panel Consensus Recommendations:
(Can be any combination of these)

- Consider treatment with a VMAT2 inhibitor
- Review and consider modifying anticholinergic TD regimen
- Review and consider modifying antipsychotic regimen
- Discuss treatment options with the patients or appropriate caregivers

Comparison of VMAT-2 Inhibitors for Tardive Dyskinesia

	Valbenazine[6,7]	Deutetrabenazine [6,8]
Brand name	**Ingrezza**	**Austedo**
Available dose formulation	Ingrezza: 40, 60, 80 mg capsules Ingrezza Sprinkle: 40, 60, 80 mg capsules	Tablets: 6, 9, and 12 mg XR (extended-release) 6, 9 and 24 mg
Other indications	Chorea associated with Huntington's disease	Chorea associated with Huntington's disease

CONTINUED
Page 6 of 8

Comparison of VMAT-2 Inhibitors for Tardive Dyskinesia continued

	Valbenazine[6,7]	Deutetrabenazine [6,8]
Brand name	**Ingrezza**	**Austedo**
Contraindications relevant to TD	None	Hepatic impairment, use of reserpine, MAOIs, tetrabenazine or valbenazine
Warnings and precaution contained in Highlights of Prescribing Information	Somnolence; QT interval prolongation	QT interval prolongation; neuroleptic malignant syndrome; akathisia, agitation, restlessness, and parkinsonism (latter not applicable to TD); sedation/somnolence
Dosing frequency	Once daily	Twice daily (IR) Once daily (XR)
Recommended dosing	Take with or without food; start at 40 mg daily; increase to 80 mg daily after one week as indicated and tolerated. Titration to 60 mg daily after one week of 40 mg, then further titration to 80 mg as indicated may be considered. A therapeutic dosage of 40 mg or 60 mg once daily may be appropriate based on patient's clinical response and tolerability.	Take with food; start at 12 mg/day, increase by 6 mg/day at weekly intervals up to 48 mg/day, based on tolerability and response
CYP2D6 poor metabolizers	Maximum recommended dose is 40 mg/ day	Maximum recommended dose is 36 mg/ day
Hepatic impairment	Moderate-to-severe hepatic impairment: maximum recommended dose is 40 mg/day	Contraindicated
Renal impairment	Dosage adjustments are not necessary for patients with mild, moderate, or severe renal impairment	Package insert does not provide any recommendations (cites a lack of studies in this population), but the metabolites are excreted renally
Drug-drug interactions	Valbenazine increases digoxin levels; consider valbenazine dose reduction with strong CYP2D6 inhibitors; with strong CYP3A4 inhibitors the maximum recommended dose is 40 mg daily; use is not recommended with MAOIs or CYP3A4 inducers	Additive sedation may occur with alcohol and other CNS depressants; with strong CYP2D6 inhibitors, the recommended maximum dose is 36 mg/day
QT prolongation recommendation	If the patient is at increased risk for QT prolongation, assess QT interval before increasing the dose	If the patient is at increased risk for QT prolongation, assess QT interval before and after increasing the dose above 24 mg/day

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Page 7 of 8

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