HIV Section Medication Formulary Workgroup (HSMFW)
Email Vote on May 2022 Action Items

On May 17, 2022, HIV Section Medication Formulary Workgroup Co-Chairs, Joanne Urban and Cathy Frazier, advised the workgroup, via email, that the HIV/AIDS Section would not implement a clinical prior authorization (PA) at this time. Since requiring a PA is not an option, they asked HSMFW members to vote again on whether the drugs that were being considered for a PA requirement (i.e., opioids, muscle relaxants, benzodiazepines) should be added to the AIDS Drug Assistance Program (ADAP) formulary. Additionally, members were asked to vote on whether the chronically used medications that were not being added to the ADAP formulary should be added to the AIDS Pharmaceutical Assistance (APA) formulary. The deadline to cast a vote was May 24, 2022. Due to a low response rate, The AIDS Institute sent a follow-up email on June 13, 2022, to non-responders requesting that they vote by close of business June 17, 2022. The AIDS Institute sent a reminder message on June 15, 2022.

The information below was provided to members for their consideration:

ADAP Formulary (Summary information provided to members)

Opioid Analgesic

Tramadol

- **Description: Opioid analgesic**
- **Indication(s):** Treatment of severe pain
- **Place in therapy (including guidelines recommendations if applicable):** Various guidelines exist regarding use of opioid analgesics in management of chronic non-cancer pain due to opioid epidemic and risk of abuse, overdose, and death. See https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm
- **Potential interaction with ARVs: Levels may be increased by PIs and cobicistat**
    - Florida Medicaid (_Yes_)
- **PAP availability:** No

Feedback received on tramadol:

Feedback
I worry about the opioids and the potential of misuse, redirection for financial profit, and overdose. I would agree that the muscle relaxants should be ordered for short term therapy, but it seems that some Pain Management specialists keep patients on for

extended periods of time. My concern is the balance of maintaining the highest quality of life vs inadvertently putting people in harm's way. (Carscallen)
Requiring on-going opioid prescriptions be written by pain management specialists would be reasonable. Any exceptions (outside of a malignancy diagnosis) should require a prior authorization. (Appelbaum)
I'm ok with requiring PA's only for clinical reasons and would recommend them for CHRONIC opioid, muscle relaxers and benzodiazepine prescriptions because of misuse potential. We should allow opioids for acute pain and for malignancy diagnoses without a PA. (Appelbaum)
I would also agree with Jonathan's comments. (Carscallen)
I would echo/agree with Jonathan's comments. (Sension)
Tramadol: Recommend adding it to the ADAP Formulary for pain. (Wall/Miami area pharmacists)

Muscle Relaxants

Metaxalone

- **Description:** Muscle relaxant
- **Indication(s):** Treatment of muscle pain/spasm
- **Place in therapy (including guidelines recommendations if applicable):** Option for short-term (e.g., 2 to 3 days) treatment of pain/muscle spasm. Used in combination with other agents such as non-steroidal anti-inflammatory drugs (NSAIDS).
- **Potential interaction with ARVs:** No significant interactions expected
- **Coverage on other formularies:**
    - Florida Medicaid (No)
- **PAP availability:** Yes

Methocarbamol

- **Description:** Muscle relaxant
- **Indication(s):** Treatment of musculoskeletal spasm and/or pain
- **Place in therapy (including guidelines recommendations if applicable):** Option for short-term (e.g., 2 to 3 days) treatment of pain/muscle spasm. Used in combination with other agents such as non-steroidal anti-inflammatory drugs (NSAIDS).
- **Potential interaction with ARVs:** No significant interactions expected
- **Coverage on other formularies:**
    - Florida Medicaid (Yes)
- **PAP availability:** No

Tizanidine

- **Description:** Muscle relaxant
- **Indication(s):** Acute and intermittent management of increased muscle tone associated with spasticity

- **Place in therapy (including guidelines recommendations if applicable):** Option for short-term (e.g., 2 to 3 days) treatment of pain/muscle spasm. Used in combination with other agents such as non-steroidal anti-inflammatory drugs (NSAIDS).
- **Potential interaction with ARVs:** No significant interactions expected
- **Coverage on other formularies:**
  - Florida Medicaid (Yes)
- **PAP availability:** No

Feedback received on muscle relaxants:

Feedback
This month we are asked to approve several muscle relaxers. This is a group of medications that again have little clinical data to support their chronic use. Perhaps they are effective in the short term but many of them are prescribed chronically. If we approve them, do we put limits on the duration of use? (Appelbaum)
I would agree that the muscle relaxants should be ordered for short term therapy, but it seems that some Pain Management specialists keep patients on for extended periods of time. My concern is the balance of maintaining the highest quality of life vs inadvertently putting people in harm's way. (Carscallen)
I'm ok with requiring PA's only for clinical reasons and would recommend them for CHRONIC opioid, muscle relaxers and benzodiazepine prescriptions because of misuse potential. We should allow opioids for acute pain and for malignancy diagnoses without a PA. (Appelbaum)
I would also agree with Jonathan's comments. (Carscallen)
I would echo/agree with Jonathan's comments. (Sension)
Methocarbamol and metaxalone This is a muscle relaxant. Cyclobenzaprine (muscle relaxant) is already on the ADAP formulary. Is there a need to add another option? Add only if this is a cost effective, better, or necessary treatment option. (Wall/Miami area pharmacists)
Tizanidine (from Krichbaum, Pain Management pharmacy specialist) **Recommendation: Add to Formulary** Reasoning: Currently on formulary there is only 1 agent for muscle spasticity, baclofen. Baclofen is often indicated 1st line for muscle spasticity; however, it requires renal dose adjustment at CrCl <80ml/min, and therefore therapeutic benefit may be unable to achieve in a patient with reduced kidney function. Tizanidine is indicated for muscle spasticity and while primarily renally eliminated, it is not renally dose adjusted until CrCL <25 mL/min. Early comparison studies between tizanidine and baclofen showed less muscle weakness with tizanidine.[1,2] Tizanidine has a different mechanism of action than baclofen for spasticity and therefore can be used as an adjunct in refractory spasticity. Notes: Tizanidine is an alpha 2 agonist and a structural analogue to clonidine so use caution in hypotensive or bradycardic patients. Tizanidine also causes more

sedation than baclofen, so use with caution in the elderly or with other CNS depressants. 1. Bass, B., et al. "Tizanidine versus baclofen in the treatment of spasticity in patients with multiple sclerosis." *Canadian journal of neurological sciences* 15.1 (1988): 15-19. 2. Groves, L., M. K. Shellenberger, and C. S. Davis. "Tizanidine treatment of spasticity: a meta-analysis of controlled, double-blind, comparative studies with baclofen and diazepam." *Advances in therapy* 15.4 (1998): 241-251.
Methocarbamol & Metaxalone (from Krichbaum, Pain Management pharmacy specialist) **Recommendation: Do not add to formulary** Reasoning: Systematic literature reviews for methocarbamol and metaxalone demonstrate minimal to no benefit vs placebo or other pharmacologic agents such as tizanidine or cyclobenzaprine for skeletal muscle spasms and/or pain.[3] The mechanism of actions for both drugs is unknown but has been shown to have NO direct effect on contractile mechanism of striated muscle, the nerve fiber, or the motor end plate.[4] 3. Chou, Roger, Kim Peterson, and Mark Helfand. "Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review." *Journal of pain and symptom management* 28.2 (2004): 140-175. 4. Metaxalone. In: Lexi-drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed March 2, 2022. Last updated Feb 12, 2022. http://online.lexi.com

Benzodiazepines

Clonazepam

- **Description:** benzodiazepine
- **Indication(s):** treatment of panic disorder, seizure disorders
- **Place in therapy (including guidelines recommendations if applicable):** Effective in reducing anxiety symptoms but long-term use generally not recommended due to risk of abuse and adverse effects. For seizure disorders, primarily used as an adjunctive therapy for myoclonic and atonic seizures.
- **Potential interaction with ARVs:** Levels may be increased by CYP 3A4 inhibitors such as protease inhibitors and cobicistat
- **Coverage on other formularies:**
  Florida Medicaid (_Yes_), Florida Blue (_Yes_)
- **PAP availability:** No

Temazepam

- **Description:** Benzodiazepine
- **Indication(s):** Short-term treatment of insomnia

- **Place in therapy (including guidelines recommendations if applicable):** Due to high abuse/dependence potential, should only be used for short-term. See American Family Physician review article on management of insomnia. https://www.aafp.org/afp/2017/0701/p29.html
- **Potential interaction with ARVs:** none expected
- **Coverage on other formularies:**
  - Florida Medicaid (Yes), Florida Blue (Yes)
- **PAP availability:** No

Feedback received on benzodiazepines

I'm ok with requiring PA's only for clinical reasons and would recommend them for CHRONIC opioid, muscle relaxers and benzodiazepine prescriptions because of misuse potential. We should allow opioids for acute pain and for malignancy diagnoses without a PA. (Appelbaum)
I would also agree with Jonathan's comments. (Carscallen)
I would echo/agree with Jonathan's comments. (Sension)

The following drugs were not added to ADAP either due to high cost (brexpiprazole, cariprazine, inclisarin), inability to order (tapentadol), or not recommended by HSFMW (fentanyl, oxycodone). HSMFW voting members are asked to vote on whether these drugs should be added to the AIDS Pharmaceutical Assistance (APA) formulary. The most recent APA formulary is here: APAFormulary.pdf (floridahealth.gov). Drugs added to this formulary should be for chronic use (e.g., duration of therapy > 6 months) and inclusion on this formulary allows Part B programs to purchase using LPAP funds.

Brexpiprazole

- **Description:** Atypical antipsychotic
- **Indication(s):** Major depressive disorder (in combination with antidepressants) and schizophrenia
- **Place in therapy (including guidelines recommendations if applicable):** Recommended option for adjunctive treatment of depression (along with antidepressants) or and schizophrenia
- **Potential interaction with ARVs:** Metabolized by CYP 3A4 and 2D6, PIs and cobicistat may increase levels
- **Coverage on other formularies:**
  - Florida Medicaid (No), Florida Blue (Yes)
- **PAP availability:** Yes

Cariprazine

- **Description:** Atypical antipsychotic
- **Indication(s):** Treatment of schizophrenia, bipolar disorder

- **Place in therapy (including guidelines recommendations if applicable):**
- **Potential interaction with ARVs:** Levels may be increased by protease inhibitors and cobicistat. Dosage reduction is necessary.
- **Coverage on other formularies:**
  - Florida Medicaid (Yes)
- **PAP availability:** Yes
  - PAP appears to have income limit of 600% of FPL- https://www.abbvie.com/patients/patient-assistance/program-qualification/vraylar-capsules-program-selection.html#myabbvie

Inclisiran

- **Description:** Injectable lipid lowering agents, inhibit pro-protein convertase subtilisin/kexin type 9 (PCSK9)
- **Indication(s):** Treatment of heterozygous or homozygous familial hypercholesterolemia or myocardial infarction prophylaxis, stroke prophylaxis, and to reduce risk of unstable angina requiring hospitalization in patients with established cardiovascular disease
- **Place in therapy (including guidelines recommendations if applicable):** Can be considered in combination with maximally tolerated statin therapy in patients who require additional LDL lowering. Ezetimibe is usually added to statin therapy first. See the 2018 ACC/AHA Guideline on Management of Blood Cholesterol at **https://www.jacc.org/guidelines/cholesterol**
- **Potential interaction with ARVs:** No interactions expected
- **Coverage on other formularies:**
  - Florida Medicaid (No)
- **PAP availability:** Yes
  - PAP appears to have income limit of 600% of FPL- https://www.abbvie.com/patients/patient-assistance/program-qualification/vraylar-capsules-program-selection.html#myabbvie

Fentanyl

- **Description: Opioid analgesic**
- **Indication(s):** Treatment of severe pain
- **Place in therapy (including guidelines recommendations if applicable):** Various guidelines exist regarding use of opioid analgesics in management of chronic non-cancer pain due to opioid epidemic and risk of abuse, overdose, and death. See https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm
- **Potential interaction with ARVs: Levels may be increased by PIs and cobicistat**
  - Florida Medicaid (Yes)
- **PAP availability:** No

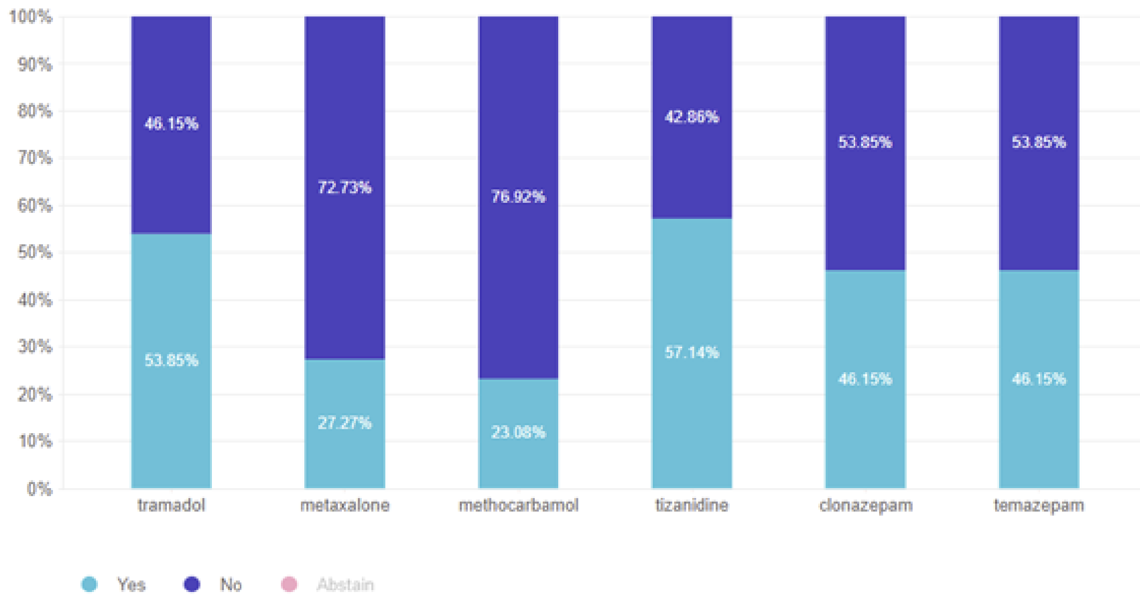
Oxycodone

- **Description:** Opioid analgesic
- **Indication(s):** Treatment of acute and chronic pain
- **Place in therapy (including guidelines recommendations if applicable):** Short acting formulation can be used for short-term (e.g., usually < 3 days) acute pain that is severe enough to require an opiate. Use of nonopioid analgesics should be maximized. Extended-release formulations should be reserved for patients who experience continuous pain despite the use of immediate release formulation for at least 1 week.
- **Potential interaction with ARVs:** Levels may be increased by protease inhibitors and cobicistat.
- **Coverage on other formularies:**
  - Florida Medicaid (Yes)
- **PAP availability:** No

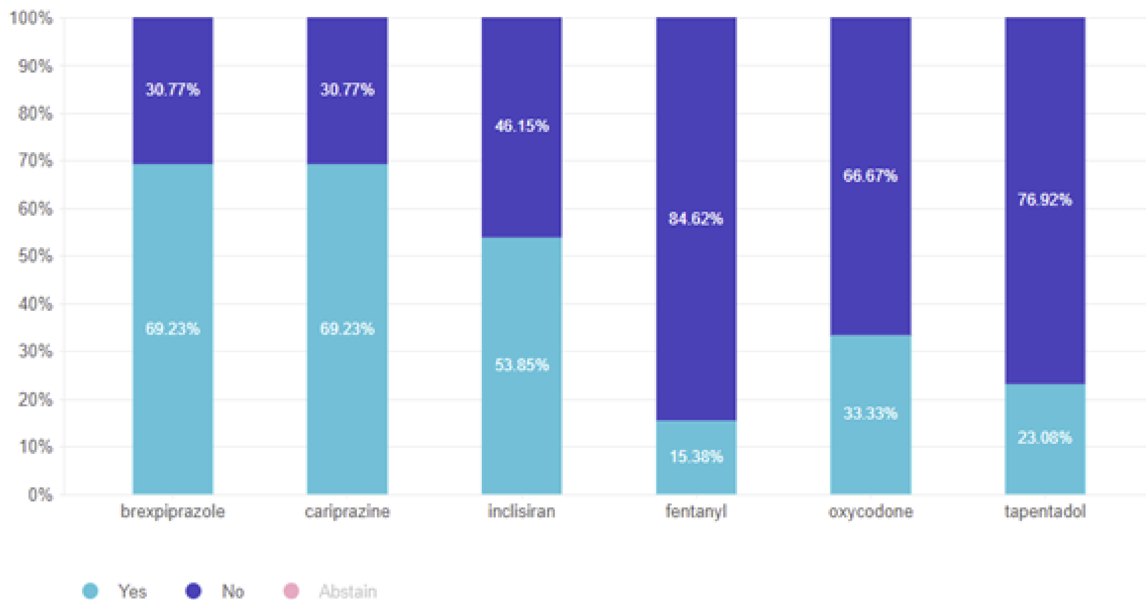
Tapentadol

- **Description: Opioid analgesic**
- **Indication(s):** Treatment of severe pain
- **Place in therapy (including guidelines recommendations if applicable):** Various guidelines exists regarding use of opioid analgesics in management of chronic non-cancer pain due to opioid epidemic and risk of abuse, overdose, and death. See https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm
- **Potential interaction with ARVs:** Levels may be increased by atazanavir due to UGT inhibition.
- **Coverage on other formularies:**
  - Florida Medicaid (No)
- **PAP availability:** No

Please see below for a voting summary:



*Abstentions are not counted to determine consensus



*Abstentions are not counted to determine consensus

SUMMARY

For a voted item to be approved, 50% of the voting members (8 of the 16) must vote. Consensus is then required. Abstentions are not counted towards consensus. Using these parameters, tramadol and tizanidine were recommended for addition to the ADAP Formulary. Brexpiprazole, cariprazine, and inclisiran were recommended for addition to the APA Formulary. Fentanyl was included on the list of drugs to consider for APA formulary addition; however, it is noted that this medication is already on the APA formulary.

Original information on the voting results was submitted to the HSMFW Co-Chairs by The AIDS Institute on May 25, 2022. Updated information was provided to the HSMFW Co-Chairs by The AIDS Institute on June 21, 2022.