NATIONAL COUNCIL for Mental Wellbeing

Identifying and Treating Tardive Dyskinesia

Speakers

Amber Hoberg
APRN, MSN, PMHNP-BC
Psychiatric Mental Health Nurse Practitioner
Morningstar Family Medicine PLLC

Gavin Clingham
Director of Public Policy
Alliance for Patient Access

Tardive Dyskinesia (TD)

AMBER HOBERG, APRN, MSN, PMHNP-BC
MORNINGSTAR FAMILY MEDICINE PLLC
BAPTIST HEALTH SYSTEM

What is Tardive Dyskinesia (TD)

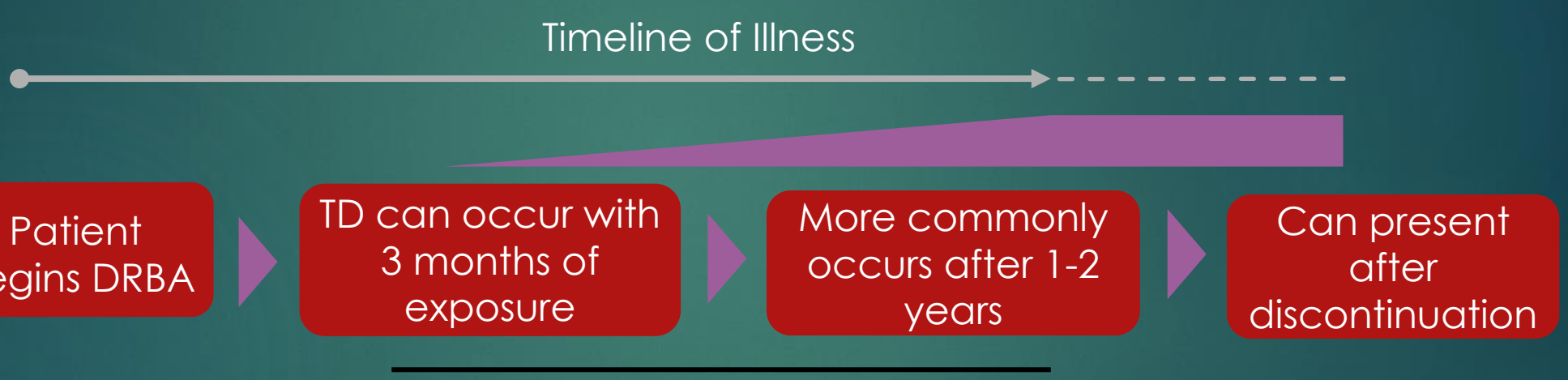
Basics of Tardive Dyskinesia

Tardive

Appearing or tending to appear late

Dyskinesia

Distortion or impairment of voluntary movement

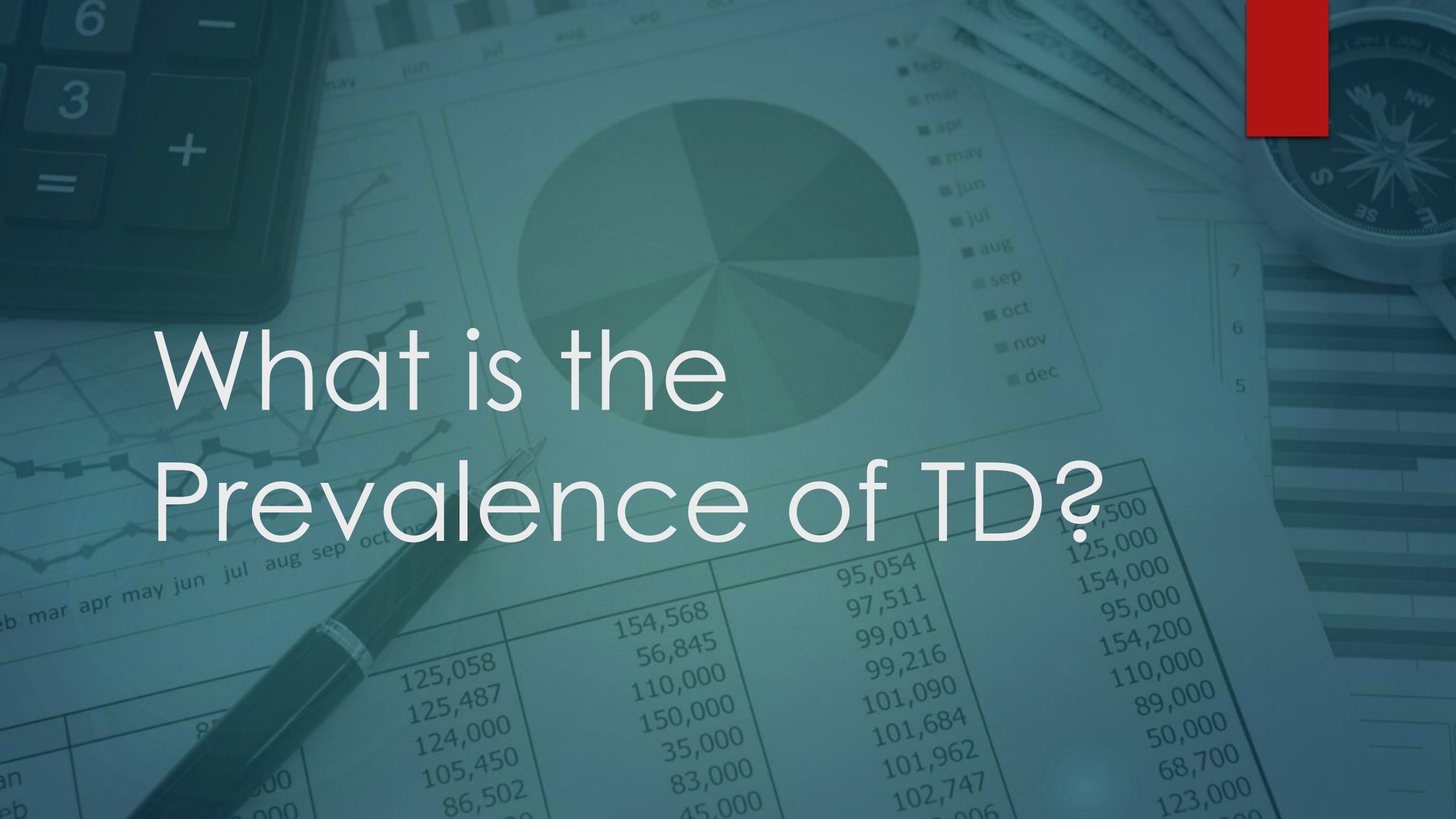


Symptoms may vary in severity over time, but are generally chronic and irreversible

The involuntary movements range from mild to severe and can be disabling

DRBA = dopamine receptor blocking agent.

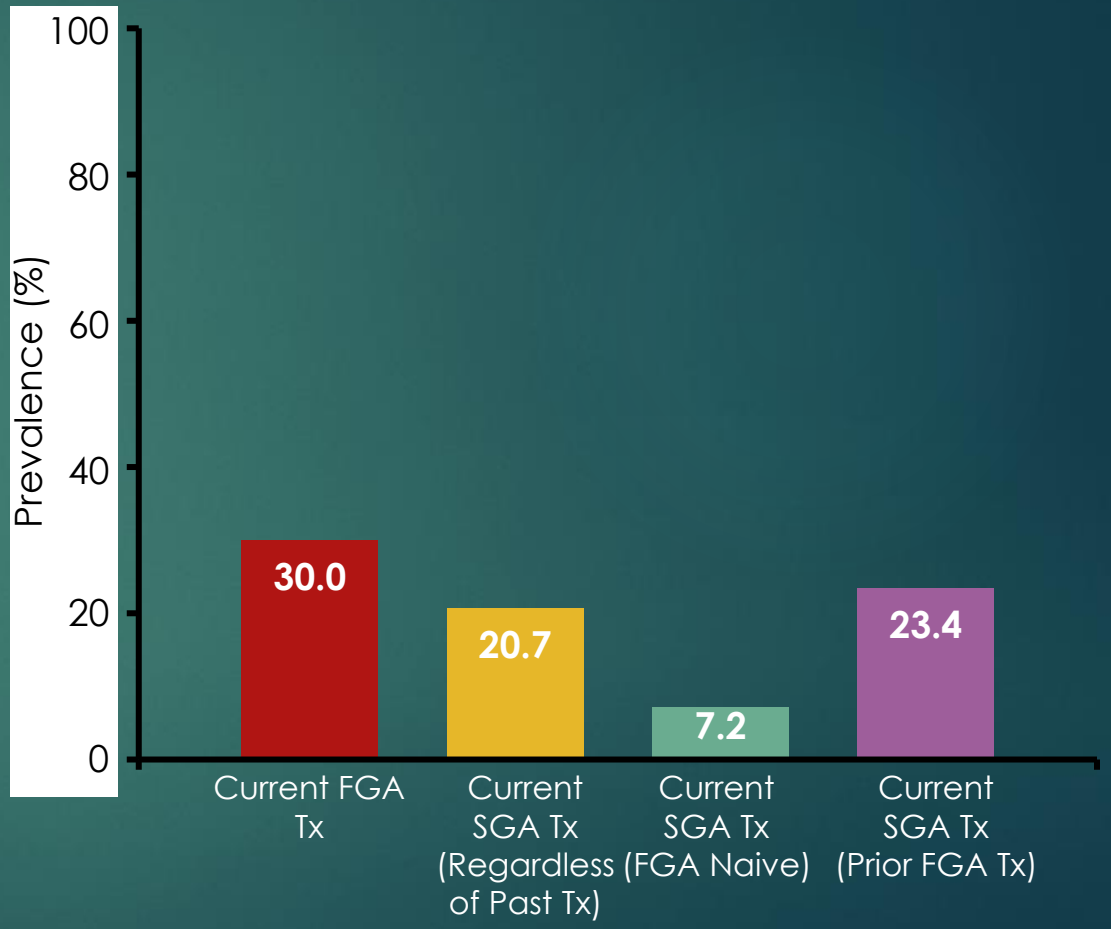
Lerner PP, et al. *Psychiatry Clin Neurosci.* 2015;69(6):321-334. Dorland's Online Medical Dictionary. www.dorlands.com. Waln O, et al. *Tremor Other Hyperkinet Mov*. 2013;3. Bhidayasiri R, et al. *Postgrad Med J*. 2011;87(1024):132-141. Zutshi D, et al. *Tremor Other Hyperkinet Mov*. 2014;4:266.



What is the Prevalence of TD?

Prevalence of Tardive Dyskinesia

- There are ~600,000 people with
  TD in the United States
  - This is more than the population of Atlanta, Georgia, or the state of Wyoming!



nationsonline.org/oneworld/map/usa_population_map.htm. Stahl. Neurotherapeutics. 2014;11:166.
Carbon. J Clin Psychiatry. 2017;78:e264-e278. worldpopulationreview.com/states.

How Does TD Impact Patients?

TD Is More Than a Movement Disorder

Physical/Functional Impact

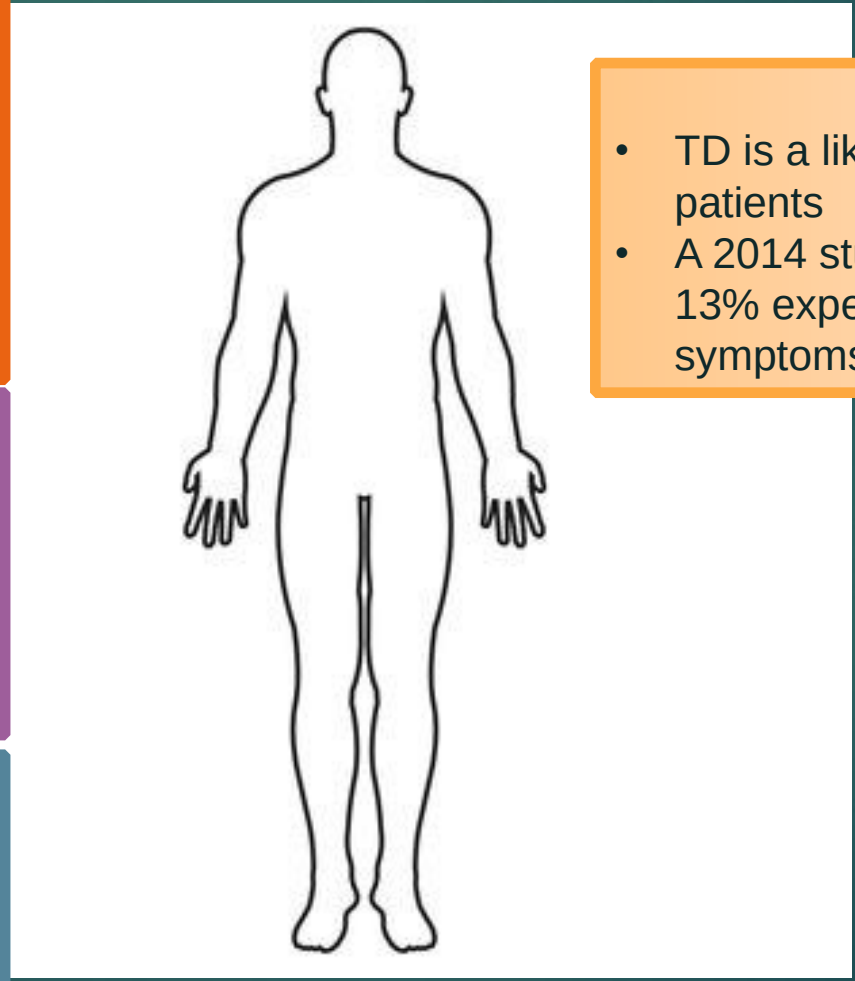
- Trouble walking/gait instability
- Pain and discomfort to muscles
- Dental damage/pain
- Gasping/grunting with respirations
- Trouble swallowing
- Ulcerations/bite marks on tongue and inside of mouth

Social/Emotional Impact

- Embarrassment
- Social isolation
- Trouble maintaining friendships/relationships
- Decrease in enjoyment of leisure activities

Psychological/Therapeutic Impact

- Feeling hopeless
- Increase in depression and anxiety
- Noncompliance with medications
- Harder to treat underlying condition



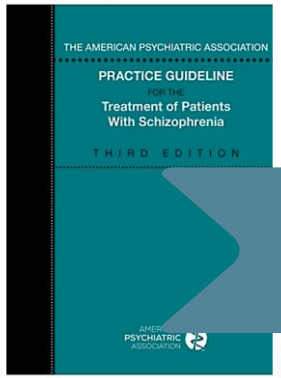
FURTHERMORE

- TD is a likely irreversible condition for most patients
- A 2014 study of 108 patients found only 13% experienced reversibility of tardive symptoms

Zutshi D, et al. *Tremor Other Hyperkinet Mov (NY).* 2014;23(4):266.

What are Risk Factors and how do you Screen for TD?

Structured Screening Is Standard of Care



Semi-structured exams between AIMS:

Before AP
All patients

Q3 months
High risk + FGA

Q6 months
FGA or high risk + SGA

Q12 months
SGA

11%

of patients on antipsychotics receive regular TD screenings, according to one study

Risk Factors

- 3–5× risk if > 60 years old
- History of akathisia, dystonia, or Parkinsonism ("EPS")
- Dosage, duration, and potency of DRBA
- Substance use disorder
- Mood disorder > Psychotic disorder diagnosis
- Intellectually disabled patients

AP = antipsychotic; FGA = first-generat

Miller WR, et al. *J Nerv Ment Dis*. 20

Patients with Schizophrenia. 3rd

Suppl 1):S113-S117. 20

Parkinsonis

et al. *J A*

Abnormal Involuntary Movement

0 No abnormal involuntary movement

1 Equivocal, may be extreme normal

2 Definite involuntary movement, mild

3 Definite involuntary movement, moderate

4 Definite involuntary movement, severe

Score the highest severity seen, not the average

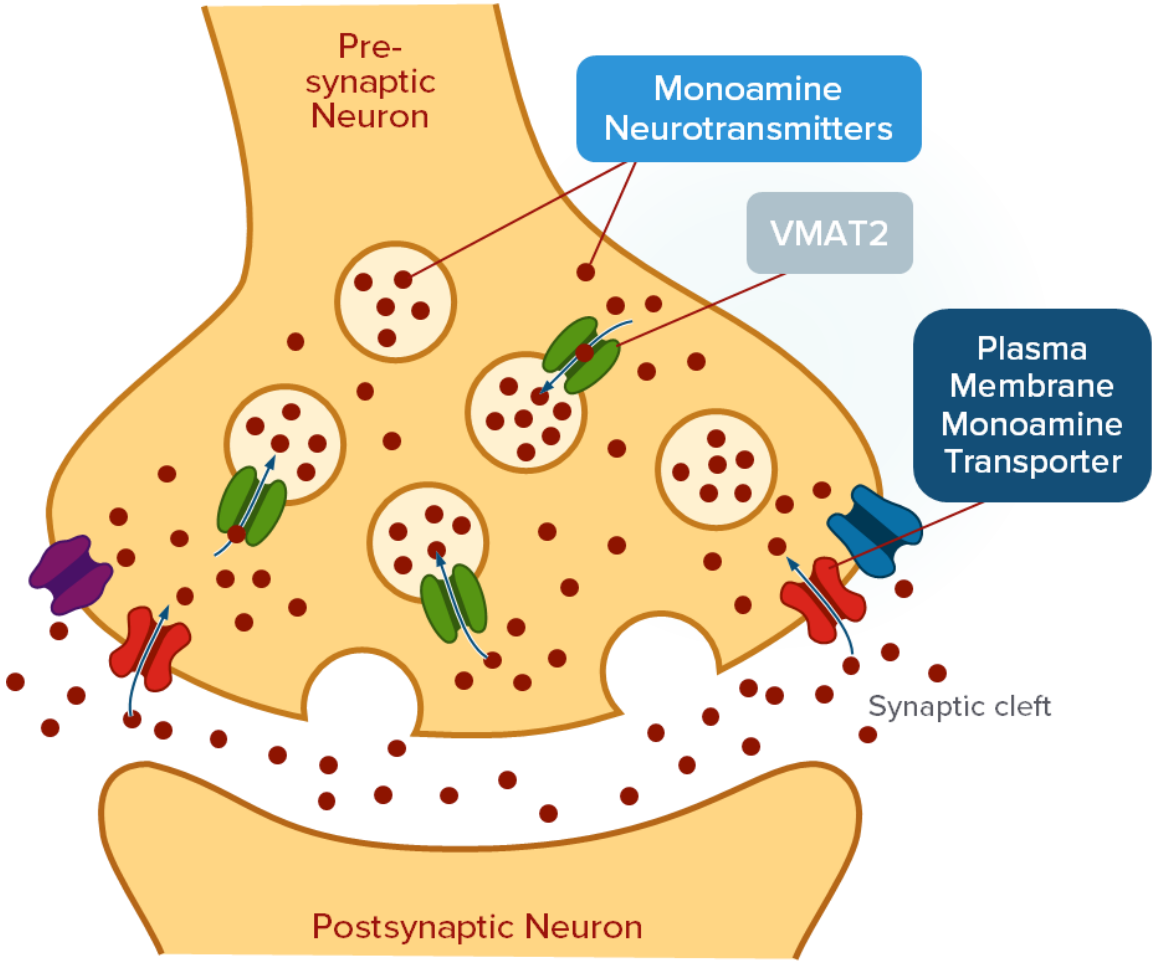
		CIRCLE ONE
FACIAL AND ORAL MOVEMENTS	1. **Muscles of Facial Expression** e.g., Movements of forehead, eyebrows, peri-orbital area, cheeks, include frowning, blinking, smiling, grimacing	0 1 2 3 4
	2. **Lips and Peri-oral Area** e.g., puckering, pouting, smacking	0 1 2 3 4
	3. **Jaws** e.g., biting, clenching, chewing, mouth opening, lateral movement	0 1 2 3 4
	4. **Tongue** Rate only increase in movement both in and out of mouth, **NOT** inability to sustain movement	0 1 2 3 4
EXTREMITY MOVEMENTS	5. **Upper (arms, wrists, hands, fingers)** Include choreic movements (i.e., rapid objectively, purposeless, irregular spontaneous), athetoid movements (i.e., slow, irregular, complex, serpentine) Do **NOT include tremor (i.e., repetitive, regular, rhythmic)**	0 1 2 3 4
	6. **Lower (legs, knees, ankles, toes)** e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot	0 1 2 3 4
TRUNK MOVEMENTS	7. **Back, shoulders, hips** e.g., rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4
GLOBAL JUDGMENTS	8. Severity of abnormal movements	None, Normal ...0 Minimal .....1 Mild .....2 Moderate .....3 Severe 4
	9. Incapacitation due to abnormal movements	None, Normal ...0 Minimal .....1 Mild .....2 Moderate .....3 Severe 4
	10. Patient's awareness of abnormal movements ***RATE ONLY PATIENT'S REPORT***	No Awareness .....0 Aware, Mild distress .....2 Aware, No distress .....1 Aware, Severe distress ...4
DENTAL STATUS	11. Current problems with teeth and/or dentures	No.....0 Yes 1
	12. Does patient usually wear dentures?	No.....0 Yes 1

Guy. ECDEU Assessment Manual for ... Psychopharmacology. 1976. p. 534. Citrome. J Neurol Sci. 2017;383:199.

How Do You Treat TD?

What Causes TD and How Do VMAT2 Inhibitors Help?

- FDA has approved 2 medications for the treatment of TD: valbenazine and deutetrabenazine, both are VMAT2 inhibitors
- VMAT2 = Vesicular Monoamine Transporter Type 2 and controls the packaging of monoamines (such as dopamine) into synaptic vesicles within a neuron
  - When a neuron fires, it releases the contents of synaptic vesicles into the synapse
  - If VMAT2 is inhibited in a dopaminergic neuron, there is less dopamine in the synaptic vesicle, and less dopamine is released (especially in the motor striatum), decreasing dyskinetic movements



Citrome L. *Expert Rev Neurother*. 2018 Apr;18(4):323-32. Bernstein AI, et al. *Neurochem Int*. 2014 Jul;73:89-97.

VMAT2 Inhibitor Characteristics

Valbenazine

- Indication: adults with TD, HD chorea
- 40, 60, and 80 mg doses available
  - 80 mg/day recommended
- Dosed once daily
- Not recommended with strong CYP3A4 inducers; contraindicated for use with another VMAT2 inhibitor or MAOIs
- Use 40 mg dose with CYP2D6 inhibitors, poor metabolizers of CYP2D6, and strong CYP3A4 inhibitors
- No clinically relevant QT prolongation at concentrations expected with recommended dosing*

Deutetrabenazine

- Indication: adults with TD, HD chorea
- 6, 12, 24 mg doses available in Extended-release (XR) form.
- Avg. daily dose in clinical trials >36mg/day. Maximum daily dose 48mg/day
- XR dosed once daily with or without food.
- Max daily dose 36 mg with CYP2D6 inhibitors or poor metabolizers of CYP2D6
- Contraindicated with hepatic impairment, use of another VMAT2 inhibitor, reserpine, or MAOIs
- No clinically relevant QT prolongation with recommended dosing

*** Use caution in patients with congenital long QT syndrome or with arrythmias associated with prolonged QT interval.**
CYP3A4 = cytochrome P450 family 3 subfamily a member 4; MAOI = monoamine oxidase inhibitors; CYP2D6 = cytochrome p450 family 2 subfamily d member 6; HD = Huntington's disease; XR = extended release; QD = daily.
Valbenazine PI. Deutetrabenazine PI.

Policies Impacting Access to Tardive Dyskinesia Care

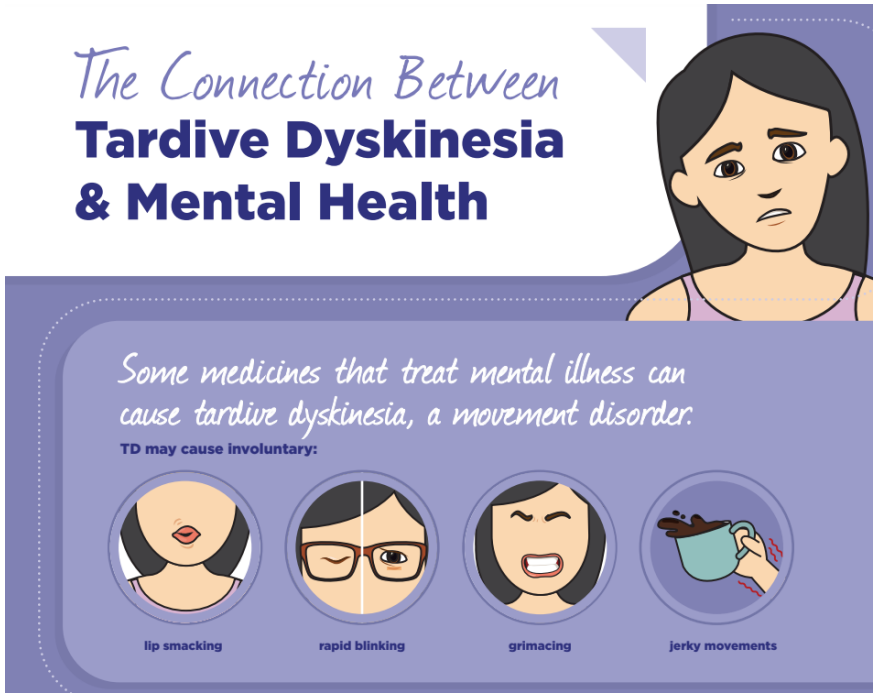
AfPA's Mission

The Alliance for Patient Access (AfPA) is a national network of health care professionals dedicated to promoting the benefits of patient-centered health care.

AfPA accomplishes its mission through educating clinicians on issues impacting patient access and empowering them to engage and inform policymakers.

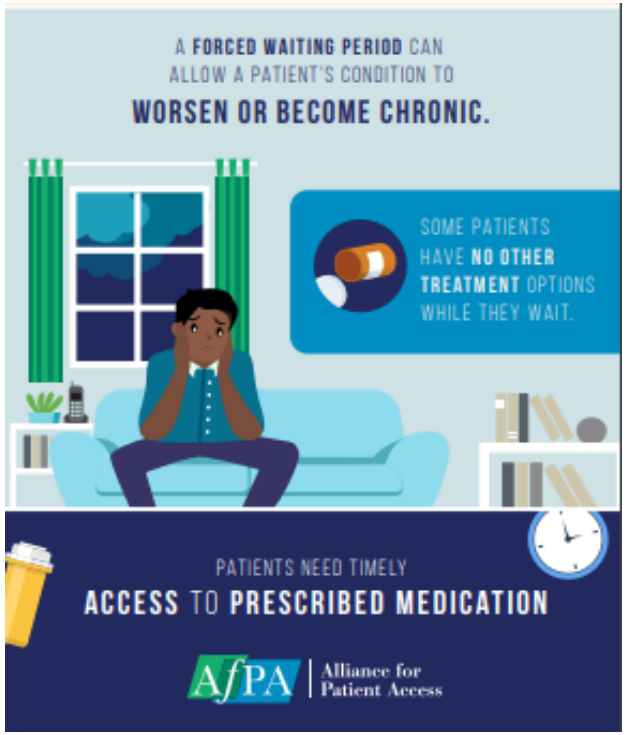
Awareness

- TD affects approximately 600,000 Americans
- Estimated that 16-50% of patients taking antipsychotics have TD
- Patients may not be aware of their disorder, or that it is treatable



Formulary Exclusions

- Two FDA-approved treatments for TD
- Despite multiple approved options, these may not be covered under certain health insurance programs
- Serves to limit options for patients and providers as they are considering the most appropriate TD treatment for their specific circumstances



Prior Authorization

- Prior to receiving coverage providers must obtain a prior authorization from the insurance company
- Prior authorization causes lengthy delays and an increased administrative burden on providers and staff
- Delaying treatment that was deemed appropriate by a patient's provider may causes symptoms to worsen

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Prior Authorization

A POSITION STATEMENT
from the Alliance for Patient Access

OVERVIEW

Patients can be denied access to their medicine for days, even weeks because of a practice called "prior authorization." It's the process whereby insurance companies must approve a physician-prescribed medicine, procedure or test before a patient can get coverage.

Delays can be frustrating, painful or even dangerous for patients—especially for patients with chronic conditions. Meanwhile, physicians and their staff spend hours filling out multi-page forms and submitting labs and patient records. Even then, approval is not guaranteed. If the insurer denies coverage, patients and their physicians can appeal. But that delays treatment even longer, and may not lead to approval.

Insurers claim prior authorization stops unnecessary use of expensive treatments. But it's become a cost-cutting tool that makes it hard for patients to access treatment, especially newer, more innovative medicines. In some cases, the frustrating process may lead patients to abandon treatment altogether.

POSITION

The Alliance for Patient Access presents the following principles for prior authorization and the laws that govern insurers' use of it:

1. **A unified prior authorization form encourages efficiency.** A single form for prior authorization and other related policies like step therapy creates a streamlined and efficient process for physicians and practices. It also ensures physicians and patients know about all requirements up front.
2. **Electronic submission and response should be standard.** Electronic submission in conjunction with a standardized prior authorization process could increase efficiency by eliminating downtime between phone calls, faxes and standard mail.
3. **Considerations of prior authorization requests should adhere to a uniform timeline.** Insurers should be required to consider and respond to a request within a set, reasonable period or the request is deemed approved.
4. **Patients deserve a straightforward appeal process.** Patients experience additional treatment delays when a prior authorization is denied and must be appealed. A straightforward appeal process that outlines requirements and timelines will help physicians and patients know what to expect. This is especially important for expedited appeals during matters of urgent care.

With these safeguards in place, legislators can make certain that insurers do not use prior authorization to the detriment of patient health.

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Step Therapy

- "Fail first" requirements
- Payer requires patient to have a "failure" or negative outcome on a certain treatment prior to receiving coverage
- Requiring a failure for a TD patient serves as a delay

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Step Therapy

A POSITION STATEMENT
from the Alliance for Patient Access

OVERVIEW

To get the medicine prescribed by their health care provider, patients must first prove that older, less expensive or insurer-preferred alternatives don't work. That's the crux of step therapy, or "fail first."

In some cases, step therapy makes sense. A logical progression of treatment options may represent best practice for certain diseases or reflect the wisdom of clinical guidelines.

In other cases, step therapy can be excessive, arbitrary and even damaging to patients' health. Insurers may use step therapy as a deliberate access hurdle meant to protect their own profits.

Doing so hurts patients, whose condition may worsen or who may suffer unnecessarily in the process of failing insurer-preferred treatments. It also undermines the relationship between the physician and patient, to whom treatment decisions rightfully belong.

POSITION

The Alliance for Patient Access presents the following principles for step therapy and the laws that govern insurers' use of it:

1. **Step therapy must be rooted in clinical evidence.** If insurers dictate a progression of treatment options, they must be able to trace their requirement to clinical guidelines from relevant medical associations. Insurers should not be able to require therapies that are inappropriate or unproven for the condition being treated.
2. **Repeated failures are inappropriate.** Patients who have tried a treatment with a previous insurer should not be asked to fail on the same drug again just to satisfy the new insurer's requirement.
3. **Insurers must offer a straightforward exemption process.** Some patients will have allergies, side effects, comorbidities or other health factors that render a step therapy protocol inappropriate. They and their health care providers need a straightforward process for bypassing the requirement.
4. **Insurers' communication must be timely and clear.** Delays associated with step therapy can impact a patient's life and health. That means that responses to a patient's request for a step therapy exemption should occur within a reasonable timeframe. Similarly, details about the exemptions process should be readily available and in plain language for patients and health care providers to access.

With these safeguards in place, legislators can ensure that insurers do not overuse or misuse step therapy to the detriment of patient health.

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Step Therapy

- "Fail first" requirements
- Payer requires patient to have a "failure" or negative outcome on a certain treatment prior to receiving coverage
- Requiring a failure for a TD patient serves as a delay and risks disease progression

AfPA

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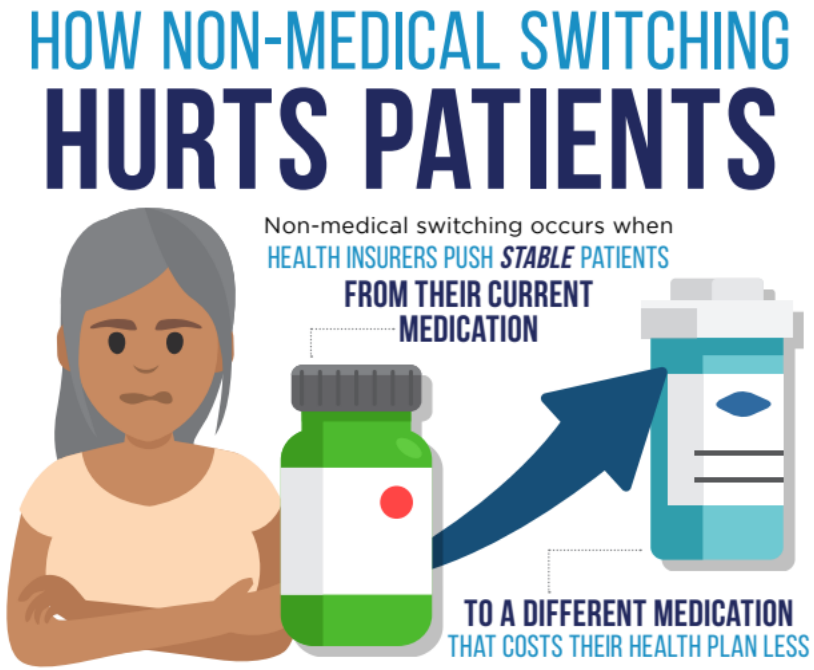
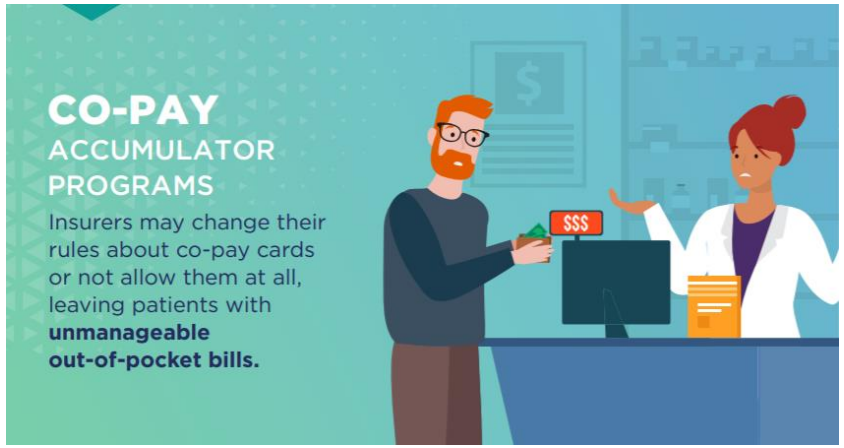
Non-Medical Switching

- Occurs when a stable patient is moved from one treatment to another for non-medical reasons
- Can lead to additional side effects, disease worsening and poor outcomes
- For the TD patient population, ensuring consistent access to the agreed upon treatment is critical



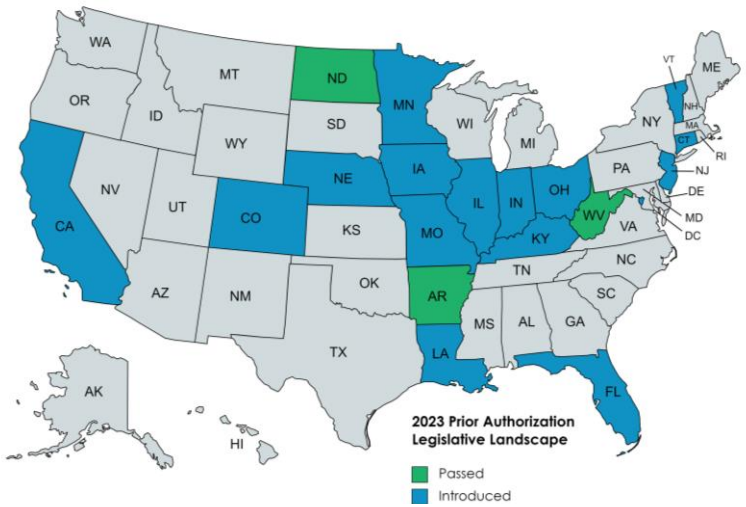
Copay Accumulators

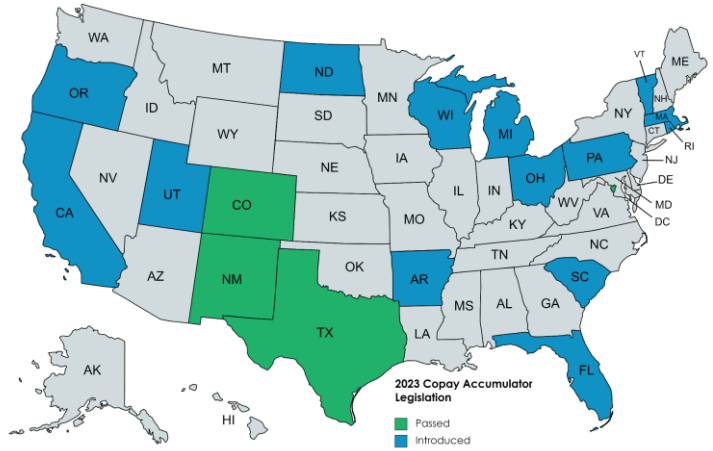
- When patients are taking an expensive medication, they may use a copay coupon from the drug manufacturer to help cover out-of-pocket costs
- A copay accumulator is when a payer does not count the copay coupon towards a patient's annual deductible
- Leaves patients with unforeseen costs when the coupon is exhausted

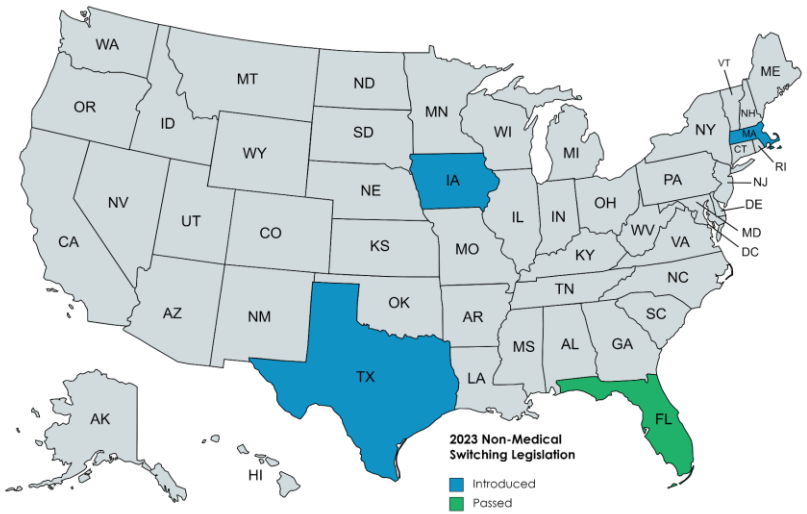


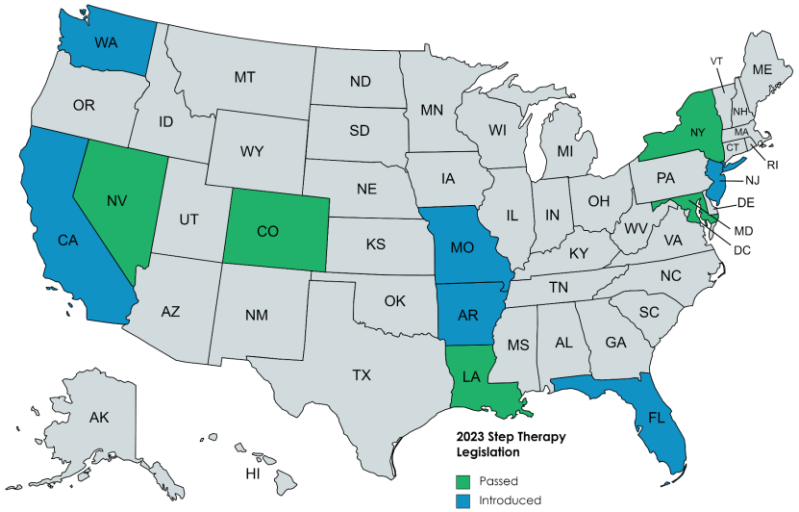
What is being done?

State Activity









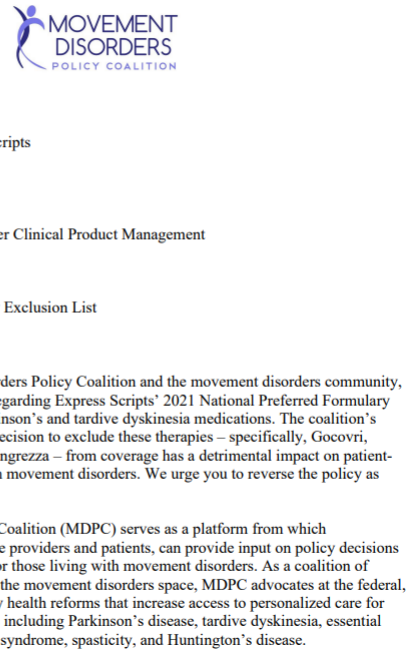
Federal Activity

- Utilization Management
  - Copay Accumulators
  - Step Therapy
  - Prior Authorization

- Telehealth
  - End of the Public Health Emergency
  - Congress has until 2024 to act on certain telehealth provisions

Health Plan Activity

- Legislation may not apply to private plans
- Plans may have exclusionary practices
- Movement Disorder Policy Coalition engagement with Express Scripts



MOVEMENT DISORDERS POLICY COALITION

April 28, 2021

Steve Miller, MD
Chief Clinical Officer, Express Scripts
1 Express Way
St. Louis, MO 63121

Snezana Mahon, PharmD
Vice President & General Manager Clinical Product Management
1 Express Way
St. Louis, MO 63121

Re: National Preferred Formulary Exclusion List

Dear Dr. Miller and Dr. Mahon,

On behalf of the Movement Disorders Policy Coalition and the movement disorders community, I am writing to express concern regarding Express Scripts' 2021 National Preferred Formulary Exclusion List placement of Parkinson's and tardive dyskinesia medications. The coalition's members are concerned that the decision to exclude these therapies – specifically, Gocovri, Ongentys, Xadago, Zelapar, and Ingrezza – from coverage has a detrimental impact on patient-centered care for those living with movement disorders. We urge you to reverse the policy as currently set.

The Movement Disorders Policy Coalition (MDPC) serves as a platform from which stakeholders, including health care providers and patients, can provide input on policy decisions impacting patient-centered care for those living with movement disorders. As a coalition of twenty stakeholder groups across the movement disorders space, MDPC advocates at the federal, state, and health plan level for key health reforms that increase access to personalized care for patients with movement disorders including Parkinson's disease, tardive dyskinesia, essential tremor, dystonia, ataxia, Tourette syndrome, spasticity, and Huntington's disease.

AfPA