This Coverage Policy applies to Individual Health Insurance Marketplace benefit plans only.

Metabolic Agents
sodium phenylbutyrate
Buphenyl® (Sodium phenylbutyrate)
Carbaglu® (carglumic acid)
Cuprimine® (penicillamine)
Cystadane® (betaine)
Depen® (penicillamine)
Kuvan® (sapropterin)
Orfadin® (nitisinone)
Ravicti® (glycerol phenylbutyrate)
Syprine® (trientine hydrochloride)
Thiola® (tiopronin)
Xuriden™ (uridine triacetate)

COVERAGE POLICY
Buphenyl, Carbaglu, Cuprimine, Kuvan, Orfadin, sodium phenylbutyrate, Ravicti, Syprine and Xuriden are covered for members who meet the following criteria:

For sodium phenylbutyrate, Buphenyl
A. Adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS), AND
B. Compliance with a protein restrictive diet

For Carbaglu
A. A documented treatment of one of the following:
   a. Adjunctive therapy in pediatric and adult patients for the treatment of acute hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS), OR
   b. Maintenance therapy in pediatric and adult patients for the treatment of chronic hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS)

For Cuprimine
A. A documented diagnosis of one of the following:
   a. Wilson's disease AND treatment with Depen was ineffective, not tolerated, or is contraindicated, OR
   b. cystinuria AND treatment with conservative measures (e.g. high fluid intake, sodium and protein restriction, urinary alkalinization) was ineffective, not tolerated, or is contraindicated AND treatment with Depen was ineffective, not tolerated, or is contraindicated, OR
   c. Rheumatoid arthritis AND a one month trial of each of the following was ineffective, not tolerated, or is contraindicated: methotrexate, leflunomide, and sulfasalazine.
For **Cystadane**

A. Treatment of homocystinuria to decrease elevated homocysteine blood level, including
   a. Cystathionine beta-synthase (CBS) deficiency
   b. 5,10-methylenetetrahydrofolate reductase (MTHFR) deficiency
   c. Cobalamin (cbl) cofactor metabolism (cbl) deficiency

B. For CBS deficiency plasma methionine concentrations should be monitored and kept below 1,000 µmol/L through dietary modification and, if necessary, a reduction of Cystadane dose.

For **Depen**

A. A documented diagnosis of one of the following:
   a. Wilson’s disease, OR
   b. Cystinuria AND treatment with conservative measures (e.g. high fluid intake, sodium and protein restriction, urinary alkalinization) was ineffective, not tolerated, or is contraindicated, OR
   c. Rheumatoid arthritis AND a one month trial of each of the following medications was ineffective, not tolerated, or is contraindicated: methotrexate, leflunomide, and sulfasalazine

For **Kuvan**

A. A documented diagnosis of phenylketonuria (PKU), AND
   a. A documented baseline phenylalanine (Phe) level of greater than 6 mg/dL (360 micromol/L), AND
   b. Kuvan will be used in conjunction with a Phe-restrictive diet

For **Orfadin**

A. A documented diagnosis of hereditary tyrosinemia type 1 (HT-1) along with dietary restriction of tyrosine and phenylalanine, AND

B. Dietary restriction of tyrosine and phenylalanine

For **Ravicti**:

Documentation of ALL of the following:

A. A documented diagnosis of chronic management of a urea cycle disorder (UCD*) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone in an adult or pediatric patient ≥2 years of age. Urea cycle disorders (UCD*) include:
   a. Carbamoyl phosphate synthetase I (CPSI) deficiency
   b. Ornithine transcarbamylase (OTC) deficiency
   c. Argininosuccinate synthetase (ASS) deficiency (also known as classic citrullinemia or type I citrullinemia, CTLN1),
   d. Argininosuccinate lyase (ASL) deficiency (also known as argininosuccinic aciduria),
   e. Arginase deficiency (also known as argininemia)

AND

B. Ravicti is NOT being administered for the treatment of UCD N-acetylglutamate synthase (NAGS) deficiency, AND

C. Ravicti will be used with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements), AND

D. Ravicti is NOT being administered for acute hyperammonemia, AND

For **Syprine**

A. A documented diagnosis of Wilson's disease, AND

B. Treatment with Depen was ineffective, not tolerated, or contraindicated
For **Thiola**
A. A documented diagnosis of severe cystinuria with urinary cystine levels greater than 500 mg/day, AND
B. treatment with conservative measures (e.g. high fluid intake, sodium and protein restriction, urinary alkalinization) was ineffective, not tolerated, or is contraindicated.

For **Xuriden**
A. A documented diagnosis of hereditary orotic aciduria

**AUTHORIZATION PERIOD AND LIMITATIONS**

**Initial Approval:** 12 months
- Kuvan- 2 months , (1 month if initiated on 20 mg/kg/day) Initial extension will ONLY be granted for members who meet Documented “response” to therapy as defined by a 30% reduction in baseline Phe level

**Extended Approval:** Kuvan- 6 month intervals, based on documentation of Maintenance of a 30% reduction in baseline Phe level

**Quantity Limit:**
- Ravicit 1.1 gm/ml= Up to 525 ml in 30 days
- Xuriden 2gm= Up to 8gm (4 packets) per day

**NON-COVERAGE**
Coverage will NOT be granted for the following:
A. Use not approved by the FDA; and
B. The use is unapproved and not supported by the literature or evidence as an accepted off-label use. (see Off-Label Use Policy for determining “accepted use”)

**REFERENCES**
8. RAVICTI [prescribing information]; Brockton, MA: Lyne Laboratories, Inc.; June 2014

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