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Coverage Policy Number **IP0251**

Compounded Medications

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for **Compounded Medications**, including the following:

- Compounded naltrexone implants
- Non-FDA approved hormone pellets
    - Compounded testosterone pellets
    - Compounded estrogen and estrogen derivative pellets (for example, estradiol, estriol, estrone)
    - Compounded progesterone and progesterone derivative pellets (for example, progestin)

Bulk chemicals used in compounded products do not meet the definition of a Prescription Drug in Cigna standard benefit plans. All benefit plan exclusions also apply. Please refer to the applicable benefit plan document to determine benefit availability and the terms and conditions of coverage.

Mixing, diluting, or repackaging an FDA approved pharmaceutical product as described in the label is considered an approved manipulation of the product and is not subject to this coverage policy.

Medical Necessity Criteria

Compounded Medications are considered medically necessary when ALL the following criteria are met:

1. There is documentation the individual has had an inadequate response, contraindication, or is intolerant to ALL FDA-approved commercially available pharmaceutical alternatives that require a prescription, and approved for the same route of administration.
2. The compound must contain at least one FDA-approved prescription ingredient that is not otherwise excluded in the plan benefit language.
3. Compounded drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products must be a distinguishable variation that is medically necessary for a particular patient.
4. The compound does not contain ingredients that have been removed from the market for safety or efficacy reasons (refer to FDA Exemption List).
5. The compound contains only human, pharmaceutical grade ingredients.
6. Components of compound formula are safe and effective for the prescribed purpose as evidenced by **EITHER** of the following (A or B):
    A. Support from results of at least two different controlled clinical studies published in peer-reviewed English language, biomedical journals or appropriate compendia, American Hospital Formulary Service (AHFS)
    B. The prescription ingredient's FDA-approved indication

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Compounded Medications are considered medically necessary for continued use when initial criteria are met.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered not medically necessary.

Compounded Hormone pellets are not FDA-approved and are considered experimental, investigational or unproven for ANY use (this list may not be all inclusive):

1. Compounded testosterone pellets
2. Compounded estrogen and estrogen derivative pellets (for example, estradiol, estriol, estrone)
3. Compounded progesterone and progesterone derivative pellets (for example, progestin)

Compounded naltrexone implants are not FDA-approved and are considered experimental, investigational, for unproven or ANY use.

The following medications are considered experimental, investigational, or unproven in any compounded formulation for topical use because their use in compounds is not approved by the FDA (this list may not be all inclusive):

Amantadine	Ketorolac
Amitriptyline	Levocetirizine

Apomorphine	Mefenamic acid
Baclofen	Meloxicam
Carbamazepine	Methadone
Clomipramine	Mometasone furoate (including nasal irrigation solutions)
Cyclobenzaprine	Morphine
Dexamethasone	Nabumetone
Duloxetine	Naltrexone
Diclofenac	Orphenadrine
Flurbiprofen	Oxycodone
Fluticasone propionate (including nasal irrigation solutions)	Oxytocin
Fluoxetine	Papaverine
Gabapentin	Pentoxifylline
Human chorionic gonadotropin	Piroxicam
Hyaluronic acid	Promethazine
Hydrocodone	Sumatriptan
Hydromorphone	Tamoxifen
Ketamine	Tizanidine
Ketoprofen	Tramadol

APPENDIX

FDA EXEMPTION LIST

Per Code of Federal Regulations Title 21, Volume 4, Section 216.24, the following drug products were withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective. The following drug products may not be compounded under the exemptions provided by section 503A(a) or section 503B(a) of the Federal Food, Drug, and Cosmetic Act:

Compound Name	Comments
Adenosine phosphate	All drug products containing adenosine phosphate
Adrenal cortex	All drug products containing adrenal cortex
Alatrofloxacin mesylate	All drug products containing alatrofloxacin mesylate
Aminopyrine	All drug products containing aminopyrine
Astemizole	All drug products containing astemizole
Azaribine	All drug products containing azaribine
Benoxaprofen	All drug products containing benoxaprofen
Bithionol	All drug products containing bithionol
Bromfenac sodium	All drug products containing bromfenac sodium (except ophthalmic solutions)
Bromocriptine mesylate	All drug products containing bromocriptine mesylate for prevention of physiological lactation
Butamben	All parenteral drug products containing butamben
Camphorated oil	All drug products containing camphorated oil
Carbetapentane citrate	All oral gel drug products containing carbetapentane citrate
Casein, iodinated	All drug products containing iodinated casein
Cerivastatin sodium	All drug products containing cerivastatin sodium
Chloramphenicol	All oral drug products containing chloramphenicol
Chlorhexidine gluconate	All tinctures of chlorhexidine gluconate formulated for use as a patient preoperative skin preparation.
Chlormadinone acetate	All drug products containing chlormadinone acetate
Chloroform	All drug products containing chloroform
Cisapride	All drug products containing cisapride

Compound Name	Comments
Cobalt	All drug products containing cobalt salts (except radioactive forms of cobalt and its salts and cobalamin and its derivatives).
Dexfenfluramine hydrocholride	All drug products containing dexfenfluramine hydrochloride
Diamthazole dihydrochloride	All drug products containing diamthazole dihydrochloride
Dibromsalan	All drug products containing dibromsalan
Diethylstilbestrol	All oral and parenteral drug products containing 25 milligrams or more of diethylstilbestrol per unit dose.
Dihydrostreptomycin sulfate	All drug products containing dihydrostreptomycin sulfate.
Dipyrone	All drug products containing dipyrone
Encainide hydrochloride	All drug products containing encainide hydrochloride
Esmolol hydrochloride	All parenteral dosage form drug products containing esmolol hydrochloride that supply 250 milligrams/milliliter of concentrated esmolol per 10-milliliter ampule
Etretinate	All drug products containing etretinate
Fenfluramine hydrochloride	All drug products containing fenfluramine hydrochloride
Flosequinan	All drug products containing flosequinan
Gatifloxacin	All drug products containing gatifloxacin (except ophthalmic solutions)
Gelatin	All intravenous drug products containing gelatin
Glycerol, iodinated	All drug products containing iodinated glycerol
Gonadotropin, chorionic	All drug products containing chorionic gonadotropins (of animal origin)
Grepafloxacin	All drug products containing grepafloxacin
Mepazine	All drug products containing mepazine hydrochloride or mepazine acetate
Metabromsalan	All drug products containing metabromsalan
Methamphetamine hydrochloride	All parenteral drug products containing methamphetamine hydrochloride
Methapyrilene	All drug products containing methapyrilene
Methopholine	All drug products containing methopholine
Methoxyflurane	All drug products containing methoxyflurane
Mibefradil dihydrochloride	All drug products containing mibefradil dihydrochloride
Nitrofurazone	All drug products containing nitrofurazone (except topical drug products formulated for dermatalogic application).
Nomifensine maleate	All drug products containing nomifensine maleate
Novobiocin sodium	All drug products containing novobiocin sodium
Ondansetron hydrochloride	All intravenous drug products containing greater than a 16 milligram single dose of ondansetron hydrochloride
Oxyphenisatin	All drug products containing oxyphenisatin
Oxyphenisatin acetate	All drug products containing oxyphenisatin acetate
Pemoline	All drug products containing pemoline
Pergolide mesylate	All drug products containing pergolide mesylate
Phenacetin	All drug products containing phenacetin
Phenformin hydrochloride	All drug products containing phenformin hydrochloride
Phenylpropanolamine	All drug products containing phenylpropanolamine
Pipamazine	All drug products containing pipamazine
Polyethylene glycol 3350, sodium chloride, sodium bicarbonate, potassium chloride, and bisacodyl	All drug products containing polyethylene glycol 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and 10 milligrams or more of bisacodyl delayed-release tablets.
Potassium arsenite	All drug products containing potassium arsenite
Potassium chloride	All solid oral dosage form drug products containing potassium chloride that supply 100 milligrams or more of potassium per dosage unit (except for controlled-release dosage forms and those products formulated for preparation of solution prior to ingestion)

Compound Name	Comments
Povidone	All intravenous drug products containing povidone
Propoxyphene	All drug products containing propoxyphene
Rapacuronium bromide	All drug products containing rapacuronium bromide
Reserpine	All oral dosage form drug products containing more than 1 milligram of reserpine
Rofecoxib	All drug products containing rofecoxib
Sibutramine hydrochloride	All drug products containing sibutramine hydrochloride
Sparteine sulfate	All drug products containing sparteine sulfate
Sulfadimethoxine	All drug products containing sulfadimethoxine
Sulfathiazole	All drug products containing sulfathiazole (except those formulated for vaginal use)
Suprofen	All drug products containing suprofen (except ophthalmic solutions)
Sweet spirits of nitre	All drug products containing sweet spirits of nitre
Tegaserod maleate	All drug products containing tegaserod maleate
Temafloxacin hydrochloride	All drug products containing temafloxacin
Terfenadrine	All drug products containing terfenadine
3,3',4',5-tetrachlorosalicylanilide	All drug products containing 3,3',4',5-tetrachlorosalicylanilide
Tetracycline	All liquid oral drug products formulated for pediatric use containing tetracycline in a concentration greater than 25 milligrams/milliliter.
Ticrynafen	All drug products containing ticrynafen
Tribomsalan	All drug products containing tribromsalan
Trichloroethane	All aerosol drug products intended for inhalation containing trichloroethane
Troglitazone	All drug products containing troglitazone
Trovafloxacin mesylate	All drug products containing trovafloxacin mesylate
Urethane	All drug products containing urethane
Valdecoxib	All drug products containing valdecoxib
Vinyl chloride	All aerosol drug products containing vinyl chloride
Zirconium	All aerosol drug products containing zirconium
Zomepirac sodium	All drug products containing zomepirac sodium

*current as of April 6, 2020

Coding / Billing Information

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

Note: Compounded products are typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions. The following drugs require medical drug coding and are listed as follows:

Note:

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven when used to report subcutaneous implantation of compounded hormone pellets:

CPT®* Codes	Description
11980	Subcutaneous hormone pellet implantation (implantation of estradiol and/or testosterone pellets beneath the skin)

Considered Experimental/Investigational/Unproven when used to report subcutaneous implantation of Naltrexone pellets:

CPT®* Codes	Description
17999	Unlisted procedure, skin, mucous membrane and subcutaneous tissue

Considered Experimental/Investigational/Unproven when used to report compounded testosterone pellets, estrogen/estrogen derivative pellets, or progesterone/progestin pellets or Naltrexone pellets:

HCPCS Codes	Description
J3490	Unclassified drugs
J3590	Unclassified biologics
J7999	Compounded drug, not otherwise classified

*Current Procedural Terminology (CPT®) ©2021 American Medical Association: Chicago, IL.

Background

Overview
A federal legend drug is one which has been approved by the FDA and requires a prescription by a licensed physician or other licensed health care provider.

The FDA defines traditional compounding as a practice in which a licensed pharmacist, a licensed physician, or, in the case of an outsourcing facility, a person under the supervision of a licensed pharmacist, combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient. Combining two drugs is considered compounding.

Occasionally patients need an alternative to an FDA-approved medication, for example inability to swallow a solid dosage form, or allergy or sensitivity to certain excipients or dyes. Compounded drugs are not FDA-approved. This means that FDA does not verify the safety, or effectiveness of compounded drugs. Consumers and health professionals rely on the drug approval process to ensure that drugs are safe and effective and made in accordance with Federal quality standards. Compounded drugs also lack an FDA finding of manufacturing quality before such drugs are marketed. There can be health risks associated with compounded drugs that do not meet federal quality standards. Compounded drugs made using poor quality practices may be sub- or super-potent, contaminated, or otherwise adulterated. Additional health risks include the possibility that patients will use ineffective compounded drugs instead of FDA-approved drugs that have been shown to be safe and effective.

The Pharmaceutical Compounding Quality and Accountability Act of 2013 establishes a clear boundary between traditional compounders and compounding manufacturers which make sterile products without or in advance of a prescription and sell those products across state lines. This act grants certain exemptions to traditional compounders, and compounding manufacturers that meet certain requirements, while giving the FDA more regulatory power over compounding manufacturers.

Professional Societies/Organizations

Compounded Hormone Products

American College of Obstetricians and Gynecologists
The American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice and the Practice Committee of the American Society for Reproductive Medicine published the following recommendations. Clinical evidence is lacking to support superiority claims of compounded bioidentical hormones over conventional menopausal hormone therapy. Customized compounded hormones pose additional risks. These preparations

have variable purity and potency and lack efficacy and safety data. Because of variable bioavailability and bioactivity, both underdosing and overdosing are possible. Conventional hormone therapy is preferred over compounded hormone therapy given the available data. Despite claims to the contrary, evidence is inadequate to support increased efficacy or safety for individualized hormone therapy regimens based on salivary, serum, or urinary testing. (ACOG, 2016)

North American Menopause Society
In their Menopause Position Statement, The North American Menopause Society (NAMS) cites the health risks associated with use of custom compounded bio-identical hormone therapy. NAMS states that in the majority of individuals, an FDA approved hormone replacement is sufficient and avoids the risks associated with compounded preparations. The organization further states it only recommends compounded estrogen replacement therapy in order to avoid allergic reactions to ingredients in FDA approved products. (NAMS, 2013)

The Endocrine Society
The Endocrine Society has commented that no published studies in peer-reviewed literature demonstrate compounded bio-identical hormone products are more safe or efficacious than FDA approved products. The organization also calls attention to the lack of quality control and safety and efficacy data for compounded preparations. The Society recommends treatment with FDA approved products and does not recommend use of compounded hormone formulations. (Stuenkel, 2015; Santen, 2010)

Compounded Naltrexone Products

American Society of Addiction Medicine and Substance Abuse and Mental Health Services Administration
Guidelines published by American Society of Addiction Medicine and Substance Abuse and Mental Health Services Administration do not address naltrexone implants. (Kampman, 2015)

World Federation of Societies of Biological Psychiatry
The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of substance use and related disorders, do not recommend naltrexone implants stating, although promising, concerns of safety require further need of evaluation. (Soyka, 2011)

Compendia and Other Published Clinical Studies

Compounded Implantable Hormones
Hormone therapy (HT) or hormone replacement therapy (HRT) includes the use of estrogen and/or progestin for vasomotor symptoms and/or vulvular and vaginal atrophy associated with menopause. Progestin products are also used in combination with estrogen to prevent endometrial hyperplasia in nonhysterectomized postmenopausal women. There are no FDA approved implantable estrogen and/or progesterone hormone pellets. Testosterone products are not FDA approved for use in women and are not recommended for hormone replacement therapy. (Goodman, 2011 and NAMS, 2013, 2017)

The term “bio-identical” has no defined meaning in any medical or conventional dictionary, and FDA does not recognize the term. Some compounders market compounded bioidentical hormone replacement therapy (BHRT) products as superior to FDA-approved drugs by making assertions that they are more natural or safer or better for patients than FDA-approved drug products. However, compounded BHRT products are not FDA-approved, which means these products have not undergone an FDA assessment of quality, safety, effectiveness and bioavailability (the extent and rate at which the drug enters the body). The FDA announced that the National Academies of Science, Engineering & Medicine (NASEM) will conduct research to help inform the public and the agency’s policies regarding compounded drugs. NASEM will provide a report evaluating the available scientific evidence relating to the safety and effectiveness of BHRT products. (FDA, 2018)

Compounded Naltrexone Implants
A systematic review and meta-analysis of naltrexone implants to treat opioid addiction states there is sparse evidence for the safety and efficacy of naltrexone implants and what available evidence exists is of moderate to very low quality. The authors conclude that naltrexone implants should only be used in a clinical trial setting, until more data becomes available supporting the safety and efficacy of this delivery system. (Larney, 2014)

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