TEXAS Health and Human Services

Medicaid Drug Use Criteria

Hydrocodone Bitartrate/Hydrocodone Polistirex

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Information on indications for use or diagnosis is assumed to be unavailable. All criteria may be applied retrospectively; prospective application is indicated with an asterisk [*]. The information contained is for the convenience of the public. The Texas Health and Human Services Commission is not responsible for any errors in transmission or any errors or omissions in the document.

Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.

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1 Dosage

In August 2014, the Drug Enforcement Administration published a final ruling to reschedule hydrocodone combination products from Schedule III to Schedule II due to their high potential of abuse. Effective October 6, 2014, all hydrocodone combination products will be Schedule II. Single-entity hydrocodone products were already classified as Schedule II.

Hydrocodone bitartrate, as combination therapy, is FDA-approved as an opioid antitussive and analgesic used for the relief of cough and moderate to moderately severe pain. Hydrocodone bitartrate is available in fixed combinations with non-opiate drugs (e.g., acetaminophen, acetylsalicylic acid, chlorpheniramine, guaifenesin, ibuprofen, phenylephrine, pseudoephedrine). This drug should be given in the smallest effective dose and as infrequently as possible to minimize the development of tolerance and physical dependence.[1-4] Hydrocodone bitartrate has recently become available in the United States as a single entity, extended-release capsule (Zohydro® ER),[1-5] formulated with abuse-deterrent beads. This hydrocodone product is FDA-approved for managing pain requiring daily, long-term, around-the-clock opiate therapy not responsive to other treatment options. Hydrocodone bitartrate extended-release tablets with abuse deterrent properties (Hysingla® ER) have also been FDA-approved to manage severe pain requiring chronic, around-the-clock opiate treatment unresponsive to other treatment regimens.[1-4, 6]

The use of hydrocodone when prescribed by multiple physicians will be reviewed.

Hydrocodone/acetaminophen combination products containing greater than 325 mg of acetaminophen have been discontinued due to increased potential for liver toxicity.

1.1 Adults

Analgesic hydrocodone dosages should be determined based on pain severity and patient response/ tolerance. In individuals with severe pain or those who have become tolerant to the analgesic effects of hydrocodone, it may be necessary to exceed the usual dosage. Reduced hydrocodone dosages are indicated in high-risk patients and the elderly. The maximum daily dosage for the acetaminophen/ hydrocodone combination is restricted by the maximum acetaminophen dose of 4 g daily to limit the risk of hepatic damage and severe hypersensitivity reactions associated with acetaminophen use.[1-13]

Hydrocodone exerts antitussive effects by directly acting on receptors in the cough center at dosages lower than those required for analgesia.[1-4]

Recommended adult hydrocodone dosages as monotherapy and combination therapy are summarized in Table 1 and Table 2. Dosages exceeding these recommendations will be reviewed.

Table 1: Recommended Adult Hydrocodone Dosages: Monotherapy

Drug / Indication	Dosage Forms / Strengths	Usual Dosage Regimen	Maximum Recommended Dose
Analgesic hydrocodone extended-release capsule (Zohydro® ER)	10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg extended-release, abuse-deterrent capsules	20 mg to 100 mg every 12 hours	maximum dose not defined; doses should be titrated per patient to maximize analgesia and minimize adverse drug reactions
Analgesic hydrocodone extended-release tablet (Hysingla® ER)	20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg, 120 mg extended-release, abuse-deterrent tablets	20 mg to 120 mg every 24 hours	maximum dose not defined; doses should be titrated per patient to maximize analgesia and minimize adverse drug reactions

Table 2: Recommended Adult Hydrocodone Dosages: Combination Therapy

Drug / Indication	Dosage Forms / Strengtl	Usual Dosage Regimen	Maximum Recommended Dos
Analgesic hydrocodone bitartrate/ acetaminophen (Lortab®, Norco®, Vicodin®, generics)	5 mg/300 mg, 7.5 mg/30(mg, 10 mg/300 mg, 2.5 mg/325 mg, 5 mg/325 mg 7.5 mg/325 mg, 10 mg/325 mg tablets; 7.5 mg/325 mg/15 ml or 10 mg/325 mg/15 ml solutio 10 mg/300 mg/15 ml elixi	2.5-10 mg every 4-6 hours as needed	60 mg/4000 mg daily*
Analgesic hydrocodone bitartrate/ ibuprofen (Vicoprofen®, Ibudone®, Reprexain®, generics)	2.5 mg/200 mg, 5 mg/200 mg, 7.5 mg/200 mg, 10 mg/200 mg tablets	2.5-10 mg every 4-6 hours as needed	5 tablets per day [maximum hydrocodon dose (10mg/200 mg): 50 mg daily]**
Antitussive hydrocodone bitartrate (in various combinations)	2.5 mg/5 ml or 5 mg/5 ml solution or 5 mg, 10 mg a tablet in combination products	5 mg every 4-6 hours as needed	single dose: 15 mg total daily dose: 20 mg to 30 mg
Antitussive hydrocodone bitartrate/ homatropine (Hydromet®, generics)	5 mg/1.5 mg/5ml solution or 5 mg/1.5 mg tablet	5 mg every 4-6 hours as needed	30 mg daily

Drug / Indication	Dosage Forms / Strengtl	Usual Dosage Regimen	Maximum Recommended Dos
Antitussive hydrocodone polistirex/ chlorpheniramine polistirex (TussiCaps®)	5 mg/ 4 mg, 10 mg/ 8 mg extended-release capsules	1 capsule every 12 hours	20 mg/16 mg every 24 hours
Antitussive hydrocodone polistirex/ chlorpheniramine polistirex (Tussionex® Pennkinetic®, generics)	10 mg/8 mg+/5 ml extended-release oral suspension	10 mg/8 mg+ every 12 hours	20 mg/16 mg+ daily

- * Dosage limit based on maximum acetaminophen daily dose; varies by product
- ** Short-term use (less than 10 days) recommended
- + Dosed as hydrocodone bitartrate and chlorpheniramine maleate

1.2 Pediatrics

Hydrocodone is not FDA-approved for use as an antitussive in pediatric patients younger than 6 years of age as safety and efficacy have not been established. For analgesia, safety and efficacy of the hydrocodone/acetaminophen combination have not been established in children younger than 2 years of age, while the hydrocodone/ibuprofen combination is not indicated for use in children younger than 16 years of age due to lack of safety and efficacy data.[1-4] The hydrocodone single-entity products, Zohydro® ER and Hysingla® ER are not FDA-approved in the pediatric population (less than 18 years of age) as safety and efficacy in this age group have not been established.[5, 6]

Analgesic hydrocodone dosages should be determined based on pain severity and patient response/ tolerance. In individuals with severe pain or those who have become tolerant to the analgesic effects of hydrocodone, it may be necessary to exceed the usual dosage. Reduced hydrocodone dosages are indicated in very young patients. Like adult patients, the maximum daily dosage for the acetaminophen/ hydrocodone combination is restricted by the maximum acetaminophen dose (as determined by age and weight – see Table 3) to limit the risk of hepatic damage and severe hypersensitivity reactions associated with acetaminophen use.[1-4]

Recommended pediatric hydrocodone dosages as combination therapy are summarized in Table 3. Dosages exceeding these recommendations will be reviewed.

Table 3. Recommended Pediatric Hydrocodone Dosages: Combination Therapy[1-4, 7, 8]

Drug / Indication	Usual Dosage Regimen	Maximum Recommended Dose
Analgesic hydrocodone bitartrate/acetaminophen (APA (Lortab®, Norco®, Vicodin®, generics)	~2-3 years of age (12 to 15 kg): ~1.875 mg every 4-6 hours as needed	750 mg daily (APAP+)*
	~4-6 years of age (16 to 22 kg): 2.5 mg every 4-6 hours as needed	1 g daily (APAP)*
	~7-9 years of age (23 to 31 kg): ~3.75 mg every 4-6 hours as needed	1.5 g daily (APAP)*
	~10-13 years of age (32 to 45 kg): 5 mg every 4-6 hours as needed	2 g daily (APAP)*
	Greater than or equal to 14 years of age (greater than or equal to 46 kg) ~7.5 mg every 4-6 hours as needed	3 g daily (APAP)*
Analgesic hydrocodone bitartrate/ibuprofen (Vicoprofen®, Ibudone®, Reprexain®, generics)	16 years and older: 2.5-10 mg/200 mg every 4-6 hours as needed	5 tablets daily**
Antitussive hydrocodone polistirex/ chlorpheniramine polistirex (TussiCaps®, Tussionex® Pennkinetic®, generics)	6-11 years of age: 5 mg/4mg every 12 hours	10 mg/8 mg daily
	Greater than or equal to 12 years of age: 10 mg/8 mg every 12 hours	20 mg/16 mg daily

- + APAP = acetaminophen
- * Dosage limit based on maximum acetaminophen daily dose
- ** Short-term use (less than 10 days) recommended

2 Duration of Therapy

When used as an analgesic, there is no basis for limiting hydrocodone therapy duration as hydrocodone may be utilized to manage chronic painful conditions as well as acute pain events. As an antitussive, hydrocodone is prescribed for a limited duration to manage cough and upper respiratory symptoms associated with the common cold or allergies in adults and pediatric patients 6 years of age and older. In isolated cases, hydrocodone may be prescribed for an extended time period in those adult patients requiring nonspecific therapy for a chronic, nonproductive cough, such as advanced cancer. In all patients, the smallest effective hydrocodone dose should be administered as infrequently as possible to minimize the development of tolerance and physical dependence.[1-8, 10-12]

3 Duplicative Therapy

Gabapentin dosage formulations are not interchangeable due to variations in chemical forms and pharmacokinetic properties. Concurrent administration of two or more gabapentin formulations is not recommended due to lack of additional therapeutic benefit and increased risk of adverse effects. Patient profiles containing concomitant prescriptions for two or more gabapentin dosage formulations for more than two months will be reviewed.

4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for hydrocodone are summarized in **Table 4**. Only those drug-drug interactions classified as clinical significance level 1/contraindicated or those considered life-threatening which have not yet been classified will be reviewed:

Table 4. Hydrocodone Drug-Drug Interactions[1-8]

Interacting Drug	Interaction	Recommendation	Clinical Significance Level*
anticholinergics (e.g., antidiarrheals	co-administration may lead increased risk of urination retention, severe constipation, including paralytic ileus, especially with chronic use, and CNS depression due to additive anticholinergic effects	observe for chronic constipation, urinary retention, and CNS depression; adjust doses and/or discontinue therapy as needed	2-major (CP)
CNS depressants (e.g., anxiolytics, sedatives, tricyclic antidepressants)	adjunctive administration may result in additive CNS and respiratory depression	monitor for additive pharmacologic/adverse effects and reduce drug dosages as necessary	major (DrugReax) 2-major (CP)
CYP2D6 inhibitors (e.g., amiodarone, fluoxetine, paroxetine, bupropion, ritonavir	hydrocodone is converted to hydromorphone, an active metabolite that also possesses analgesic effects through CYP2D6; concurrent administration with CYP2D6 inhibitors may result in increased hydrocodone serum levels and reduced hydromorphone levels and the potential for enhanced or diminished pharmacologic/ adverse effects	monitor for effective analgesia and signs/symptoms of adverse effects (e.g., enhanced sedation, respiratory depression); modify doses as necessary	3-moderate (CP)
CYP3A4 inducers (e.g., rifampin, barbiturates)	adjunctive use may result in decreased hydrocodone plasma levels/reduced therapeutic effects, including withdrawal, as hydrocodone is CYP3A4 substrate	monitor for effective therapeutic effects; modify doses as necessary	major (DrugReax) 3-moderate (CP)
CYP3A4 inhibitors	concurrent administration with CY3A4 inhibitors may result in increased hydrocodone serum levels and the potential for enhanced pharmacologic/ adverse effects through inhibition of CYP3A4-mediated hydrocodone metabolism	monitor for effective analgesia and signs/symptoms of adverse effects (e.g., enhanced sedation, respiratory depression); modify doses as necessary	major (DrugReax) 2-major (CP)

Interacting Drug	Interaction	Recommendation	Clinical Significance Level*
Gabapentin	potential for decreased hydrocodone peak concentrations and AUC with concomitant gabapentin-hydrocodone administration in dose-dependent fashion; minor increases in gabapentin AUC	observe patients for decreased hydrocodone efficacy or additive drowsiness	minor (DrugReax) 3-moderate (CP)
monoamine oxidase inhibitors (MAOIs)	combined administration may result in severe, unpredictable additive effects	although no specific adverse interactions have been reported with the hydrocodone-MAOI combination, hydrocodone should not be administered in patients who have received MAOIs within 14 days	major (DrugReax) 2-major (CP)
opiate agonist/ antagonists (OAAs) (e.g., buprenorphine, pentazocine)	concomitant administration may result in partial blockade of hydrocodone pharmacologic effects and may precipitate a withdrawal syndrome in some patients requiring chronic hydrocodone therapy; antagonist effects are more likely to occur when OAAs used concurrently with low to moderate doses of a pure opioid agonist; adjunctive therapy may be required in some instances, which may result in additive CNS depressant, respiratory, and hypotensive effects	patients requiring concurrent therapy with hydrocodone and a mixed OAA should be monitored for enhanced or attenuated pharmacologic effects, which may necessitate hydrocodone dosage adjustments and/or pharmacotherapy modifications	major (DrugReax) 2-major (CP)
opiate agonists (OAs)	concurrent administration of pure OAs and narcotic analgesics like hydrocodone, or administration of OAs within 7 to 10 days of narcotic analgesic therapy may induce an acute abstinence syndrome	unless clinically significant respiratory depression is present, OAs should not be administered concurrently with hydrocodone	contraindicated (DrugReax) 2-major (CP)

- *CP = Clinical Pharmacology
- AUC = area under the curve

- CNS = central nervous system

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