Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed alcohol use disorders at the February 2015 NPTC Meeting, defining the disease, describing the pathogenesis, prevalence and clinical manifestations of AUDs and summarizing the medications used for treatment. The committee reviewed the Food and Drug Administration (FDA) approved medications for this indication: disulfiram, naltrexone, extended release naltrexone, and acamprosate. Topiramate, gabapentin, baclofen, selective serotonin receptor inhibitors (SSRIs) and ondansetron were also briefly reviewed.

Discussion:
Alcohol use disorders (AUDs) are prevalent in the United States (US) with the highest frequency in American Indians or Alaskan Natives. They are caused by a complicated interplay of genetics (responsible for ~50% of vulnerabilities to AUDs), psychosocial and environmental factors and result in significant morbidity and mortality. Despite the severe health consequences of AUDs, only 13.5% of people with alcohol use disorders received any type of treatment, most of which were in self-help groups. Less than 10% of patients reported treatment in a hospital or clinic based setting.

Referrals to social services or behavioral counseling are an important part of treatment, but these are often insufficient to treat moderate to severe alcohol use disorders. Medication-assisted treatment is an important component of management. Compared to either alone, the addition of pharmacotherapy to psychosocial treatment improves outcomes. Medications can help relieve cravings and symptoms of protracted withdrawal and allow neurons to readapt to a nonalcoholic state. This helps patients increase motivational readiness for change, leading to longer periods of abstinence.

The FDA has approved four medications for the treatment of alcohol dependence: two forms of naltrexone (oral and extended-release injectable), acamprosate, and disulfiram. There are data to support the safety and efficacy of all of these medications. In particular, many experts consider naltrexone first-line therapy given its proven efficacy and safety profile, both during supervised withdrawal and in the primary care setting. Despite availability, these medications are extremely underutilized. In a US Department of Veterans Affairs healthcare system, only 1.9 % of patients with alcohol dependence were prescribed naltrexone. A national survey of US physicians who treat addictions showed that only 3–13 % use pharmacotherapy for the treatment of alcohol dependence. Although physicians demonstrate low prescribing patterns, a majority of patients with alcohol dependence report an interest in medication-assisted treatment.

Findings:
Naltrexone: A multicenter randomized, controlled trial (RCT) in 2006 showed efficacy in decreasing heavy drinking and improving clinical outcomes in the primary care setting. A Cochrane Review in 2008 concluded that short term (16 week) treatment of naltrexone decreased the chance of alcohol relapses by 36% (NNT = 7) and lowered the risk of withdrawal in alcohol dependent patients by 28% (NNT = 13). Treatment up to 1 year gave no benefit for relapse prevention, but decreased overall alcohol consumption and diminished cravings

Acamprosate: Of 17 RCTs in 12 countries with 5000 patients measuring 3 months to over a year, 14 of 17 showed increased abstinence, time to first drink and decreased LFT levels. Combined abstinence rate at the end of treatment was 35% in acamprosate versus 21% in placebo groups. Of 3 studies that failed, only a 2 month treatment period was used suggesting that longer periods of treatment are required.

Disulfiram: On review of all 18 RCTs with administering disulfiram under direct supervision, 17 of 18 showed improved abstinence, treatment retention and/or proportion of days of alcohol consumption. The
most comprehensive review of literature covering 1937-2005 concluded that supervised disulfiram is an effective treatment for alcohol dependence but disulfiram is similar to placebo when not under close supervision.

There is some promising data for the use of topiramate, gabapentin, baclofen, SSRIs and ondansetron for the treatment of alcohol use disorders but more data is needed.

Guidelines:
The NICE 2011 Guidelines for AUDs states that after a successful withdrawal for people with moderate and severe alcohol dependence, patients should be offered acamprosate or oral naltrexone in combination with an individual psychological intervention (cognitive behavioral therapies, behavioral therapies or social network and environment-based therapies) focused specifically on alcohol misuse.

The Treatment Improvement Protocol published by the US Department of HHS, SAMHSA and CSAT in 2009 stated that the medications were an important part of managing patients with AUDs and physicians should become familiar with these medications as AUDs are treatable medical conditions and treatment can improve health outcomes.

Conclusions:
Naltrexone should be used as first line therapy for those with moderate to severe AUDs unless there is severe liver disease or concomitant opioid use. Acamprosate should be considered first line if there is a contraindication to naltrexone. It can be used as second line if there is partial or no response to other medications. Disulfiram should be used in motivated patients with close supervision. It can also be used as an adjunct to other medications or to support abstinence if attending events that involve alcohol.

Given the increased prevalence, high morbidity and mortality of alcohol use disorders in the American Indian/Alaskan Native population, and given the recommendation for all these patients to have access to medications for the treatment of AUDs, the NPTC added naltrexone to the IHS 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:
- US Department of HHS, SAMHSA, Center for Behavioral Health Statistics and Quality. Results from the 2012 National Survey on Drug Use and Health. Rockville, MD: Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality; 2012.