

Absolute Total Care

Appropriate Use & Safety Edits

US Script (USS) provides a variety of safety edits to promote the use of the right medication, in the right patient, at the right time. These edits are routinely updated as new medication entries come to market and in cases of new medication safety alerts in an effort to maintain best-in-class safety protocols. The items listed below represent the most recent strategies implemented to improve quality of care and cost containment. It is important to note that this is not a comprehensive list of USS utilization management strategies. For specific medication restriction information, please see the specific Centene Health Plan Preferred Medication List (PDL).

Dose Consolidation Edits

Restrictions on claims implemented to prevent members from receiving multiple strengths of the same medication. Current medication classes with dose consolidation edits include, but are not limited to:

- Atypical Antipsychotics
- Long-Acting ADHD Medications (stimulants & non-stimulants)
- Selective Serotonin Receptor Inhibitors (SSRI) & Serotonin Norepinephrine Receptor Inhibitors (SNRI)
- Short-Acting ADHD Medications (stimulants only)

Duplicate Therapy Edits

Restrictions on claims implemented to prevent members from receiving excessive medication regimens within the same, or similar, medication class. *Please note that members may utilize up to two medications in any classes listed below with an asterisk (*).* Current medication classes with duplicate therapy edits include, but are not limited to:

- ACE Inhibitor/Angiotensin Receptor Blockers (ARB)
- Alpha Agonists (pediatrics only)
- Antidepressants* (all classes)
- Atypical Antipsychotics
- Benzodiazepines*
- Diabetic Medications (sulfonylurea/meglitinides)
- Long-Acting ADHD Medications (stimulants & non-stimulants)
- Muscle Relaxants
- Sedative-Hypnotics
- Selective Serotonin Receptor Inhibitors (SSRI) & Serotonin Norepinephrine Receptor Inhibitors (SNRI)
- Short-Acting ADHD Medications (stimulants only)*
- Tricyclic Antidepressants (TCA)



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Fraud and Abuse Edits

Restrictions on claims implemented to assist in limiting opioids to prevent potentially inappropriate utilization. Current medication classes with fraud and abuse edits include, but are not limited to:

- Opioid Claim Restrictions (restricts members to two opioid claims per month)
- Opioid Cumulative Quantity Limits (regimens restricted to a total of 180 units of opioids per month)
- Detox Agents & Opioid (prevents members from receiving detox agents when opioid use is ongoing)

Gender Edits

Restrictions on claims implemented to prevent patients from receiving certain medications which are only approved for a specific gender. Current medication classes with gender edits include, but are not limited to:

- Hormone Replacement Therapy (HRT)
- Contraceptives
- Prenatal vitamins

Lower Age Limits

Restrictions on age implemented to prevent children from utilizing medications below FDA recommended age limits. Current medication classes with lower age limits include, but are not limited to:

- Atypical Antipsychotics
- Benzodiazepines
- Long-Acting ADHD Medications (stimulants & non-stimulants)
- Migraine Rescue Medications (triptans & non-triptans)
- Sedative-Hypnotics
- Short-Acting ADHD Medications (stimulants only)
- Smoking Deterrents



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Upper Age Limits

Restrictions on age implemented to prevent adults from receiving medications commonly indicated for pediatric use only (without proper documentation of diagnosis) or for pregnancy (generally under age 45). Current medication classes with upper age limits include, but are not limited to):

- Long-Acting ADHD Medications (stimulants & non-stimulants)
- Most chewable, liquid, and suspension formulations
- Prenatal vitamins
- Short-Acting ADHD Medications (stimulants only)
- Advair Diskus

Quantity Limits

Restrictions on claim quantity per day implemented to prevent daily doses above FDA recommendations. Multiple medications within different medication classes have quantity limit requirements. Current medication classes with quantity limits include, but are not limited:

- | | | |
|--------------------------------|--|---|
| ▪ Antibiotics | ▪ Diabetic Medications | ▪ Non-Steroidal Anti-Inflammatory Drugs (NSAID) |
| ▪ Anti-Cholesterolemia Therapy | ▪ Gastrointestinal Treatment & Prophylaxis | ▪ Opioid Analgesics |
| ▪ Antiemetics | ▪ HIV Therapy | ▪ Osteoporosis Therapy |
| ▪ Antifungals | ▪ Hormone Replace Therapy (HRT) | ▪ Sedative/Hypnotics |
| ▪ Anti-Hypertensives | ▪ Migraine Therapy | ▪ Skeletal Muscle Relaxants |
| ▪ Asthma Medications | | ▪ Topical Steroids |
| ▪ Cough & Cold Therapy | | |

Step Therapy Edits

Restrictions on claims implemented to steer members toward the preferred medication in a particular medication class. Current medication classes with step therapy restrictions include, but are not limited to:

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|---|---|
| ▪ Aromatase Inhibitors (exemestane/letrozole) | ▪ Lodoxamide/Nedocramil Ophthalmic Solution |
| ▪ Canagliflozin | ▪ Olanzapine-Fluoxetine |
| ▪ Exenatide | ▪ Valsartan (with or without HCTZ) |
| ▪ Isotretinoin | |

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Teratogenic Edits

Restrictions on claims implemented to prevent female members from receiving potentially harmful medications prior to confirmation of pregnancy status. Current medications/medication classes with teratogenic edits include, but are not limited to:

Pregnancy Category 1

- 5-alpha Reductase Inhibitors
- ACE Inhibitors
- Alkylating Agents
- Anabolic Steroids
- Androgens
- Antiestrogens
- Antineoplastic Enzyme Inhibitors
- Combination Antihyperlipidemics
- Combination Antihypertensives
- Coumarin Anticoagulants
- HMG-CoA Reductase Inhibitors
- Methotrexate
- Migraine Products
- Nicotine
- Paroxetine
- Phenothiazines and Tricyclic Agents
- Progesterone Receptor Antagonists
- Tetracyclines
- Thiazides and Thiazide-like Diuretics

Pregnancy Category 2

- Antimanic Agents
- Antithyroid Agents
- Barbiturate Hypnotics
- Benzodiazepine Anticonvulsants
- Carbamazepine
- Chloridiazepoxide-Clidinium
- Efavirenz
- Fluconazole
- Inosine Monophosphate Dehydrogenase Inhibitors
- Phenytoin
- Primidone
- Topiramate
- Valproic Acid
- Voriconazole

**Centene Medicaid
US Script Drug Restriction / Benefit Design**

Safety Edits - Human Immunodeficiency Virus (HIV) Medications¹

Restrictions on claims implemented to prevent members from receiving combination medication regimens that are contraindicated or may be potentially toxic and life threatening. In addition, restrictions are in place to ensure that certain anti-retroviral products are utilized in a boosted fashion as many of these agents must be used in combination with augmenting products to increase the virological benefit/medication exposure. Current medications with safety edits are subdivided by area of concern and include, but are not limited to:

Duplicative Therapy

Many anti-retroviral agents have duplicative ingredients. The safety edits below have been established to prevent members from utilizing two products with the same ingredient(s) at the same time

¹ Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at <http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf>. Updated 5/1/14. Section accessed 12/7/14. Table 9 & 19.

**Centene Medicaid
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Atripla (efavirenz-emtricitabine-tenofovir) *plus*:

- Complera (rilpivirine-emtricitabine-tenofovir)
- Emtriva (emtricitabine)
- Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)
- Sustiva (efavirenz)
- Truvada (emtricitabine-tenofovir)
- Viread (tenofovir)

Combivir (lamivudine-zidovudine) *plus*:

- Epivir (lamivudine)
- Epzicom (lamivudine-abacavir)
- Retrovir (zidovudine)
- Triumeq (abacavir-dolutegravir-lamivudine)
- Trizivir (abacavir-lamivudine-zidovudine)

Complera (rilpivirine-emtricitabine-tenofovir) *plus*:

- Atripla (efavirenz-emtricitabine-tenofovir)
- Edurant (rilpivirine)
- Emtriva (emtricitabine)
- Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)
- Truvada (emtricitabine-tenofovir)
- Viread (tenofovir)

Epzicom (lamivudine-abacavir) *plus*:

- Combivir (lamivudine-zidovudine)
- Epivir (lamivudine)
- Triumeq (abacavir-dolutegravir-lamivudine)
- Trizivir (abacavir-lamivudine-zidovudine)
- Ziagen (abacavir)

Kaletra (lopinavir-ritonavir) *plus* Norvir (ritonavir)

Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) *plus*:

- Atripla (efavirenz-emtricitabine-tenofovir)
- Complera (rilpivirine-emtricitabine-tenofovir)
- Truvada (emtricitabine-tenofovir)
- Tybost (cobicistat)
- Viread (tenofovir)
- Vitekta (elvitegravir)
- Emtriva (emtricitabine)

Tivicay (dolutegravir) *plus* Triumeq (abacavir-dolutegravir-lamivudine)

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Triumeq (abacavir-dolutegravir-lamivudine) *plus*:

- Combivir (lamivudine-zidovudine)
- Epivir (lamivudine)
- Epzicom (lamivudine-abacavir)
- Tivicay (dolutegravir)
- Trizivir (abacavir-lamivudine-zidovudine)
- Ziagen (abacavir)

Trizivir (abacavir-lamivudine-zidovudine) *plus*:

- Combivir (lamivudine-zidovudine)
- Epivir (lamivudine)
- Epzicom (lamivudine-abacavir)
- Retrovir (zidovudine)
- Triumeq (abacavir-dolutegravir-lamivudine)
- Ziagen (abacavir)

Truvada (emtricitabine-tenofovir) *plus*:

- Atripla (efavirenz-emtricitabine-tenofovir)
- Complera (rilpivirine-emtricitabine-tenofovir)
- Emtriva (emtricitabine)
- Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)
- Viread (tenofovir)

Tybost (cobicistat) *or* Vitekta (elvitegravir) *plus* Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)

Ziagen (abacavir) *plus* Triumeq (abacavir-dolutegravir-lamivudine)

Inappropriate/Interaction Combination Use

Many anti-retroviral agents have dangerous and/or life threatening interactions when taken together; therefore, the safety edits listed below have been implemented to protect members from these situations.

Reyataz (atazanavir) *plus* Crixivan (indinavir)

(Atazanavir and indinavir can cause Grade 3 to 4 hyperbilirubinemia and jaundice)

Atripla (efavirenz-emtricitabine-tenofovir) *or* Complera (rilpivirine-emtricitabine-tenofovir) *or* Emtriva (emtricitabine) *or* Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) *or* Truvada (emtricitabine-tenofovir) *plus*:

(Emtricitabine and lamivudine have similar resistance profiles and have minimal additive antiviral activity)

- Epivir (lamivudine)
- Combivir (lamivudine-zidovudine)
- Epzicom (lamivudine-abacavir)
- Triumeq (abacavir-dolutegravir-lamivudine)
- Trizivir (abacavir-lamivudine-zidovudine)

Videx (didanosine) *plus* Zerit (stavudine)

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(Didanosine and stavudine as a dual-NRTI backbone can result in a high incidence of toxicities, particularly peripheral neuropathy, pancreatitis, and lactic acidosis)

Zerit (stavudine) plus:

(Stavudine and zidovudine should not be used in combination because of antagonism demonstrated in vitro and in vivo)

- Combivir (lamivudine-zidovudine)
- Retrovir (zidovudine)
- Trizivir (abacavir-lamivudine-zidovudine)

Intelence (etravirine) plus Aptivus (tipranavir)

(Tipranavir (ritonavir-boosted as a standard) significantly reduces etravirine concentrations)

Sustiva (efavirenz) plus:

(Two-non-nucleoside reverse transcriptase inhibitor (2-NNRTI) combinations can cause a higher frequency of clinical adverse events that leads to treatment discontinuation)

- | | |
|---|---|
| <ul style="list-style-type: none"> ▪ Complera (rilpivirine-emtricitabine-tenofovir) ▪ Edurant (rilpivirine) | <ul style="list-style-type: none"> ▪ Intelence (etravirine) ▪ Rescriptor (delavirdine) ▪ Viramune (nevirapine) |
|---|---|

Rescriptor (delavirdine) plus:

- | | |
|---|---|
| <ul style="list-style-type: none"> ▪ Atripla (efavirenz-emtricitabine-tenofovir) ▪ Complera (rilpivirine-emtricitabine-tenofovir) | <ul style="list-style-type: none"> ▪ Edurant (rilpivirine) ▪ Intelence (etravirine) ▪ Sustiva (efavirenz) ▪ Viramune (nevirapine) |
|---|---|

Viramune (nevirapine) plus:

- | | |
|---|--|
| <ul style="list-style-type: none"> ▪ Atripla (efavirenz-emtricitabine-tenofovir) ▪ Complera (rilpivirine-emtricitabine-tenofovir) | <ul style="list-style-type: none"> ▪ Edurant (rilpivirine) ▪ Intelence (etravirine) ▪ Rescriptor (delavirdine) ▪ Sustiva (efavirenz) |
|---|--|

Intelence (etravirine) plus:

- | | |
|--|---|
| <ul style="list-style-type: none"> ▪ Atripla (efavirenz-emtricitabine-tenofovir) ▪ Complera (rilpivirine-emtricitabine-tenofovir) ▪ Edurant (rilpivirine) ▪ Lexiva (fosamprenavir) | <ul style="list-style-type: none"> ▪ Rescriptor (delavirdine) ▪ Reyataz (atazanavir) ▪ Sustiva (efavirenz) ▪ Viracept (nelfinavir) ▪ Viramune (nevirapine) |
|--|---|

Atripla (efavirenz-emtricitabine-tenofovir) plus:

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- Complera (rilpivirine-emtricitabine-tenofovir)
- Edurant (rilpivirine)
- Rescriptor (delavirdine)
- Sustiva (efavirenz)
- Viramune (nevirapine)

Complera (rilpivirine-emtricitabine-tenofovir) plus:

- Atripla (efavirenz-emtricitabine-tenofovir)
- Edurant (rilpivirine)
- Rescriptor (delavirdine)
- Sustiva (efavirenz)
- Viramune (nevirapine)

Edurant (rilpivirine) plus:

- Atripla (efavirenz-emtricitabine-tenofovir)
- Intelence (etravirine)
- Rescriptor (delavirdine)
- Sustiva (efavirenz)
- Viramune (nevirapine)

Viracept (nelfinavir) plus:

- Aptivus (tipranavir)
- Crixivan (indinavir)
- Invirase (saquinavir)
- Lexiva (fosamprenavir)
- Prezista (darunavir)
- Reyataz (atazanavir)
- Kaletra (lopinavir-ritonavir)

Isentress (raltegravir) plus:

(Two integrase inhibitor combinations can cause a higher frequency of clinical adverse events that leads to treatment discontinuation)

- Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)
- Tivicay (dolutegravir)
- Triumeq (abacavir-dolutegravir-lamivudine)

Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) plus:

- Isentress (raltegravir)
- Tivicay (dolutegravir)
- Triumeq (abacavir-dolutegravir-lamivudine)

Tivicay (dolutegravir) plus:

- Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)
- Isentress (raltegravir)

Triumeq (abacavir-dolutegravir-lamivudine) plus:

- Isentress (raltegravir)

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- Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)

Viracept (nelfinavir) plus:

(Greater than two protease inhibitor (PIs) combinations can cause a higher frequency of clinical adverse events that leads to treatment discontinuation)

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|--------------------------|---------------------------------|
| ▪ Aptivus (tipranavir) | ▪ Prezista (darunavir) |
| ▪ Crixivan (indinavir) | ▪ Reyataz (atazanavir) |
| ▪ Invirase (saquinavir) | ▪ Kaletra (lopinavir-ritonavir) |
| ▪ Lexiva (fosamprenavir) | ▪ Norvir (ritonavir) |

Aptivus (tipranavir) plus:

- | | |
|--------------------------|---------------------------------|
| ▪ Viracept (nelfinavir) | ▪ Prezista (darunavir) |
| ▪ Crixivan (indinavir) | ▪ Reyataz (atazanavir) |
| ▪ Invirase (saquinavir) | ▪ Kaletra (lopinavir-ritonavir) |
| ▪ Lexiva (fosamprenavir) | |

Crixivan (indinavir) plus:

- | | |
|--------------------------|---------------------------------|
| ▪ Viracept (nelfinavir) | ▪ Prezista (darunavir) |
| ▪ Aptivus (tipranavir) | ▪ Reyataz (atazanavir) |
| ▪ Invirase (saquinavir) | ▪ Kaletra (lopinavir-ritonavir) |
| ▪ Lexiva (fosamprenavir) | |

Invirase (saquinavir) plus:

- | | |
|--------------------------|---------------------------------|
| ▪ Viracept (nelfinavir) | ▪ Prezista (darunavir) |
| ▪ Aptivus (tipranavir) | ▪ Reyataz (atazanavir) |
| ▪ Crixivan (indinavir) | ▪ Kaletra (lopinavir-ritonavir) |
| ▪ Lexiva (fosamprenavir) | |

Lexiva (fosamprenavir) plus:

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|-------------------------|---------------------------------|
| ▪ Viracept (nelfinavir) | ▪ Prezista (darunavir) |
| ▪ Aptivus (tipranavir) | ▪ Reyataz (atazanavir) |
| ▪ Crixivan (indinavir) | ▪ Kaletra (lopinavir-ritonavir) |
| ▪ Invirase (saquinavir) | |

Prezista (darunavir) plus:

- | | |
|-------------------------|------------------------|
| ▪ Viracept (nelfinavir) | ▪ Aptivus (tipranavir) |
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- Crixivan (indinavir)
- Invirase (saquinavir)
- Lexiva (fosamprenavir)
- Reyataz (atazanavir)
- Kaletra (lopinavir-ritonavir)

Reyataz (atazanavir) *plus*:

- Viracept (nelfinavir)
- Aptivus (tipranavir)
- Crixivan (indinavir)
- Invirase (saquinavir)
- Lexiva (fosamprenavir)
- Prezista (darunavir)
- Kaletra (lopinavir-ritonavir)

Kaletra (lopinavir-ritonavir) *plus*:

- Viracept (nelfinavir)
- Aptivus (tipranavir)
- Crixivan (indinavir)
- Invirase (saquinavir)
- Lexiva (fosamprenavir)
- Prezista (darunavir)
- Reyataz (atazanavir)
- Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)
- Tybost (cobicistat)

Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) *plus*:

- Kaletra (lopinavir-ritonavir)
- Norvir (ritonavir)

Norvir (ritonavir) *plus* Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)

Tybost (cobicistat) *plus* Kaletra (lopinavir-ritonavir)

Norvir (ritonavir) *plus* Tybost (cobicistat)

(Two booster agents can cause a higher frequency of clinical adverse events that leads to treatment discontinuation)

Tybost (cobicistat) *plus* Norvir (ritonavir)

Unboosted Protease Inhibitor Therapy

Many anti-retroviral agents must be boosted with other protease inhibitors to increase the virological benefit or increase medication exposure.

Intelence (etravirine) *plus*:

(Etravirine may induce the metabolism and significantly reduce the drug exposure of unboosted protease inhibitors)

- Combivir (lamivudine-zidovudine)
- Emtriva (emtricitabine)
- Epivir (lamivudine)
- Epzicom (lamivudine-abacavir)

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- Fuzeon (enfuvirtide)
- Isentress (raltegravir)
- Kaletra (lopinavir-ritonavir)
- Retrovir (zidovudine)
- Selzentry (maraviroc)
- Tivicay (dolutegravir)
- Trizivir (abacavir-lamivudine-zidovudine)
- Truvada (emtricitabine-tenofovir)
- Videx (didanosine)
- Viread (tenofovir)
- Zerit (stavudine)
- Ziagen (abacavir)
- Crixivan (indinavir) + Norvir (ritonavir)
- Invirase (saquinavir) + Norvir (ritonavir)
- Prezista (darunavir) + Norvir (ritonavir)
- Viracept (nelfinavir) + Norvir (ritonavir)

Aptivus (tipranavir) plus Norvir (ritonavir)

The virologic benefit of this protease inhibitor has been demonstrated only when used with concomitant ritonavir

Invirase (saquinavir) plus Norvir (ritonavir) or Tybost (cobicistat)

The virologic benefit of this protease inhibitor has been demonstrated only when used with concomitant ritonavir or cobicistat

Prezista (darunavir) plus Norvir (ritonavir) or Tybost (cobicistat)

The virologic benefit of this protease inhibitor has been demonstrated only when used with concomitant ritonavir or cobicistat

Reyataz (atazanavir) plus Norvir (ritonavir) or Tybost (cobicistat)

The virologic benefit of this protease inhibitor has been demonstrated only when used with concomitant ritonavir or cobicistat

Vitekta (elvitegravir) plus:

(The virologic benefit of this integrase inhibitor has been demonstrated only when used with concomitant protease inhibitor and ritonavir)

- Aptivus (tipranavir) + Norvir (ritonavir)
- Kaletra (lopinavir/ritonavir)
- Lexiva (fosamprenavir) + Norvir (ritonavir)
- Prezista (darunavir) + Norvir (ritonavir)
- Reyataz (atazanavir) + Norvir (ritonavir)

Document Revision Log

Revision	Performed by	Date
Updated document formatting for consistency by adding revision log for version control. Added section for gender edits with respective criteria. Updated Quantity Edits sections by adding specific examples of medication classes. Updated Lower Age Edit by addition of smoking deterrents criteria. Updated Upper Age Edit to include prenatal vitamins and dosage formulations typically reserved for pediatric use. Updated Step Therapy Edits to be reflective of current Centene Core PDL (removed acne therapy, antibiotic, nasal steroid, non-sedating antihistamines,	Nelson A.	3/16

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and sedative/hypnotics)		
Updated HIV section. Deleted previous information for anti-retrovirals and replaced with information regarding HIV duplicative use, inappropriate interactions, and unboosted protease inhibitor details. Updated teratogenic edits section and replaced ABCDX pregnancy categories with Category 1 & 2 edits actually in place.	Nelson A.	8/16