Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Bipolar Disorder***
-February 2022-

Background:

In February 2022, the Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed the current available outpatient treatment options for bipolar disorder in adults, as well as guidelines for the treatment of bipolar disorder in adults, to determine if changes to the IHS National Core Formulary were warranted. The IHS National Core Formulary currently lists atypical antipsychotics (any product), requiring facilities to maintain any one atypical antipsychotic agent on formulary but deferring the selection of the specific agent to the discretion of the local facility. The IHS National Core Formulary also lists five mood stabilizers and 10 antidepressants which may be used in the treatment of bipolar disorder. Following the recent NPTC clinical and pharmacoeconomic reviews, **the NPTC made no modifications to the National Core Formulary.**

Discussion:

Bipolar disorder is a brain disorder that causes changes in a person's mood, energy, and ability to function. People with bipolar disorder experience intense emotional states that typically occur during distinct periods of days to weeks, called mood episodes. These mood episodes are categorized as manic/hypomanic (abnormally happy or irritable mood) or depressive (sad mood). Bipolar disorder is a category that includes four different diagnoses:[1]

- Bipolar I disorder
- Bipolar II disorder
- Cyclothymic disorder
- Unspecified bipolar disorder

An estimated 82.9% of adults in the United States (U.S.) with bipolar disorder have serious impairment or disability, while the remaining 17% of U.S. bipolar adults have some degree of moderate impairment or disability. The median age of onset for bipolar disorder is 25 years. Illness can start in early childhood or as late as 40 to 50 years of age. More than two-thirds of people with bipolar disorder have at least one close, first- or second-degree relative with the illness or with unipolar major depression.[2, 3] The percentage of American Indian and/or Alaska Native (AI/AN) people living in the U.S. was 0.9% (2.9 million) in 2010 vs. 1.1% (3.7 million) in 2020. Of particular note, AI/AN people are 1.5 times more likely to experience serious psychological distress than in the general population. The annual prevalence of mental illness among Non-Hispanic AI/AN adults in the U.S. is 18.7%. The lifetime prevalence of DSM-I bipolar I disorder is greatest among AI/AN populations in men (3.6%) and women (6.9%).[4-6]

Patients with Bipolar I disorder have a history of at least one episode of mania which is preceded or followed by a hypomanic, major depressive, mixed, or unspecified episode. Patients with Bipolar II disorder have a history of major depressive episodes and hypomanic episodes only. These episodes may be preceded or followed by one or more episodes of hypomania, but the individual experiences no manic or mixed episodes.[7]

The treatment for bipolar disorder can be broken down into six categories:

- Non- pharmacological Approaches
- Acute Management of Bipolar I Mania
- Management of Bipolar I Depression
- Bipolar I Maintenance Therapy
- Acute Management of Bipolar II Depression
- Maintenance Management of Bipolar II Depression

The evidence-based guideline review for the treatment of bipolar disorder in adults focused on both national and international guidance from the American Psychiatric Association, the Canadian Network for Mood and Anxiety Treatments and International Society for Bipolar Disorders, the National Institute for Health and Care Excellence, the British Association for Psychopharmacology, the Royal Australian and New Zealand College of Psychiatrists, and the Veteran Affairs/Department of Defense.

According to clinical guidelines, multiple medications across several differing medication classes are used in the treatment of bipolar disorder, including mood stabilizers, antipsychotics, antidepressants, or a combination of these medications.

The IHS National Core Formulary currently lists the following available medications commonly used for the treatment of bipolar disorder:[8-13]

Mood Stabilizers	Antipsychotics	Antidepressants
Carbamazepine	*First generation antipsychotics*	Bupropion
Divalproex	Haloperidol (injectable only)	
Lamotrigine		*Serotonin and norepinephrine reuptake inhibitors (SNRIs)*
Lithium	*Second generation antipsychotics or Atypicals*	Duloxetine
Oxcarbazepine	Aripiprazole (injectable only)	Venlafaxine
	Any product	
		Selective serotonin reuptake inhibitors (SSRIs)
		Citalopram
		Escitalopram
		Fluoxetine
		Paroxetine
		Sertraline
		Tricyclic Antidepressants (TCAs)
		Amitriptyline
		Nortriptyline

In August 2018, the Agency for Healthcare Research and Quality performed a comprehensive systematic review of varying pharmacotherapeutic treatments in adults with bipolar disorder. Eight antipsychotics from 47 publications were reviewed. Most antipsychotic drugs had few studies to contribute to the findings. Studies for antipsychotics plus mood stabilizers were even more sparse. Low-strength evidence showed improved mania symptoms for most all FDA-approved antipsychotics when compared to placebo in adults with bipolar I disorder. Most manic symptom improvements were of modest clinical significance but still large enough to determine that reasonable proportions of participants likely received a benefit. Evidence was largely insufficient to draw conclusions regarding the effects of drug treatments for depression in adults with bipolar disorder for the primary outcomes of interest (relapse, symptom scores, and function).[14]

Findings:

All drug classes of agents or specific medications used in the treatment of bipolar disorder, including mood stabilizers, antipsychotics, and antidepressants are currently available on the IHS National Core Formulary. Clinical evidence from published literature and national guidelines, in concert with internal Agency reviews of pharmacoeconomic analyses fail to demonstrate superiority of any particular medication agents or classes. Furthermore, the NPTC recognizes the broad variance in regional/state-based preference(s) at specific IHS facilities. Collectively, these issues supported the NPTC's decision to make no modifications to the National Core Formulary.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

References:

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