Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: *Long-Acting Injectable Antipsychotics*
-November 2020-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a drug class review of the long-acting injectable antipsychotic agents (LAAs) at their November 2020 meeting. This review included both first- and second-generation LAAs and their various formulations. The IHS National Core Formulary does not currently contain any LAAs although "atypical antipsychotics" (any product) were named to the National Core Formulary in 2015. The goal of this review was to determine if clinical evidence and guidelines supported the addition of these agents. Following clinical review and analysis, the NPTC voted to **ADD both (1) haloperidol decanoate** and **(2) aripiprazole lauroxil** to the National Core Formulary.

Discussion:

Long-acting antipsychotics are an important part of treatment of psychotic disorders such as schizophrenia, schizoaffective disorder, and bipolar disorder (often termed "SMI" for serious mental illness). With the cognitive impairment that can lead to lack of insight in having an illness, associated symptoms of psychosis that often occur with these conditions (such as paranoia), and side effects of medications, there is marked difficulty with treatment adherence to oral antipsychotics[1]. This leads to revolving-door inpatient admissions that frequently involve law enforcement and involuntary treatment, incarceration, homelessness, a shortened life span and significant disability and human suffering[2].

Since the 1960's, there has been recognition of the need for LAAs for the reasons listed above. The first LAA, fluphenazine decanoate, was FDA-approved in 1967. Haldol decanoate followed and these two first- generation antipsychotics have been in use for decades. Following initial FDA approvals of second-generation antipsychotics in the late 1990's, rapid development ensued for these medications with the creation of various forms of risperidone, aripiprazole, olanzapine, and paliperidone. Currently, there are six LAA medications (but nine LAA formulations) in total on the market.

The primary advantage of second-generation antipsychotic agents is the marked reduction in an irreversible neurological side effect called tardive dyskinesia seen with first-generation antipsychotics. The side effect profile of second-generation antipsychotics however includes increased cardiovascular risk from weight gain, insulin insensitivity, hypertension and elevated cholesterol in addition to higher cost. Balancing the risk of tardive dyskinesia and cardiovascular risk as well as cost is an important aspect of decision making around the choice of LAA for psychiatric providers. Both first- and second-generation antipsychotics are now widely used to treat psychotic disorders although at a lower rate of utilization than hoped by national groups dedicated to ensuring evidence-based treatment for the SMI population[3].

The American Psychiatric Association Practice Guidelines for schizophrenia recommend the use of LAAs for appropriate patients[4]. An extensive evidence base for the effectiveness of LAAs spans the 50 years of their availability on the market. A recent Cochrane review demonstrated the benefit of first- generation antipsychotics and second-generation antipsychotics compared to placebo, and multiple studies subsequently demonstrated superiority of various LAAs to placebo[5]. This same evidence review showed similar efficacy between LAAs when compared to each other[6]. A recent meta-analysis of comparison trials of the first-generation vs second-generation antipsychotics demonstrated similar efficacy between groups and varying side effect profiles[7].

Findings:

LAAs are an effective, evidence-based treatment that can address medication adherence issues experienced by individuals with psychotic conditions such as schizophrenia. The decision on which one to use is based on patient preference and consideration of side effect profile and cost.

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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