<table>
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<tr>
<th>#</th>
<th>DRUGS</th>
<th>INDICATION/S</th>
<th>HOW SUPPLIED**</th>
<th>DOSE</th>
<th>ROUTE</th>
<th>SIDE EFFECT</th>
<th>EVIDENCE LEVEL</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Agalsidase-alpha (Replagal®)</td>
<td>Fabry disease</td>
<td>1mg/ml solution for infusion</td>
<td>0.2 mg /kg every 2 weeks as IV infusion over 40 minutes.(1, 2)</td>
<td>IV</td>
<td>headache, tingling, tremors, fatigue, change in temperature sensation, increased blood pressure, upset stomach, diarrhea, coughing, sore throat, difficulty sleeping, change in the taste of food, change in smell, difficulty speaking, acne, dry skin and eye problems. About 1 out of 10 patients may have a reaction during or shortly after infusion of Replagal. These effects include chills and facial flushing (warmth and redness).</td>
<td>1b</td>
</tr>
</tbody>
</table>
2 | Agalsidase-beta (Fabrazyme®) | Fabry disease | 5 mg and 35 mg single-use vials for reconstitution to yield (5mg/mL) | 1mg/kg every 2 weeks as IV infusion over 2-4 hours.(1, 3) | IV | However some effects may be serious and may need treatment.

Infusion reaction consisted of one or more of the following: chills, fever, feeling hot or cold, dyspnea, nausea, flushing, headache, vomiting, paresthesia, fatigue, pruritus, pain in extremity, hypertension, chest pain, throat tightness, abdominal pain, dizziness, tachycardia, nasal congestion, diarrhea, edema peripheral, myalgia, back pain, pallor, bradycardia, urticaria, hypotension, face edema, rash, and somnolence
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<tr>
<td>3</td>
<td>Alanine</td>
<td>Maple syrup urine disease (MSUD)</td>
<td>300 mg and 500 mg capsules 300 mg, 500 mg, and 1000 mg tablets. powder</td>
<td>150 - 400 mg/kg/day adjusted according to plasma amino acids.(4)</td>
<td>PO</td>
<td>Non</td>
<td>4</td>
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<tr>
<td>4</td>
<td>Alglucosidase-alpha (Myozyme®)</td>
<td>Pompe disease (GSD II)</td>
<td>50 mg single-use vials for reconstitution to yield (5mg/mL)</td>
<td>20mg/kg every 2 weeks IV infusion over 4 hours.(5-7)</td>
<td>IV</td>
<td>pneumonia, respiratory failure, respiratory distress, catheter-related infection, respiratory syncytial virus infection, gastroenteritis, fever and infusion reactions.</td>
<td>1b</td>
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<tr>
<td>5</td>
<td>Allopurinol</td>
<td>- Disorders causing hyperuricemia - As a challenge drug to induce orotic aciduria</td>
<td>100 and 300 mg tablets 20 mg/mL suspension (extemporaneous preparation)</td>
<td>Children: 2-20 mg/kg/day. Adults: 100-600 mg/day. The dosage range is wide. Generally the recommended dose is what is required to keep the serum uric acid level &lt; 6 mg/dl and avoid xanthine calculi (the side effect of allopurinol). The dose should be reduced in renal failure.(8-17)</td>
<td>PO</td>
<td>Dermatologic: Rash (less than 1%), Stevens-Johnson syndrome (less than 1%), Toxic epidermal necrolysis (less than 1%).  Hematologic: Agranulocytosis, Aplastic anemia, Eosinophilia, Myelosuppression, Thrombocytopenia (0.6%).  Hepatic:</td>
<td>4</td>
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<tr>
<td>#</td>
<td>Drug/Compound</td>
<td>Condition/Disease</td>
<td>Dose Form</td>
<td>Dosage</td>
<td>Adverse Effects/Interactions</td>
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<td>6</td>
<td>Alpha-lipoic acid</td>
<td>Inborn errors of pyruvate dehydrogenase complex</td>
<td>50 mg, 100 mg, and 250 mg capsules, 100 mg, 200 mg, and 300 mg tablets, Oral liquid</td>
<td>25-50mg/kg/day, dose adjusted according to biochemical and clinical response.(18, 19)</td>
<td>PO muscle cramps, paresthesia and neuropathy symptoms may worsen at first, platelet disorders, purpura, shortness of breath, tension headache, urticaria, eczema.</td>
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<td>7</td>
<td>Ammonium tetrathiomolybdate (Coprex®)</td>
<td>Neurological presentation of Wilson disease</td>
<td>20 mg capsules</td>
<td>120 mg/day as: 20 mg three times daily with meals and 20 mg 3 times daily between meals for 2 weeks, and then 60 mg/day as: 10 mg three times daily with meals and 10 mg three times daily between meals.(20, 21)</td>
<td>PO Nausea and cytopenia</td>
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<tr>
<td>8</td>
<td>Arginine</td>
<td>Chronic management of hyperammonemia</td>
<td>250 mg tablets, 600 mg and 700 mg</td>
<td>- For argininosuccinic acid synthetase deficiency (ASS) and</td>
<td>PO hyperchloremic metabolic acidosis,</td>
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<tr>
<td></td>
<td>Drug Name</td>
<td>Indication</td>
<td>Formulation</td>
<td>Dosing/injection details</td>
<td>Adverse Effects</td>
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|9  | Arginine hydrochloride (R-Gene®)  | Acute management of hyperammonemic crises in suspected or confirmed urea cycle disorders, except arginase deficiency | 10% solution for injection (100 mg/ml) | - For suspected urea cycle or ASS or ASL, give: 600mg/kg if (< 20kg) or 12 gram/m² if (> 20kg) as a loading dose over 90 minutes followed by 600 mg/kg if (< 20kg) or 12 gram/m² if (> 20kg) as maintenance infusion over 24 hours.  
- For OTC and CPS: 200mg/kg if (< 20kg) or 4 gram/m² if (> 20kg) as a loading dose over 90 minutes followed by 200 mg/kg if (< 20kg) or 4 gram/m² if (> 20kg) as maintenance infusion over 24 hours. | IV hyperchloremic metabolic acidosis, hypekolemia, diarrhea, elevated BUN, creatinine levels, flushing, nausea, vomiting, abdominal cramps, bloating numbness, headache |
|10 | Aspirin                           | As an antithrombotic agent used in homocystinuria                                               | 81, 100, 325 mg tablets              | 50-100 mg daily. | PO Gastrointestinal ulcer, bleeding, tinnitus, bronchospasm angioedema, Reye's syndrome |
| 11 | Baclofen | Musculoskeletal relaxant | 10 mg, 20 mg and 25 mg tablets  
5 mg/mL and 10 mg/mL suspension (extemporaneous preparation) | < 2 years: 10-20 mg/day div. Q8 hr; titrate dose every 3 days in increments of 5-15 mg/day to a maximum of 40 mg daily.  
2 - 7 years: 20-30 mg/day div. Q8 hr; titrate dose every 3 days in increments of 5-15 mg/day to a maximum of 60 mg daily.  
≥ 8 years: 30-40 mg/day div. Q8 hr; titrate dosage as above to a maximum of 120 mg daily.  
**Alternatively:** start at 0.3 mg/kg/day div. Q8 hr and increase every 1-2 week(s) until reaching maintenance dose of:  
0.75-2mg/kg/day  
For > 10 years of age you can reach up to 2.5mg/kg/day  
**Adults:** 5 mg three times daily; may increase by 5 mg/dose every 3 days to a maximum of 80 mg/day. 30 - 75mg) /day is considered the standard dosage range (24, 25) | PO | Cardiovascular: Hypotension (0% to 9%)  
Gastrointestinal: Constipation  
Musculoskeletal: Poor muscle tone  
Neurologic: Asthenia (0.7% to 15%), Dizziness, Headache, Somnolence  
Other: Fatigue (2% to 4%), Shivering (0.5% to 1.3%) | 4 |
| 12 | Betaine | Classical Homocystinuria Remethylation defects | Capsules Tablets Powder | The aim is to normalize homocysteine level.  
- Classical homocystinuria and MTHFR deficiency:  
Children: 100-150 mg/kg/day ÷ BID increase weekly by 50 mg/kg increments, as needed.  
Maximum: 9 grams/day.  
Adults: 3 grams twice daily, up | PO | Diarrhea, Drug-induced gastrointestinal disturbance, Nausea | 4 |
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</table>
| 13 | Biotin | - Co-factor for carboxylases  
- Biotinidase deficiency  
- Biotin Responsive Basal Ganglia disease (BRBGD)  
- Multiple carboxylase deficiency | 10, 50 mg tablets / capsules  
1 mg capsule  
IV (available as part of a multivitamin complex) | Biotinidase deficiency, co-factor for carboxylases and Multiple carboxylase deficiency: 5-20 mg/day. (8, 9, 30, 31)  
BRBGD: 5-10 mg/kg/day.(32-34) |
|   |   |   |   |
| 14 | Chenodeoxycholic acid (Chenodiol®) | - 3β-dehydrogenase deficiency (3Bd)  
- Delta 4-3-oxosteroid 5 beta-reductase deficiency (3-ORD)  
- Cerebrotendinous xanthomatosis (CTX) | 250 mg tablets | 3Bd: 12 - 18 mg/kg/day for first 2 months then 9 - 12 mg/kg/day or 7 mg/kg/day with cholic acid.  
3-ORD: 8mg/kg/day.  
CTX: 750 mg/day in 3 divided doses.(8, 9, 35-38) |
|   |   |   |   |
| 15 | Cholesterol | Smith-Lemli-Opitz (SLO) | 150 mg tablets | Children: 100 mg/kg/day in 3 divided doses (doses up to 150mg/kg/day have been used).  
Adults: 40mg/kg/day or 500 mg/day in 3 divided doses.(9) (39-41) |
|   |   |   |   |
| 16 | Cholestyramine | Familial Hypercholesterolemia | 4 g resin in packets | -Children ≤10 years:  
Initial: 2 g/day; titrate dose based on efficacy and tolerance;  
PO Abdominal discomfort, constipation,  
1b |
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<tr>
<th>No.</th>
<th>Treatment</th>
<th>Condition</th>
<th>Formulation</th>
<th>Dosage</th>
<th>Side Effects</th>
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<tbody>
<tr>
<td>17</td>
<td>Cholic acid</td>
<td>3-ORD 3Bd deficiency</td>
<td>Powder</td>
<td>With chenodeoxycholic acid: 3Bd: 7 mg/kg/day. (9, 35) 3-ORD: 8 mg/kg/day. (8, 9, 35) Alone: 6 - 15 mg/kg/day in 2 divided doses (don’t exceed total dose of 500 mg/day). (35, 46)</td>
<td>PO unknown</td>
</tr>
<tr>
<td>18</td>
<td>Copper histidine</td>
<td>Menkes diseases</td>
<td>500 mcg/mL solution for injection (prepared extemporaneously)</td>
<td>Neonates: 50 - 150 mcg/kg daily injection. Infants and children: 1 mg/day. (8, 9, 47, 48)</td>
<td>SC unknown</td>
</tr>
</tbody>
</table>
| 19  | Creatine monohydrate          | -Guanidinoacetate methyltransferase (GAMT) deficiency  
-Arginine:glycine amidinotransferase (AGAT) deficiency  
Creatine transporter defect | Tablet Powder                      | 300 - 400 mg/kg/day up to 2 g/kg /day in three to six divided doses. (49) | Dehydration gastrointestinal distress, diarrhea muscle cramping renal dysfunction weight gain, water retention |
| 20  | Cysteamine bitartrate (Cystagon®) | Cystinosis                             | 50 mg and 150 mg capsules         | Begin with 10 mg/kg/day and increase weekly until reaching the maintenance dose (60 to 90) | Dermatologic: Rash (7%)  Gastrointestinal: |
mg of free base/kg/day) or (1.3 to 1.95 g/m² per day).
The recommended adult dose is
500 mg free base q6 hours;
however, for both children and
adults, the dose is titrated to
reduce, if possible, leukocyte
cystine concentration (measured
5-6 hours after a dose) to below
1 nmol half-cystine/mg
protein(50-52)

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<tr>
<th>No.</th>
<th>Drug</th>
<th>Condition</th>
<th>Dosage &amp; Administration</th>
<th>Side Effects</th>
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</table>
| 21  | Cysteamine hydrochloride (Cystoran®)      | Cystinosis                 | Ophthalmic drops 0.55% solution with benzalkonium chloride 0.01% as a preservative: 10-12 times/day in each eye(53, 54) | Eyes: Neurologic: Headache (greater than or equal to 10%)

Ophthalmic: Eye irritation, Pain in eye, Photophobia (greater than or equal to 10%), Red eye (greater than or equal to 10%), Visual field defect (greater than or equal to 10%) |

| 22  | Dextromethorphan                          | Non-Ketotic Hyperglycinemia | 15 mg tablets 15 mg/ 5mL syrup 5 - 35 mg/kg/day in 4 divided doses. Blood concentration can be monitored; the therapeutic level is not defined, but should be greater than zero (0) and lower than 100 nmol/L(55-59) | PO: Dizziness, Somnolence, fatigue |

<p>| 23  | Dichloroacetate                           | Primary lactic acidosis    | Powder 50 mg/kg/day ÷ q12 hr IV 25 mg/kg/day ÷ q12 hr PO(60) | IV/ PO: unknown |</p>
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<tr>
<td>24</td>
<td>Diazoxide</td>
<td>Hyperinsulinism hyperammonemia (HIHA)</td>
<td>50 mg capsules oral Suspension (5 – 340 mg/mL)</td>
<td>5 to 15 mg/kg/day in 3 divided doses. The dose should be adjusted to achieve adequate control of both fasting hypoglycemia and protein-induced hypoglycemia. (61, 62)</td>
<td>PO Cardiovascular: Hypotension (7%) Endocrine metabolic: Hyperglycemia Gastrointestinal: Nausea and vomiting (4%) Neurologic: Asthenia, Dizziness (2%)</td>
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<tr>
<td>25</td>
<td>Entacapone</td>
<td>Disorders of BH₄ synthesis</td>
<td>200 mg tablet</td>
<td>15 mg/kg/day in 2-3 divided doses. (8, 63)</td>
<td>PO Endocrine metabolic: Hyperpyrexia Musculoskeletal: Rhabdomyolysis Neurologic: Dyskinesia (25%), Hyperactive behavior (10%), Neuroleptic malignant syndrome Psychiatric: Hallucinations (4%)</td>
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<tr>
<td>26</td>
<td>Ezetimibe</td>
<td>Familial hypercholestrolaemia</td>
<td>10 mg tablet</td>
<td>10 mg/day (64, 65)</td>
<td>PO Hepatitis, increase liver enzymes, Rhabdomyolysis</td>
</tr>
<tr>
<td>27</td>
<td>Folic acid</td>
<td>Long term supplementation to compensate for the so-</td>
<td>1 mg and 5 mg tablets</td>
<td>Variable, 5-30mg/day (66, 67)</td>
<td>PO Bad taste in mouth, large doses: loss of appetite, nausea,</td>
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<td>called methylfolate trap in remethylation defect</td>
<td>irritability, sleep pattern disturbance and confusion</td>
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<td>28</td>
<td>Folinic acid</td>
<td>DHPR deficiency UMP synthase deficiency (hereditary orotic aciduria) methylene synthase deficiency methionine synthase deficiency hereditary folate malabsorption cerebral folate transporter defect-Folinic Acid Responsive Seizure -Remethylation defect</td>
<td>Hereditary folate malabsorption: Adult: 150-200 mg/day PO once daily Infants and children: 50 mg or 10-15 mg/kg PO once daily.(68, 69) Or 1.5-7.5 mg IM once daily(69-71). However, The dose should be adjusted in the individual to achieve a normal CSF folate level that is normal for age.(72) Other indications: 5-15mg/day PO or IV BID.(8, 73)</td>
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<td>5 mg, 10 mg, 15 mg, 25 mg tablets 10mg/mL injection solution 50 mg, 100 mg, 200 mg, 350 mg powder for reconstitution (injection)</td>
<td>PO or IV or IM</td>
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<td>Allergy</td>
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<tr>
<td>29</td>
<td>Galsulfase (Neglazyme®)</td>
<td>Mucopolysaccharidosis VI</td>
<td>5 mg/mL solution for injection</td>
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<td>1 mg/kg/wk(74-77)</td>
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<td>IV</td>
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<td></td>
<td>Fever, headache, arthralgia, abdominal pain, ear pain, diarrhea and vomiting and infusion reaction</td>
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<tr>
<td>30</td>
<td>Gemfibrozil</td>
<td>Mixed or combined hyperlipidemia</td>
<td>300 mg and 600 mg tablets 300 mg capsules</td>
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<td>1.2 grams daily, usually in 2 divided doses; range: 0.9 - 1.5 grams daily.(78, 79)</td>
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<td>PO</td>
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<td></td>
<td>Abdominal pain (9.8%), Acute appendicitis (1.2%), Indigestion (19.6%)</td>
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<tr>
<td>31</td>
<td>G-CSF = Filgrastim</td>
<td>Neutropenia in GSD 1b</td>
<td>300 mcg/mL vial, 600 mcg/mL prefilled-syringe</td>
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<td>2.5 mcg/kg once daily. If the mean absolute neutrophil count (ANC) in the subsequent 2-week period was less than 1 × 10⁹ cells/L, the dose should be</td>
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<td>SC</td>
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<td></td>
<td></td>
<td>Nausea and vomiting (57%) and bone pain (24% to 33%)</td>
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escalated to 5 mcg/kg/day for the next 2 weeks. Subsequent dose escalations to 10, 20, and 30 mcg/kg/day after 2 weeks of therapy if the mean ANC remained at less than $1 \times 10^9$ cells/L. Maximum dose 30 mcg/kg/day. Therapy could be continued for up to 6 weeks in patients with an ANC remaining at less than $0.5 \times 10^9$ cells/L. If after 6 weeks of therapy at the highest dose level, the ANC failed to increase more than $0.5 \times 10^9$ cells/L, then G-CSF should be discontinued.

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<tbody>
<tr>
<td>32</td>
<td>Glutamine</td>
<td>MSUD</td>
<td>Powder</td>
<td>150 - 400 mg/kg/day according to plasma amino acids results. (4)</td>
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<tr>
<td>33</td>
<td>Glycine</td>
<td>-Isovaleric acidemia - HMG-CoA lyase deficiency. - May be used in 3-Methylcrotonyl glycinuria</td>
<td>Powder</td>
<td>250 mg/kg/day (150 - 300 mg/kg/day) in 4 divided doses. (8, 9, 81, 82)</td>
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Peripheral edema, nausea, vomiting, insomnia, depression, fever and rigor

Blurred vision, temporary blindness, chest pain, hypotension, bradycardia, EKG changes, coma, confusion, seizures, dyspnea, electrolyte disturbance:
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<tr>
<th>#</th>
<th>Compound</th>
<th>Condition</th>
<th>Formulation</th>
<th>Dosage</th>
<th>Route</th>
<th>Adverse Effects</th>
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<tbody>
<tr>
<td>34</td>
<td>Heme arginate (Normosang®)</td>
<td>Acute porphyria</td>
<td>25 mg/mL solution for injection</td>
<td>3 - 4 mg/kg once daily for 4 days. (8, 83)</td>
<td>IV</td>
<td>Phlebitis, fever and headache</td>
</tr>
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<td></td>
<td>Hydroxocobalamin (vitamin B12)</td>
<td>Disorders of cobalamin metabolism</td>
<td>1000 mcg/mL injection for solution Tablets</td>
<td>1 mg IM daily or Oral dose: 10 mg once or twice daily. (8, 9, 84-86)</td>
<td>IM or PO</td>
<td>Increase blood pressure, Erythema, nausea, decrease lymphocyte count, Headache, red color urine</td>
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<tr>
<td>35</td>
<td>5-Hydroxytryptophan</td>
<td>Disorders of neurotransmitter synthesis</td>
<td>25 mg, 50 mg, 100 mg, and 200 mg capsules</td>
<td>Start at low dose (1 - 2 mg/kg/day) increasing gradually to 8 - 10 mg/kg/day in 4 divided doses. The dose is adjusted according to clinical response, monitoring CSF neurotransmitters and prolactin level. (8, 87)</td>
<td>PO</td>
<td>ataxia, headache, insomnia, mania, mental stimulation/agitation coryza, diaphoresis, tremulousness, hallucinations dermatomyositis, scleroderma (2 patients), drowsiness dyspnea, hyperventilation eosinophilia, eosinophilia-myalgia syndrome, dysarthria,</td>
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<tr>
<td></td>
<td>Idursulfase (Elaprase®)</td>
<td>Hunter syndrome (mucopolysaccharidosis II)</td>
<td>IV solution must be diluted in 100 ml of 0.9 sodium chloride injection, each vial contains 2mg/ml solution of idursulfase protein (6mg) in an extractable volume of 3 ml and for single use only</td>
<td>0.5 mg/kg weekly over 1-3 hour(s). (88-90)</td>
<td>IV</td>
<td>Hypertension, pruritic rash, headache, fever, urticaria and infusion reaction</td>
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<td>Hunter syndrome (mucopolysaccharidosis II)</td>
<td>IV solution must be diluted in 100 ml of 0.9 sodium chloride injection, each vial contains 2mg/ml solution of idursulfase protein (6mg) in an extractable volume of 3 ml and for single use only</td>
<td>0.5 mg/kg weekly over 1-3 hour(s). (88-90)</td>
<td>IV</td>
<td>Hypertension, pruritic rash, headache, fever, urticaria and infusion reaction</td>
</tr>
<tr>
<td>37</td>
<td>Imiglucerase (Cerezyme®)</td>
<td>Gaucher disease</td>
<td>200 units and 400 units powder for reconstitution</td>
<td>Various regimens: Adults: Non-neuropathic Gaucher's disease, chronic, symptomatic: a) Usual dosage, 60 units/kg IV over 1 to 2 hr every 2 weeks; may range from 2.5 units/kg 3 IV infusion over 1-2 hours</td>
<td>IV</td>
<td>Hypotension, tachyarrhythmia, cyanosis, flushing, pruritus, rash, urticaria, shivering, abdominal pain,</td>
</tr>
</tbody>
</table>
b) Children: safety and effectiveness have not been established in children younger than 2 years of age
a) Non-neuropathic Gaucher's disease, chronic, symptomatic:
1) (2 yr and older) usual dosage, 60 units/kg IV over 1 to 2 hr every 2 weeks; may range from 2.5 units/kg 3 times weekly to 60 units/kg once every 2 weeks. (91-93)
   The absence of an improvement in the visceral, haematological and biochemical markers within 6 months may indicate that a higher dose is required. If bone crises continue, the dose should be increased by at least 50%. (92, 93)
   For type III Gaucher disease some clinician recommend higher dosage: 120 U/kg/2 weeks. (8)

<p>| 38 | Ketamine | NKH | 10 mg/mL, 50 mg/mL, and 100 mg/mL solution for injection (maybe be used orally after mixing the dose with 0.2 – 0.3 mL/kg of cola or other beverages | 1 mg/kg/day in 4 divided doses. Titrate it up to 30 mg/kg/day according to clinical and biochemical response. (94-97) | Oral or IV or IM | Hypertension, tachycardia | 4 |</p>
<table>
<thead>
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</thead>
<tbody>
<tr>
<td>39</td>
<td>Laronidase (Aldurazyme®)</td>
<td>Mucopolysaccharidosis type 1</td>
<td>2.9 mg/5 mL solution for injection</td>
<td>100 U/kg/week.(98)</td>
<td>IV</td>
<td>Flushing, injection site reaction (18%), Rash (36%), antibody development (91%), complication of infusion (32%) headache upper respiratory infection (32%) and fever</td>
</tr>
<tr>
<td>40</td>
<td>L-carnitine</td>
<td>Primary and secondary carnitine deficiency</td>
<td>300 mg/mL Oral liquid 300 mg capsules 500 mg Tablets 200 mg/mL Solution for injection</td>
<td>Acute crises(carnitine boluses): 100 mg/kg/dose three to four times daily i.e.(300–400 mg/kg/day) should be given. Urine output should be appropriate prior to dosing (or hemofiltration be ongoing). Chronic: 100 - 300 mg/kg/day ÷ q8 hr.(8, 99-101)</td>
<td>PO or IV</td>
<td>Diarrhea, nausea, stomach cramps, vomiting</td>
</tr>
<tr>
<td>41</td>
<td>L-citrulline</td>
<td>-Carbamoyl phosphate synthetase (CPS) deficiency -Ornithine transcarbamylase (OTC) deficiency Lysinuric protein intolerance (LPI)</td>
<td>500 mg capsules Powder</td>
<td>CPS and OTC deficiency: 170 mg/kg/day or 3.8 gram/m²/day.(102-105) LPI: 100 mg/kg/day, however, the aim is to keep the citrulline at normal ranges. In some patients 400 mg/kg/day were used.(106-108)</td>
<td>PO</td>
<td>Unknown</td>
</tr>
<tr>
<td>42</td>
<td>L-dopa</td>
<td>Neurotransmitters replacement</td>
<td>250 mg and 500 mg capsules OR Combined preparation with carbidopa</td>
<td>Different dosages are suggested; generally start at low dose 1-2 mg/kg/day increasing by 1-2 mg/kg/day every few days or weeks up to maintenance dose of</td>
<td>PO</td>
<td>Nausea (5.5% to 5.7%)</td>
</tr>
<tr>
<td>No.</td>
<td>Amino Acid</td>
<td>Disease/Condition</td>
<td>Form</td>
<td>Dose and Administration</td>
<td>Other Information</td>
<td></td>
</tr>
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<tr>
<td>43</td>
<td>L-isoleucine</td>
<td>Maple syrup urine disease</td>
<td>Powder</td>
<td>10 - 12 mg/kg/day. Dosage can be monitored by measuring CSF levels of neurotransmitter metabolites or verifying normalization of serum prolactin levels. <em>(8, 63, 87, 109, 110)</em></td>
<td>PO unknown</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>L-Lysine-HCL</td>
<td>LPI</td>
<td>Powder</td>
<td>10 - 40 mg/kg/day in 3 divided doses. <em>(8, 107, 111, 112)</em> or 0.05-0.5 mmol/kg, three times per day. Monitor plasma lysine level. <em>(113)</em></td>
<td>PO Fanconi's syndrome, renal failure</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>L-serine</td>
<td>- 3-phosphoglycerate dehydrogenase deficiency (3-PGDH) deficiency -Phosphoserine aminotransferase (PSAT) deficiency - Phosphoserine phosphatase (PSPH) deficiency</td>
<td>Powder</td>
<td>• 3-PGDH: Infantile form: 500 - 600 mg/kg/day in 3 divided doses Juvenile form: 100-150 mg /kg/day in 3 divided doses. • PSAT: 500mg/kg/day • PSPH: 200 - 300mg/kg/day However, the doses are varied aiming to normalize CSF serine. <em>(114)</em></td>
<td>PO unknown</td>
<td></td>
</tr>
<tr>
<td>46</td>
<td>L-tryptophan</td>
<td>NKH</td>
<td>500mg tablets / capsules</td>
<td>100 mg/kg/day in 3 divided doses. <em>(8, 115)</em></td>
<td>PO unknown</td>
<td></td>
</tr>
<tr>
<td>47</td>
<td>L-valine**</td>
<td>Maple syrup urine disease (MSUD)</td>
<td>Powder</td>
<td>With the help of metabolic dietitian: 20-120 mg/kg/day. Dose adjusted as necessary to achieve normal plasma aminoacids levels. <em>(4)</em></td>
<td>PO unknown</td>
<td></td>
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<tr>
<td>48</td>
<td>Magnesium oxide</td>
<td>Primary hyperoxaluria type 1</td>
<td>400 mg tablets</td>
<td>500mg/m²/day.(116)</td>
<td>PO</td>
<td>Hypermagnesemia, hypokalemia, hyponatremia, nausea, vomiting, headache</td>
</tr>
<tr>
<td>49</td>
<td>Mannose</td>
<td>Congenital disorder of glycosylation type 1b</td>
<td>Liquid</td>
<td>0.15mg/kg/dose or 1g/kg/day divided in 5 doses However, the mannose doses depend on plasma mannose measurement, and the frequency of mannose uptakes are crucial because of the short clearance half-time of mannose.(8, 117-119)</td>
<td>PO</td>
<td>unknown</td>
</tr>
<tr>
<td>50</td>
<td>Mercaptopropionylglycine (Tiopronin)</td>
<td>Cystinuria</td>
<td>Tablet, 100 mg</td>
<td>The dosage is wide 15-50 mg/kg/day in 2 or 3 divided doses, maximum 1000 mg/day. However, the dose depends on monitoring free urine cystine level and modify the dose in order to maintain a level below 200 mmol/mmol of creatinine.(8, 9, 120, 121)</td>
<td>PO</td>
<td>pharyngitis, oral ulcers, gastrointestinal symptom, taste sense altered immune hypersensitivity reaction sense of smell altered</td>
</tr>
<tr>
<td>51</td>
<td>Methionine</td>
<td>Several remethylation defects</td>
<td>Available in different dosage forms, Capsules, powder and tablets</td>
<td>40–50 mg/kg per day adjust the dose to maintain upper normal ranges of plasma and CSF methionine.(67) However, some investigators argue against its usage in such disorders because it may result in sustained hyperhomocystinaemia.(66)</td>
<td>PO</td>
<td>headache, nausea, diarrhea, increased salivation, urinary frequency</td>
</tr>
<tr>
<td>52</td>
<td>Metax®</td>
<td>Hyperhomocystineimia of</td>
<td>Each tablet contains: 1 tablet twice daily.(122)</td>
<td>PO</td>
<td>Allergic reactions</td>
<td></td>
</tr>
</tbody>
</table>
various etiologies

L-methylfolate Calcium 3 mg, Pyridoxal 5′-phosphate 35 mg, Methylcobalamin 2 mg

have been reported following the use of oral L-methylfolate Calcium. Acne, skin reactions, allergic reactions, photosensitivity, nausea, vomiting, abdominal pain, loss of appetite, increased liver function test results, paresthesia, somnolence, nausea and headaches have been reported with pyridoxal 5′-phosphate. Mild transient diarrhea, polycythemia vera, itching, transitory exanthema and the feeling of swelling of the entire body has been associated with methylcobalamin.

Metronidazole

Propionic acidemia and methylmalonic acidemia

250 mg & 500 mg tablet 125 mg/5 mL suspension 500 mg/100 mL injection

Many regimen used, the most common one 10-20 mg/kg/day Q8 for 1 week then 3 weeks

PO

Nausea, Jarisch Herxheimer reaction, dizziness,
<p>| | | | | |</p>
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</thead>
<tbody>
<tr>
<td>54</td>
<td>Miglustat (Zavesca)</td>
<td>Gaucher disease (GD) in patients unable to receive intravenous ERT, Niemann-Pick disease Type C ((NPC))</td>
<td>100 mg capsule</td>
<td>GD: 100 mg/kg/day TID.(124-127) NPC: 200 mg TID.(128, 129) for adult. 8-12 years according to surface area: &gt;1.25: 200 mg three times a day &gt;0.88–1.25: 200 mg twice a day &gt;0.73–0.88: 100 mg three times a day &gt;0.47–0.73: 100 mg twice a day ≤0.47 : 100 mg once a day</td>
</tr>
<tr>
<td>55</td>
<td>N-carbamoylglutamate (Carbaglu®)</td>
<td>Unknown hyperammonemia, NAGS deficiency, CPS-1 deficiency, propionic acidemia or methylmalonic acidemia</td>
<td>200 mg tablet</td>
<td>100-250 mg/kg/day then adjusted individually in order to maintain normal ammonia plasma levels and divided into 2 to 4 doses.(130-137) Base on limited unpublished data the maintenance dose less than 100 mg/kg/day.</td>
</tr>
<tr>
<td>56</td>
<td>Nicotinamide</td>
<td>Hartnup disorder</td>
<td>50 mg, 100, 250 mg tablet</td>
<td>50-300 mg/day.(8, 138)</td>
</tr>
<tr>
<td>57</td>
<td>Nicotinic acid (Niacin)</td>
<td>Hyperlipidemia</td>
<td>50 mg 100 mg 250 mg 500 mg tablets and capsules</td>
<td>100-200 mg 3 times daily, increase gradually over 2-4 weeks to 1-2 gram 3 times daily.(8, 139)</td>
</tr>
<tr>
<td>58</td>
<td>Nitisinone, 2-(nitro-4-trifluoromethylbenzoyl)1,3-cyclohexanedione (NTBC) ORFADIN®</td>
<td>Tyrosinemia type 1</td>
<td>Capsules: 2 mg, 5 mg and 10 mg</td>
<td>1mg/kg/day in 2 divided doses.(140-142)</td>
</tr>
<tr>
<td></td>
<td>Pantothenic acid</td>
<td>3-methylglutaconic aciduria type II</td>
<td>Capsules and tablets 100 mg, 200 mg, and 250 mg</td>
<td>Liquid 200 mg/5 mL</td>
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<tr>
<td></td>
<td>Penicillamine Cuprimine®</td>
<td>Wilson disease Cystinuria</td>
<td>Capsules and tablets 250 mg</td>
<td>Wilson disease: 0.75 and 1.5 g in 2-4 divided doses that results in an initial 24-hour cupriuresis of over 2 mg should be continued for about three months, by which time the most reliable method of monitoring maintenance treatment is the determination of free copper in the serum. This equals the difference between quantitatively determined total copper and ceruloplasmin copper. Adequately treated patients will usually have less than 10 mcg free copper/dL of serum. It is seldom necessary to exceed a dosage of 2 g/day.</td>
</tr>
<tr>
<td></td>
<td>Polycitra (Tricitrate)</td>
<td>Chronic treatment for primary hyperoxaluria type 1 and primary</td>
<td>Oral solution contains: potassium citrate monohydrate 550mg</td>
<td>Adult: 15-30 ml diluted with water taken 4 times a day Pediatrics: 5-15ml, diluted in</td>
</tr>
<tr>
<td>No.</td>
<td>Pyridoxine</td>
<td>Pyridoxine responsive pyridoxine responsive cystathionine β synthase deficiency (CBS), pyridoxine dependent epilepsy (PDE), pyridoxine responsive Ornithine Aminotransferase Deficiency (OAT), primary hyperoxaluria type 1 (PH1)</td>
<td>Sodium citrate dihydrate 500mg Citric acid monohydrate 334mg per 5 mL</td>
<td>water 4 times a day after meals and at bedtime. The dose adjusted with blood gas monitoring. (147)</td>
</tr>
<tr>
<td></td>
<td>Pyridoxal phosphate (PLP)</td>
<td>Pyridoxal phosphate-dependent seizures</td>
<td>50 mg tablet</td>
<td>30 mg/kg/day divided in three or four doses enterally, for three to five days. 30-50 mg/kg/day divided in 4-6 doses. (73, 153)</td>
</tr>
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</tr>
<tr>
<td>64</td>
<td>Riboflavin</td>
<td>Glutaric aciduria (GA1), Multiple acyl Co A dehydrogenase deficiency (MAD), Mitochondrial complex 1 deficiency</td>
<td>25 mg, 50 mg, 100 mg tablet 400 mg capsule</td>
<td>GA1: There is no firm evidence that riboflavin improves the neurological outcome of GA. (100) however, responsiveness to 100-150 mg/day divided in 2-3 doses have been demonstrated in few patients. (154, 155) MAD: 100-400mg/day in 2-3 divided doses. (156, 157) SCAD: 10 mg/kg/day, divided into three doses with a maximum of 150 mg/day. (158) Mitochondrial complex 1 deficiency: 3-20 mg/kg/day divided in 3 doses. (9, 159)</td>
</tr>
<tr>
<td>65</td>
<td>Sapropterin dihydrochloride (Kuvan®)</td>
<td>hyperphenylalaninemia (HPA) due to BH4 responsive</td>
<td>100 mg tablet</td>
<td>BH4 loading test: 20 mg/kg/dose once daily for 2 consecutive days.</td>
</tr>
<tr>
<td>No.</td>
<td>Drug</td>
<td>Indications</td>
<td>Formulation</td>
<td>Dosage</td>
</tr>
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</tr>
<tr>
<td>66</td>
<td>Selegiline (1-deprenyl)</td>
<td>Disorders of BH₄ synthesis</td>
<td>5 mg capsule and tablet</td>
<td>0.1-0.25mg/kg/day in 3-4 divided doses. Dosage can be monitored by measuring CSF levels of neurotransmitter metabolites or verifying normalization of serum prolactin levels.(163, 164)</td>
</tr>
<tr>
<td>67</td>
<td>Sodium benzoate</td>
<td>Hyperammonaemia in urea cycle disorders and in undiagnosed patients with hyperammonaemia, no evidence to support use of sodium benzoate in acute crises of propionic or methylmalonic academia.(101)</td>
<td>Powder</td>
<td>Acute crises: 0.25 g/kg (&lt;20 kg) or 5.5 g/m² (&gt;20kg) as a loading dose followed by same dose as maintenance dose over 24 hours.(22, 104) In difficult to control chronic hyperammonemia, a dose of 250 mg/kg PO divided in 3 doses may be considered.(101) In NKH up to 750 mg/kg/day have been used.(57)</td>
</tr>
<tr>
<td>68</td>
<td>Sodium bicarbonate</td>
<td>Persistent metabolic acidosis</td>
<td>0.5 mEq/mL solution or dilute the 1 mEq/mL solution 1:1 with sterile water</td>
<td>Adults: HCO₃-(mEq) = 0.2 x weight (kg) x base deficit (mEq/L) or HCO₃-(mEq) = 0.5 x weight (kg) x [24 - serum HCO₃-(mEq/L)]</td>
</tr>
</tbody>
</table>
| 69 | Sodium phenylacetate | Hyperammonaemia in urea cycle disorders and in undiagnosed patient with hyperammonaemia, no evidence support its use in acute crises of propionic or methylmalonic acidemia | Acute crises: 0.25 g/kg (<20 kg) or 5.5 g/m² (>20 kg) as a loading dose followed by same dose as maintenance dose over 24 hours.(22, 104) | IV or PO | **Endocrine metabolic:** Hyperammonemia (5%), Hypokalemia (7%), Metabolic acidosis (4%)
**Hematologic:** Anemia (4%), Disseminated intravascular coagulation (3%)
**Neurologic:** Cerebral edema (5%), Coma (3%), Neurotoxicity, Seizure (6%) | 4 |
<table>
<thead>
<tr>
<th>Page</th>
<th>Sodium phenylbutyrate</th>
<th>Chronic management of urea cycle disorders</th>
<th>500 mg tablet Available also as powder</th>
<th>0.45-0.6 g/kg/day if &lt;20 kg; 9.9-13 g/m²/day in larger patients.(22, 104, 105)</th>
<th>PO</th>
<th>Endocrine metabolic: Acidosis (14% ), Hypoalbuminemia (11% )</th>
<th>Hematologic: Anemia (9% )</th>
<th>Reproductive: Amenorrhea (23% ), Irregular periods (23%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>71</td>
<td>Statins</td>
<td>Hyperlipidaemias. Simvastatin used in Smith–Lemli–Opitz syndrome</td>
<td>Atorvastatin (lipitor) Fluvastatin (lescol) Lovastatin (mevacor) Pravastatin(pravachol) Simvastatin(zocor) Rosuvastatin (crestor)</td>
<td>Depends on the type of statin used (17, 166). For more details about the dosage please refer to reference 172.</td>
<td>PO</td>
<td>Unknown</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72</td>
<td>Tetrahydrobiopterin (BH4)</td>
<td>BH4 loading test, disorders of BH4 synthesis, BH4 responsive PKU. Currently, replaced by Kuvan®</td>
<td>50 mg tablet</td>
<td>BH4 loading test: 20 mg/kg/dose once daily for 2 consecutive days. Others: 5-20 mg/kg/day, monitor phenylalanine levels and adjust the dose accordingly.(160, 167)</td>
<td>PO</td>
<td>Abdominal pain, diarrhea, nausea, vomiting, headache, nasal discharge, throat pain, URTI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>73</td>
<td>THAM TROMETHAMINE</td>
<td>Refractory severe metabolic acidosis with hypernatremia</td>
<td>THAM acetate solution</td>
<td>IV dose based on buffer base deficit of extracellular fluid: THAM(R) (mL of 0.3 molar solution) = weight (kg) X base deficit (mEq/L) X 1.1.(168, 169)</td>
<td>PO</td>
<td>Hypervolemia, Hypoglycemia, respiratory depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>74</td>
<td>Thiamine</td>
<td>Thiamine responsive MSUD, Thiamine responsive pyruvate dehydrogenase deficiency</td>
<td>50 mg, 100 mg, 250 mg, 500 mg tablet 100 mg/mL injection</td>
<td>Various dosage have been used: 100mg/day,(170)10mg/kg/day², the dose ranges between10-1000mg/day.(4, 8, 171, 172)</td>
<td>PO/IV</td>
<td>Injection site reaction</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td><strong>75</strong> Triethylene tetramine (trientine)</td>
<td>Wilson disease in cases of penicillamine intolerance</td>
<td>250 mg capsules</td>
<td>500-750 mg/day for pediatric patients and 750-1250 mg/day for adults given in divided doses two, three or four times daily. This may be increased to a maximum of 2000 mg/day for adults or 1500 mg/day for children. Adjust the dose by determination of free copper in the serum, which equals the difference between quantitatively determined total copper and ceruloplasmin. Adequately treated patients will usually have less than 10 mcg free copper/dL of serum. (20, 21)</td>
<td>PO</td>
<td>Myasthenia gravis, spasticity, dystonia, contact dermatitis</td>
<td>1b</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>76</strong> Triheptanoin</td>
<td>Very long chain fatty acid oxidation defect, pyruvate carboxylase deficiency, Adult-onset acid maltase deficiency (GSD II)</td>
<td></td>
<td>To provide 30-35% of total calories. (173-175)</td>
<td>PO</td>
<td>Unknown</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>77</strong> Ubiquinone (Coenzyme Q10)</td>
<td>Primary CoQ10 deficiency,</td>
<td>50 mg, 100 mg, 200 mg soft gels capsule</td>
<td>The dosage employed is highly variable, Adult: 200-600 mg QID, Pediatrics: 2-15 mg/kg/day BID. (176) Other used: 30 mg/kg/day. (177) As high as 2000 mg/day have been used. (178)</td>
<td>PO</td>
<td>diarrhea, nausea, heartburn, appetite suppression headache, dizziness irritability, agitation mild increase in liver enzymes skin rash, pruritus, exantherma</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>78</td>
<td>Uridine</td>
<td>UMP synthase deficiency (Hereditary orotic aciduria)</td>
<td>100 mg cap 50 units/ mL drops</td>
<td>100-150 mg/kg/day in divided doses. (179, 180)</td>
<td>PO</td>
<td>Unknown</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
| 79 | Velaglucerase alfa | Gaucher disease | Powder for solution for injection/ 200 U/vial and 400 U/vial | 60 U/kg administered every other week over 1 hour. (181) Adjust based upon disease activity. | IV | Gastrointestinal: Abdominal pain (15% to 18.5%), Nausea (5.6% to 10%)  
Hematologic: Partial thromboplastin time increased (11.1%)  
Musculoskeletal: Arthralgia (7.5% to 14.8%), Backache (16.7% to 17.5%)  
Neurologic: Dizziness (7.5% to 22.2%), Headache (30% to 35.2%)  
Respiratory: Upper respiratory infection (30 to 31.5%)  
Other: Asthenia (12.5% to 13%), Complication of infusion (22.5% to 51.9%), Fatigue (12.5% to 13%), Fever (12.5% to 22.2%) | 1b |
<table>
<thead>
<tr>
<th>Page</th>
<th>Vitamin</th>
<th>Condition</th>
<th>Dose and Formulations</th>
<th>Dosage</th>
<th>Route</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>Vitamin C</td>
<td>Glutathione Synthetase deficiency (GS) Hawkinsinuria, Tyrosinemia type III and Transient tyrosinemia of newborn</td>
<td>100 mg tablet 100 mg/mL drops 1g effervescent tablet</td>
<td>GS deficiency: 100mg/kg/day. Others: 200-1000mg/day.</td>
<td>PO</td>
<td>Nephrolithiasis, diarrhea, iron overload</td>
</tr>
<tr>
<td>81</td>
<td>Vitamin E</td>
<td>Glutathione Synthetase deficiency (GS)</td>
<td>100 mg capsule 50 units/ mL drops</td>
<td>GS deficiency: 10mg/kg/day.</td>
<td>PO</td>
<td>Bleeding, hepatotoxicity, retinal hemorrhage, pulmonary embolism, sepsis</td>
</tr>
<tr>
<td>82</td>
<td>Zinc</td>
<td>Acrodermatitis enteropathica (AE) Wilson disease</td>
<td>50 mg (elemental zinc) capsule and tablet 15 mg/ 10mL suspension (extemporaneous preparation)</td>
<td>AE: No consensus regarding the dosage but generally the recommended initial dose is 5-10mg/kg/day and maintenance doses of 1-2gram/kg/day. Wilson disease: The adult dose is 50 mg t.i.d., each dose separated from food and beverages other than water by at least 1 h. The paediatric dose is 25 mg b.i.d. until 5 years of age, 25 mg t.i.d. until 16 years of age, or until 125 lbs body weight, and then 50 mg t.i.d.</td>
<td>PO</td>
<td>Nausea, vomiting</td>
</tr>
</tbody>
</table>

* Table references provided in separate file as supplementary material. **= available under different brand names; sometimes in various dosage forms and strengths (only few examples are given).
TABLE REFERENCES:


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