AMERICAN ACADEMY OF NEUROLOGY®

Summary of Evidence-based Guideline for **CLINICIANS**

TREATMENT OF TARDIVE SYNDROMES

This is a summary of the American Academy of Neurology (AAN) guideline regarding management of tardive syndromes (TDS), including tardive dyskinesias (TDD).

Please refer to the full guideline at www.aan.com *for more information, including definitions of the classifications of evidence and recommendations.*

Drug Warning

Some of the drugs described here may have serious side effects or other risks associated with them. For more information, visit the US Food and Drug Administration website at *www.fda.gov*.

Is withdrawal of dopamine receptor blocking agents (DRBAs) an effective TDS treatment?

Insufficient evidence	Data are insufficient to support or refute TDS treatment of DRBA withdrawal (**Level U**).

Clinical context

The American Psychiatric Association Task Force recommends antipsychotic withdrawal only in patients who can tolerate it. Despite limited evidence, clinical impression indicates that short-term withdrawal may worsen dyskinesias, whereas adding antipsychotics with stronger extrapyramidal symptoms can reduce TDS. Psychotic relapse predictors include younger age, higher baseline antipsychotic dosage, and shorter hospitalization.

Does switching from typical to atypical DRBAs reduce TDS symptoms?

Insufficient evidence	Data are insufficient to support or refute TDS treatment by changing to atypical antipsychotics (**Level U**, Class IV studies).

What is the efficacy of pharmacologic agents in treating TDS?

AMANTADINE

Weak evidence	Amantadine reduced TDS when used conjointly with a neuroleptic during the first 7 weeks (1 Class II study, 2 Class III studies). Amantadine with neuroleptics may be considered to treat TDS for short-term use (**Level C**).

ACETAZOLAMIDE

Insufficient evidence	Acetazolamide and thiamine reduced TDS in one Class III study. Data are insufficient to support or refute TDS treatment with acetazolamide and thiamine (**Level U**).

Clinical context

Only flupentixol decanoate, chlorpromazine, haloperidol, trifluoperazine, and thioridazine were tested with amantadine in these studies. The efficacy of amantadine plus other neuroleptics in TDS treatment is unknown. Because safety data are unavailable concerning long-term use of only typical neuroleptics as TDS suppressive agents and because of these agents' propensity to cause TDS, the evidence suggests only potential efficacy short-term.

FIRST-GENERATION ANTIPSYCHOTICS

Insufficient evidence	Haloperidol possibly reduces TDS movements for up to 2 weeks (2 Class II studies, 1 Class III study) but is associated with increased akinetic-rigid syndrome (1 Class II study). Data are insufficient to support or refute the use of thiopropazate in reducing oral dyskinesia (1 Class III study). Data are insufficient to support or refute the use of thiopropazate, molindone, sulpiride, fluperlapine, and flupenthixol in treating TDS (**Level U**).

Clinical context

Although haloperidol and thiopropazate possibly reduce TDS, they are not recommended because of the competing risk of akinetic-rigid syndrome. Safety data are unavailable concerning the long-term use of typical antipsychotics as TDS suppressive agents, and these drugs themselves can cause TDS; these significant risks outweigh the benefits of any short-term use of typical antipsychotics.

SECOND-GENERATION ANTIPSYCHOTICS

Insufficient evidence	Data are conflicting regarding the use of clozapine (conflicting Class III studies). Risperidone (2 Class II studies, 1 Class III study) is probably effective in reducing TDD. Olanzapine is possibly effective in reducing TDD (2 Class III studies). The safety of risperidone and olanzapine as a TDS suppressant for use beyond 48 weeks has not been addressed. There is no evidence to determine the efficacy of quetiapine, ziprasidone, aripiprazole, and sertindole in TDS treatment. **Because neuroleptic agents may themselves cause TDS and may mask its symptoms rather than treat it, these drugs cannot be recommended for TDS treatment (Level U)**. Caution is advised when using risperidone or olanzapine to reduce TDS.

ELECTROCONVULSIVE THERAPY

Insufficient evidence	Data are insufficient to determine the efficacy of electroconvulsive therapy for TDD treatment (**Level U**).

DOPAMINE-DEPLETING AGENTS

Weak evidence	Tetrabenazine (TBZ) possibly reduces TDS symptoms (2 consistent Class III studies). TBZ possibly reduces TDS symptoms (2 consistent Class III studies). TBZ may be considered in treating TDS (**Level C**).
Insufficient evidence	One study (Class III) found reserpine and α-methyldopa effective in treating TDS. Data are insufficient to determine the efficacy of reserpine or α-methyldopa in treating TDS (**Level U**).

Clinical context

TBZ reduces TDS symptoms; there is no evidence that long-term TBZ administration induces TDS, but it can cause parkinsonism.

DOPAMINE AGONISTS

Insufficient evidence	Data are insufficient to support or refute the use of bromocriptine for TDS treatment (**Level U**).

CHOLINERGIC AND ANTICHOLINERGIC DRUGS

Weak evidence	Galantamine is possibly ineffective in treating TDS (1 Class II study). Galantamine might not be considered in treating TDS (**Level C negative**).
Insufficient evidence	Data are insufficient to determine the effectiveness of other cholinergic drugs in treating TDS (**Level U**).
	Data are insufficient to determine the effectiveness of anticholinergic drugs in treating TDS (**Level U**).

BIPERIDEN (AKINETON) DISCONTINUATION

Insufficient evidence	Data are insufficient to determine the effectiveness of biperiden discontinuation in treating TDS (**Level U**, 1 Class III study).

ANTIOXIDANTS

Moderate evidence	Ginkgo biloba (EGb-761) is probably useful in TDS treatment (1 Class I study), but data are limited to inpatients with schizophrenia (**Level B**).
Weak evidence	Based on 1 Class II study, eicosapentaenoic acid is possibly ineffective in treating TDS and might not be considered (**Level C negative**).
Insufficient evidence	Based on 4 Class II and numerous Class III studies, data are conflicting regarding vitamin E efficacy in treating TDS. Data are insufficient to determine the efficacy of vitamin E (**Level U**).
	Melatonin is possibly ineffective in treating TDS at a 2-mg/d dose (1 Class II study) but is possibly effective in treating TDS at a 10-mg/d dose (1 Class II study). Evidence regarding TDS treatment with melatonin is conflicting (**Level U**).
	Data are insufficient to support or refute the use of other antioxidants, including vitamin B_6, selegiline, and yi-gan san, in treating TDS (**Level U**).

GABA AGONISTS

Moderate evidence	Based on 1 Class I study, clonazepam is probably effective in decreasing TDD symptoms short-term (approximately 3 months) and should be considered for short-term TDD treatment (**Level B**).
Insufficient evidence	Data are insufficient to support or refute baclofen use in treating TDD (**Level U**).

LEVETIRACETAM

Insufficient evidence	Data are insufficient to recommend levetiracetam as TDS treatment (**Level U**, 1 Class III study).

CALCIUM CHANNEL BLOCKERS

Moderate evidence	Diltiazem probably does not reduce TDD and should not be considered as treatment (**Level B negative**, 1 Class I study).
Insufficient evidence	Data are insufficient to support or refute nifedipine use in treating TDD (**Level U**).

BUSPIRONE

Insufficient evidence	Data are insufficient to support or refute buspirone use in treating TDD (**Level U**, 1 Class III study).

Do patients with TDS benefit from chemodenervation with botulinum toxin (BoNT)?

Insufficient evidence	Data are insufficient to support or refute BoNT use to treat TDS symptoms (**Level U**).

Do patients with TDS benefit from surgical therapy?

Insufficient evidence	Data are insufficient to support or refute pallidal deep brain stimulation use in treating TDS (**Level U**, Class IV studies).

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Copies of this summary and additional companion tools are available at *www.aan.com* or through AAN Member Services at (800) 879-1960.