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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	April 6, 2018
Subject:	Opioid Cough Medications	**Page:**	1 of 9

Last Review Date: December 8, 2023

Opioid Cough Medications

Description

Codeine with phenylephrine and promethazine, Codeine with promethazine, FlowTuss* (hydrocodone bitartrate, guaifenesin), Hycofenix (hydrocodone bitartrate, pseudoephedrine, guaifenesin), Hydromet (hydrocodone bitartrate, homatropine), Obredon* (hydrocodone bitartrate, guaifenesin), TussiCaps (hydrocodone polistirex, chlorphineramine polistirex), Tussigon (hydrocodone bitartrate, homatropine), Tussionex Pennkinetic (hydrocodone bitartrate, chlorpheniramine), Tuxarin ER, Tuzistra XR (codeine, chlorpheniramine), Zutripro (hydrocodone bitartrate, pseudoephedrine, chlorpheniramine)

* Prior authorization for the brand formulation applies only to formulary exceptions due to being a non-covered medication.

Background
Opioids, such as codeine and hydrocodone, are often used in prescription cough medications to suppress cough. Many formulations of opioid cough medications include other drugs that treat cough and cold including chlorpheniramine (an antihistamine), pseudophedrine (a decongestant), and guaifenesin (an expectorant). The FDA has drastically increased safety measures regarding opioids in the past few years, including opioid use in children. It is now required that a contraindication label be on all codeine products stating that these products should not be used in children less than 12 years of age. Additionally, the FDA recently held an

expert round table to address the use of cough and cold medications in individuals less than 18 years of age and ultimately decided that in most cases, the risks of using prescription opioid cough products outweigh the potential benefits. Specifically regarding cough medications, alternative medications should be utilized such as over the counter (OTC) cough suppressants like dextromethorphan and legend benzonatate products (1-2).

Regulatory Status
FDA approved indications: Opioid cough medications are indicated for the temporary relief of coughs nasal congestion, to loosen mucus and upper respiratory symptoms associated with allergy or the common cold (3-14).

Limitations of Use:
Boxed warning regarding the use of codeine in adolescents: Life-threatening respiratory depression and death have occurred in children who received codeine. Most of the reported cases occurred following tonsillectomy and/or adenoidectomy and many of the children had evidence of being an ultra-rapid metabolizer of codeine due to a CYP2D6 polymorphisms. Codeine containing compounds are contraindicated in children under 12 years of age (1-4, 12-13).

Boxed warning for all opioid products: Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol (3-14).

This policy does not apply to Robitussin AC or its therapeutic equivalents as it is excluded from coverage by the plan.

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Opioid cough medications may be considered **medically necessary** if the conditions indicated below are met.

Opioid cough medications may be considered **investigational** for all other indications.

Prior-Approval Requirements

Prior authorization is not required if prescribed by an oncologist and/or the member has paid pharmacy claims for an oncology medication(s) in the past 6 months

Age 18 years of age or older

Diagnosis

Patient must have the following:

Cough

AND ALL of the following:

1. **NO** dual therapy with other opioid analgesic(s)
2. Alternative treatment options have been ineffective, not tolerated or inadequate for controlling the patient's cough
    a. These include: Over-the-counter medications (dextromethorphan), and legend medications (benzonatate)
3. Prescriber agrees to assess patient for serotonin syndrome (see Appendix 1)
4. **NO** dual therapy with opioid addiction treatment or methadone
5. **NO** dual therapy with an anti-anxiety benzodiazepine(s)
    a. Alprazolam (Xanax)
    b. Clonazepam (Klonopin)
    c. Diazepam (Valium)
    d. Lorazepam (Ativan)
    e. Oxazepam (Serax)
    f. Chlordiazepoxide (Librium)
    g. Clorazepate dipotassium (Tranxene)

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

Age 12 years of age or older

Quantity

Drug Name	Quantity Limit
Codeine with phenylephrine and promethazine	32 ounces (960 mL) per 90 days **OR**
Codeine with promethazine	
Hydrocodone bitartrate, guaifenesin (generic FlowTuss)	
Hycofenix (hydrocodone bitartrate, pseudoephedrine, guaifenesin)	
Hydromet (hydrocodone bitartrate, homatropine)	
Hydrocodone bitartrate, guaifenesin (generic Obredon)	
Tussionex Pennkinetic (hydrocodone bitartrate, chlorpheniramine)	
Tuzistra XR (codeine, chlorpheniramine)	
Zutripro (hydrocodone bitartrate, pseudoephedrine, chlorpheniramine)	
TussiCaps (hydrocodone polistirex, chlorphineramine polistirex)	90 capsules/tablets per 90 days
Tussigon tablets (hydrocodone bitartrate, homatropine)	
Tuxarin ER tablets (codeine, chlorpheniramine)	

Prior – Approval Limits

Quantity

Drug Name	Quantity Limit

Codeine with phenylephrine and promethazine	64 ounces (1920 mL) per 90 days **OR**
Codeine with promethazine	
Hydrocodone bitartrate, guaifenesin (generic FlowTuss)	
Hycofenix (hydrocodone bitartrate, pseudoephedrine, guaifenesin)	
Hydromet (hydrocodone bitartrate, homatropine)	
Hydrocodone bitartrate, guaifenesin (generic Obredon)	
Tussionex Pennkinetic (hydrocodone bitartrate, chlorpheniramine)	
Tuzistra XR (codeine, chlorpheniramine)	
Zutripro (hydrocodone bitartrate, pseudoephedrine, chlorpheniramine)	
TussiCaps (hydrocodone polistirex, chlorphineramine polistirex)	180 capsules/tablets per 90 days
Tussigon tablets (hydrocodone bitartrate, homatropine)	
Tuxarin ER tablets (codeine, chlorpheniramine)	

Drug with approved MFE only	**Quantity**
FlowTuss	64 ounces (1920 mL) per 90 days
Obredon	64 ounces (1920 mL) per 90 days

Duration 6 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Opioids, such as codeine and hydrocodone, are often used in prescription cough medications to suppress cough. It is now required that a contraindication label be on all codeine products stating that these products should not be used in children less than 12 years of age. Additionally, the FDA recently held an expert round table to address the use of cough and cold medications in individuals less than 18 years of age and ultimately decided that in most cases, the risks of using prescription opioid cough products outweigh the potential benefits (1-2). Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of opioid cough medications while maintaining optimal therapeutic outcomes.

References

1. FDA News Release. FDA acts to protect kids from serious risks of opioid ingredients contained in some prescription cough and cold products by revising labeling to limit pediatric use. January 11, 2018. Website: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm592109.htm.
2. FDA Drug Safety Communication: FDA requires labeling changes for prescription opioid cough and cold medicines to limit their use to adults 18 years and older. January 11, 2018. Website: https://www.fda.gov/Drugs/DrugSafety/ucm590435.htm.
3. Codeine with phenylephrine and promethazine [package insert]. Baudette, MN: ANI Pharmaceuticals, Inc.; August 2017.
4. Codeine with promethazine [package insert]. Baudette, MN: ANI Pharmaceuticals, Inc.; August 2017.
5. FlowTuss [package insert]. San Antonio, TX: Mission Pharmacal Co.; January 2017.
6. Hycofenix [package insert]. San Antonio, TX: Mission Pharmacal Co.; January 2017.
7. Hydromet [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; January 2017.
8. Obredon [package insert]. Ashland, VA: ABER Pharmaceuticals, LLC.; January 2017.
9. TussiCaps [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals LLC.; September 2014.
10. Tussionex Pennkinetic [package insert]. Smyrna, GA: UCB, Inc.; January 2017.
11. Tussigon [package insert]. New York, NY: Pfizer Inc.; February 2018.
12. Tuxarin ER [package insert]. Irvine, CA: Nexgen Pharma, Inc.; January 2017.
13. Tuzistra XR [package insert]. Berwyn, PA: Vernalis Therapeutics, Inc.; August 2017.
14. Zutripro [package insert]. Morristown, NJ: Cypress, Pharmaceutical, Inc.; January 2017.

Policy History

Date	Action
April 2018	Addition to PA
June 2018	Annual review
February 2019	Addition of Tuxarin ER tablets
March 2019	Annual review and reference update
December 2019	Moved brand Obredon and Flowtuss to MFE with PA only
March 2020	Annual review
September 2021	Annual review
September 2022	Annual review
September 2023	Annual review
December 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.

Appendex 1 - List of Serotonergic Medications

Selective Serotonin Reuptake Inhibitors (SSRIs)

paroxetine	Paxil, Paxil CR, Pexeva, Brisdelle
fluvoxamine	Luvox, Luvox CR
fluoxetine	Prozac, Prozac Weekly, Sarafem, Selfemra, Symbyax
sertraline	Zoloft
citalopram	Celexa
escitalopram	Lexapro

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

venlafaxine	Effexor XR
desvenlafaxine	Pristiq, Khedezla
duloxetine	Cymbalta
milnacipran	Savella

Tricyclic Antidepressants (TCAs)

amitriptyline	No brand name currently marketed
desipramine	Norpramin
clomipramine	Anafranil
imipramine	Tofranil, Tofranil PM
nortriptyline	Pamelor, Aventyl
protriptyline	Vivactil
doxepin	Zonalon, Silenor
trimipramine	Surmontil

Monoamine Oxidase Inhibitors (MAOIs)

isocarboxazid	Marplan
phenelzine	Nardil
selegiline	Emsam, Eldepryl, Zelapar
tranylcypromine	Parnate

Other Psychiatric Medicines

amoxapine	No brand name currently marketed
maprotiline	No brand name currently marketed
nefazodone	No brand name currently marketed
trazodone	Oleptro
buspirone	No brand name currently marketed
vilazodone	Viibryd
mirtazapine	Remeron, Remeron Soltab
llthium	Lithobid

Migraine Medicines

almotriptan	Axert
frovatriptan	Frova
naratriptan	Amerge
rizatriptan	Maxalt, Maxalt-MLT
sumatriptan	Imitrex, Imitrex Statdose, Alsuma, Sumavel Dosepro, Zecuity, Treximet
zolmitriptan	Zomig, Zomig-ZMT

Antiemetics

ondansetron	Zofran, Zofran ODT, Zuplenz
granisetron	Kytril, Sancuso
dolasetron	Anzemet
palonosetron	Aloxi

Other Serotonergic Medicines

dextromethorphan	Bromfed-DM, Delsym, Mucinex DM, Nuedexta
linezolid	Zyvox
cyclobenzaprine	Amrix
methylene blue	
St. John’s wort	
tryptophan	