BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.70.058

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	December 18, 2016
Subject:	Butalbital Analgesics	**Page:**	1 of 7

Last Review Date: December 13, 2024

Butalbital Analgesics

Description

Allzital (butalbital-acetaminophen), butalbital-aspirin-caffeine, butalbital-aspirin-caffeine-codeine, butalbital-acetaminophen, butalbital-acetaminophen-caffeine, butalbital-acetaminophen-caffeine-codeine, Vanatol LQ (butalbital-acetaminophen-caffeine liquid oral solution)

Background
Butalbital containing products are non-opioid analgesics that contain a combination of different drug products indicated for the relief of the symptom complex of tension (or muscle contraction) headache pain. Butalbital is a short to intermediate-acting barbiturate that works in concert with acetaminophen, an antipyretic non-salicylate agent, aspirin, a pain-relieving NSAID, and caffeine, a stimulant that works in the CNS, to decrease pain via a mechanism that isn't well understood. Butalbital is a habit-forming drug that potentiates the effects of other commonly abuse drugs or substances like alcohol. Caffeine might help increase vasodilation and smooth muscle relaxation, while butalbital is thought to help balance the CNS stimulation caused by caffeine and produces depressant effects (1).

The following two statements apply only to butalbital products containing codeine:
Maximum daily limit of any combination of opioid medications without a PA is 90 MME/day.
Maximum daily limit of any combination of opioid medications with a PA is 200 MME/day.

Regulatory Status
FDA-approved indication: Butalbital containing products are used in the relief of the symptom complex of tension or muscle contraction headaches (2-8).

Frequent use of acute medications is generally thought to cause medication-overuse headache. To decrease the risk of medication-overuse headache ("rebound headache" or "drug-induced headache") many experts limit acute therapy to two headache days per week on a regular basis. Based on concerns of overuse, medication-overuse headache, and withdrawal, the use of butalbital-containing analgesics should be limited and carefully monitored. The Allzital limit is set to the maximum of 12 doses per day for acute treatment of 8 headaches per month as this product contains less butalbital than other products. The quantity limit for all other butalbital products is set to the maximum of 6 doses per day for acute treatment of 8 headaches per month (7).

Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product. Instruct patients to look for acetaminophen or APAP on package labels and not to use more than one product that contains acetaminophen. (5-6).

The FDA has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for all opioid analgesics intended for outpatient use to ensure that the benefits of these drugs continue to outweigh the risks. The Opioid Analgesic REMS is a strategy to reduce the risk of abuse, misuse, addiction, overdose, and deaths due to prescription opioid analgesics. Prescribers should counsel patients and caregivers about the use of naloxone for opioid overdose (9).

The safety and effectiveness of Allzital, butalbital-acetaminophen, butalbital-acetaminophen-caffeine, and Vanatol LQ in patients less than 12 years of age have not been established. The safety and effectiveness of butalbital-acetaminophen-caffeine-codeine, butalbital-aspirin-caffeine, and butalbital-aspirin-caffeine-codeine in patients less than 18 years of age have not been established (2-8).

Related policies

5-HT1 Agonists, Dihydroergotamine Nasal Sprays, Elyxyb, Maxalt, Migraine CGRP Antagonists IV, Migraine CGRP Antagonists Nasal, Migraine CGRP Antagonists Oral, Migraine CGRP Antagonists SC, Migraine Powders

Policy

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

Butalbital containing analgesics may be considered **medically necessary** if the conditions indicated below are met.

Butalbital containing analgesics may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

1. Tension or muscle contraction headaches

Allzital, butalbital-acetaminophen and butalbital-acetaminophen-caffeine

AND ALL of the following:
- a. 12 years of age or older
- b. **NO** previous or current liver function concerns or cirrhosis
- c. Prescriber agrees to counsel regarding concurrent use of a product(s) containing acetaminophen

Vanatol LQ

AND ALL of the following:
- a. 12 years of age or older
- b. Inadequate response to generic butalbital-containing products
- c. **NO** previous or current liver function concerns or cirrhosis
- d. Prescriber agrees to counsel regarding concurrent use of a product(s) containing acetaminophen

Butalbital-acetaminophen-caffeine-codeine, butalbital-aspirin-caffeine, and butalbital-aspirin-caffeine-codeine

AND ALL of the following:
- a. 18 years of age or older
- b. **NO** previous or current liver function concerns or cirrhosis
- c. If acetaminophen containing product**:**
  - i. Prescriber agrees to counsel regarding concurrent use of a product(s) containing acetaminophen
- d. If codeine containing product:

i. **NO** dual therapy with an opioid addiction therapy or methadone
ii. Prescriber agrees to evaluate patient's response to therapy before changing dose or adding additional opioid medications
iii. Prescriber agrees to participate in the Opioid Analgesic REMS program and to monitor for abuse, misuse, addiction, and overdose and discontinue if necessary (*https://opioidanalgesicrems.com*)
iv. **NO** cumulative morphine milligram equivalent (MME) over 200 MME/day
(e.g., https://www.mdcalc.com/morphine-milligram-equivalents-mme-calculator, https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf, https://www.cdc.gov/opioids/providers/prescribing/app.html)

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

Quantity

- **For butalbital products <u>with codeine</u> only**: Maximum daily limit of any combination of opioid medications without a PA is 90 MME/day. Patients using dual therapy with opioid addiction treatment or methadone in the last 30 days will not be eligible for Pre-PA allowance.

AGE 12 YEARS OF AGE AND OLDER	Quantity Limits
Allzital (butalbital 25 mg / APAP 325 mg)	144 tabs per 90 days **OR**
Bupap (butalbital 50mg / APAP 300mg)	
Tencon (butalbital 50mg / APAP 325mg)	
Fioricet (butalbital 50mg / APAP 300mg / caffeine 40mg)	
Esgic (butalbital 50mg / APAP 325mg / caffeine 40mg)	
Esgic Plus (butalbital 50mg / APAP 500mg / caffeine 40mg)	
Vanatol LQ (butalbital / APAP / caffeine solution)	2,160 mL per 90 days

<u>OR</u>

AGE 18 YEARS OF AGE AND OLDER	Quantity Limits
Allzital (butalbital 25 mg / APAP 325 mg)	144 tabs per 90 days (1.6 units per day for **codeine-containing** products)
Bupap (butalbital 50mg / APAP 300mg)	
Tencon (butalbital 50mg / APAP 325mg)	
Fioricet (butalbital 50mg / APAP 300mg / caffeine 40mg)	

Esgic (butalbital 50mg / APAP 325mg / caffeine 40mg)	
Esgic Plus (butalbital 50mg / APAP 500mg / caffeine 40mg)	
Fiorinal (butalbital 50mg / aspirin 325mg / caffeine 40mg)	
Fiorinal with **Codeine*** (butalbital / aspirin / caffeine / **codeine**)	
Fioricet with **Codeine*** (butalbital / APAP/ caffeine / **codeine**)	
Vanatol LQ (butalbital / APAP/ caffeine solution)	2,160 mL per 90 days

***For butalbital products <u>with codeine</u> only**: Maximum daily limit of any combination of opioid medications without a PA is 90 MME/day.

Prior - Approval Limits

Quantity

- **For butalbital products <u>with codeine</u> only**: Maximum daily limit of any combination of opioid medications with a PA is 200 MME/day.

Medication / Strength	Quantity Limit
Allzital (butalbital 25 mg / APAP 325 mg)	288 tabs per 90 days **OR**
Bupap (butalbital 50mg / APAP 300mg)	216 tabs per 90 days **OR**
Tencon (butalbital 50mg / APAP 325mg)	216 tabs per 90 days **OR**
Fioricet (butalbital 50mg / APAP 300mg / caffeine 40mg)	216 tabs per 90 days **OR**
Esgic (butalbital 50mg / APAP 325mg / caffeine 40mg)	216 tabs per 90 days **OR**
Esgic Plus (butalbital 50mg / APAP 500mg / caffeine 40mg)	216 tabs per 90 days **OR**
Fiorinal (butalbital 50mg / aspirin 325mg / caffeine 40mg)	216 tabs per 90 days **OR**
Vanatol LQ (butalbital / APAP / caffeine solution)	3,240 mL per 90 days

Capsules ≤ 200 MME/day

Medication / Strength	Morphine Milligram Equivalent (MME) <u>per unit</u>
Fiorinal with **Codeine*** (butalbital / aspirin / caffeine / **codeine**)	4.5 MME
Fioricet with **Codeine*** (butalbital / APAP / caffeine / **codeine**	4.5 MME

***For butalbital products <u>with codeine</u> only:** Maximum daily limit of any combination of opioid medications with a PA is 200 MME/day**.**

Duration 6 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Butalbital is a short to intermediate-acting barbiturate that causes CNS depression. Caffeine is a CNS stimulant that is thought to help increase vasodilation (smooth muscle relaxation). Acetaminophen might help decrease pain sensation in the peripheral nervous system by blocking those signals. Aspirin is an NSAID that decreases pain and swelling by blocking prostaglandins. Butalbital-containing analgesics are FDA approved for the treatment of the symptom complex of tension or muscle contraction headache. These products can have pronounced sedative effects and butalbital is habit-forming (1-8).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of butalbital-containing analgesics, while maintaining optimal therapeutic outcomes.

References

1. Bryczkowski, C., Geib, A.J. Combined Butalbital/Acetaminophen/Caffeine Overdose: Case Files of the Robert Wood Johnson Medical School Toxicology Service. Journal of Medical Toxicology, Sept. 26, 2012.
2. Vanatol LQ [package insert]. Arlington, TX GM Pharmaceuticals, Inc.; November 2019.
3. Fiorinal [package insert]. Madison, NJ: Allergan USA, Inc.; April 2021.
4. Fiorinal with Codeine [package insert]. Madison, NJ: Allergan USA, Inc.; April 2021.
5. Fioricet [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; January 2021.
6. Fioricet with Codeine [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc.; March 2021.
7. Allzital [package insert]. Canton, MS: Larken Laboratories, Inc.; June 2022.
8. Beithon J, Gallenberg M, Johnson K, et al. Institute for Clinical Systems Improvement. Diagnosis and Treatment of Headache. https://www.icsi.org/guidelines__more/catalog_guidelines_and_more/catalog_guidelines/catalog_neurological_guidelines/headache. Updated January 2013.
9. Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). Drug Safety and Availability: U.S. Food & Drug Administration. September 19, 2018.

Policy History

Date	Action
December 2016	New addition to PA

March 2017	Addition of age requirements to the Pre – PA Allowance
June 2017	Annual review
June 2017	Addition of no dual therapy with methadone
September 2017	Annual review
March 2018	Annual editorial review and reference update
October 2018	Addition of Opioid Analgesic REMS requirement to codeine-containing products
November 2018	Annual review and reference update. Addition of Opioid Analgesic REMS link per SME
March 2019	Annual review
December 2019	Annual review. Addition of requirement of no cumulative MME over 300. Revised requirement for prescriber to agree to counsel regarding using concurrent APAP medications
March 2020	Annual review and reference update
June 2020	Annual review
March 2021	Annual review and reference update
September 2021	Annual review
December 2021	Per FEP, for codeine-containing products: decreased the requirement that cumulative MME cannot exceed 200 MME/day from 300 MME/day; added requirement “Prescriber agrees to evaluate patient’s response to therapy before changing dose or adding additional opioid medications”; and revised PA quantity chart to remove quantity limits and add MME per unit. Added 90 MME/day PA limit for patients 17 and under.
February 2022	Updated the REMS link. Per FEP: added “Prescribers should counsel patients and caregivers about the use of naloxone for opioid overdose” under regulatory status, and added MME calculating links
March 2022	Annual review and reference update
March 2023	Annual review. Changed policy number to 5.70.058
September 2023	Annual review
December 2023	Annual review
March 2024	Annual review
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.