Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed the medical management of Post-Traumatic Stress Disorder (PTSD) at the August 2021 Summer meeting. There is a growing recognition of the impact of adverse childhood events for adult morbidity and mortality. Some of the long term impacts of developmental trauma are now being captured by the diagnosis of complex PTSD, which is newly recognized in the International Classification of Diseases 11th Revision (ICD-11), as of 2018. The review sought to determine whether medications listed on the IHS National Core Formulary remained current in the management of complex as well as simple PTSD. The Committee found that although treatment recommendations may differ in terms of emphasis in the setting of complex PTSD, all recommended psychotropic medications needed to treat both simple and complex PTSD were currently included on the National Core Formulary. In particular, the role of prazosin was highlighted as one of the few medications which is effective in both forms of PTSD. As a result of the evaluation, the NPTC made no modifications to the National Core Formulary.

Discussion:
PTSD is a highly prevalent disorder in health care settings as 14 to 48% of clinical samples have a lifetime history of PTSD. Underdiagnosis is common and clinically significant because the presence of PTSD predicts the later development of suicidality, substance abuse, and depressive and anxiety disorders. When PTSD remits, these psychiatric comorbidities tend to lessen. PTSD is associated with increased medical morbidities as well. In addition, first-line pharmacotherapies for PTSD can be routinely prescribed in primary care settings and are an important alternative when community-based psychotherapy is not readily available. Interestingly, a 2016 meta-analysis of 55 studies (N = 6,313) compared psychopharmacology to general psychotherapy and revealed both were similarly effective in PTSD treatment [effect size of first-line drugs: -0.43 (-0.49 to -0.36)], [effect size of general psychotherapies -0.45 (-0.89 to -0.01)].

There are several key treatment considerations that can be implemented in primary care settings which can have a significant impact on the treatment of PTSD. Prazosin, an alpha-1-noradrenergic receptor inhibitor, is a highly efficacious medication for traumatic nightmares, boasting an effect size three times greater than the effect sizes observed for antidepressants [prazosin effect size for reducing nightmares: -1.13 (-1.91 to -0.36)]. Therefore, it is important to specifically query for the presence of traumatic nightmares to determine if the patient could benefit from the initiation of prazosin. This is in distinction to the usual treatment of mental health disorders in primary care. Depression, anxiety and PTSD all have the same first-line psychopharmacology recommendation, namely an antidepressant. Therefore, a patient can often benefit from an antidepressant even when there is not a high level of diagnostic precision. But unless traumatic nightmares are specifically identified, a patient is unlikely to receive prazosin which highlights the importance of this line of focused patient inquiry.

It is also important that IHS clinicians are familiar with the concept of complex PTSD because it has therapeutic implications. Complex PTSD was newly introduced to the ICD-11 in 2018. The classic cause of complex PTSD in adults is a history of childhood abuse. Due to a history of settler colonialism and historical trauma, Native Americans have the highest rates of childhood abuse of any ethnic group. The more adverse childhood events a patient has experienced, the more that complex PTSD is likely to be present. Complex PTSD is thought to be biologically distinct from simple PTSD and appears to require a different psychopharmacological approach.

In simple PTSD, the first line of treatment is the selective serotonin reuptake inhibitor (SSRI) class of medications which consist of fluoxetine, sertraline, paroxetine, escitalopram, citalopram (although citalopram above 40mg has a black box warning of sudden death). Network meta-analysis reveals that fluoxetine is better tolerated but equally efficacious to the other SSRIs [fluoxetine effect size: -0.30 (0.51 to -0.09)]. Although venlafaxine is a serotonin-norepinephrine reuptake inhibitor, it can be added to this list because it has the neurotransmitter profile of an SSRI when dosed up to 150 mg and is similarly efficacious in PTSD [venlafaxine effect size: -0.32 (0.53 to -0.11)] versus other SSRIs when dosed in the SSRI range.

Although SSRIs are the first line of treatment for simple PTSD, a recent meta-analysis published in 2020 revealed that if there is a history of childhood abuse, neither SSRIs, monoamine oxidase inhibitors or tricyclic antidepressants may be effective. Again, prazosin stands out as uniquely efficacious. Not only is prazosin helpful for traumatic nightmares as
previously discussed, but it appears to be helpful in overall PTSD symptom reduction [prazosin overall PTSD symptom reduction effect size, complex trauma: -0.52 (-1.03 to -0.02)], presumably because it calms the noradrenergic-mediated symptoms of PTSD such as hypervigilance and exaggerated startle. Should an antidepressant be trialed in a patient with a history of childhood abuse, the more highly serotonin-selective antidepressants, such as escitalopram, may be more effective. In PTSD, benzodiazepines should be avoided because they can cause an overall worsening of PTSD severity, mediated by deepening the avoidance which is characteristic of the disorder.

Findings:

In 2018, the ICD-11 introduced a new diagnostic category, complex PTSD, which is highly relevant for the IHS patient population. While the SSRI class of medications are considered the first-line treatment for PTSD, the SSRIs may not be as efficacious for complex PTSD. The more highly serotonin-selective SSRIs such as escitalopram presently show the most promise for effectiveness. While many of the agents that are effective in simple PTSD have questionable efficacy in complex PTSD, prazosin stands out as a medication that is effective in both PTSD subtypes for the treatment of nightmares. Prazosin has also been shown to be effective for general symptom reduction for complex PTSD. Prazosin is currently included on 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: