

# INDICATION and IMPORTANT SAFETY INFORMATION

## INDICATION

BUPHENYL® (sodium phenylbutyrate) Tablets for oral administration and BUPHENYL® (sodium phenylbutyrate) Powder for oral, nasogastric, or gastrostomy tube administration are indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders (UCDs) involving deficiencies of carbamoyl phosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS).

BUPHENYL is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy.

BUPHENYL must be used with dietary protein restriction and, in some cases, essential amino acid supplementation.

Any episode of acute hyperammonemia should be treated as a life-threatening emergency.

## IMPORTANT SAFETY INFORMATION

### CONTRAINDICATIONS

- *Acute hyperammonemia*: BUPHENYL should not be used to manage acute hyperammonemia, which is a medical emergency.

### WARNINGS AND PRECAUTIONS

BUPHENYL should not be administered to patients with known hypersensitivity to sodium phenylbutyrate or any component of this preparation.

- Use caution with administering BUPHENYL to patients with:
  - Congestive heart failure or severe renal insufficiency, and in clinical states in which there is sodium retention with edema.
  - Hepatic or renal insufficiency or inborn errors of beta oxidation.
- Probenecid may affect renal excretion of the conjugated product of BUPHENYL as well as its metabolite.
- Use of corticosteroids may cause the breakdown of body protein and increase plasma ammonia levels.
- There have been published reports of hyperammonemia being induced by haloperidol and by valproic acid.

### ADVERSE REACTIONS

- The most common adverse reactions ( $\geq 3\%$ ) reported in BUPHENYL clinical trials were decreased appetite, body odor, bad taste or taste aversion.
- In female patients, amenorrhea/menstrual dysfunction (irregular menstrual cycles) occurred in 23% of the menstruating patients.
- Neurotoxicity was reported in cancer patients receiving intravenous phenylacetate. Manifestations were predominately somnolence, fatigue, and lightheadedness; with less frequent headache,

dysgeusia, hypoacusis, disorientation, impaired memory, and exacerbation of a pre-existing neuropathy.

- Laboratory adverse events occurring in >2% of UCD patients by body system were:
  - *Metabolic*: acidosis, alkalosis, hyperchloremia, and hypophosphatemia
  - *Nutritional*: hypoalbuminemia and decreased total protein
  - *Hepatic*: increased alkaline phosphatase and increased liver transaminases
  - *Hematologic*: anemia, leukopenia, leukocytosis, and thrombocytopenia

#### USE IN SPECIFIC POPULATIONS

- *Pregnancy*: BUPHENYL should be used with caution in patients who are pregnant or planning to become pregnant. Animal reproduction studies have not been conducted with BUPHENYL. It is not known whether BUPHENYL can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.
- *Lactation*: breastfeeding is not recommended during treatment with BUPHENYL. There are no data on the presence of BUPHENYL in human milk.

**DIGITAL:** Please see [Full Prescribing Information](#).

**PRINT:** Please see accompanying Full Prescribing Information [in the pocket, etc.].