HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ELCYS safely and effectively. See full prescribing information for ELCYS.

ELCYS (cysteine hydrochloride injection), for intravenous use
Initial U.S. Approval: 1971

---------- INDICATIONS AND USAGE ----------
ELCYS is a sulfur-containing amino acid indicated to meet the nutritional requirements of newborn infants requiring total parenteral nutrition (TPN); and of adult and pediatric patients with severe liver disease who may have impaired enzymatic processes and require TPN. It can also be added to amino acid solutions to provide a more complete profile of amino acids for protein synthesis. (1)

---------- DOSAGE AND ADMINISTRATION ----------
- ELCYS is for *admixing use* only. *Not for direct intravenous infusion.* (2.1)
- See full prescribing information for information on preparation, administration, instructions for use, dosing considerations, including the recommended dosage in pediatric patients and adults. (2.1, 2.2, 2.3, 2.4, 2.5)

---------- DOSAGE FORMS AND STRENGTHS ----------
Injection: 500 mg/10 mL (50 mg/mL) cysteine hydrochloride, USP in a 10 mL single-dose vial. (3)

---------- CONTRAINDICATIONS ----------
- Hypersensitivity to one or more amino acids (4)
- Inborn errors of amino acid metabolism (4)
- Pulmonary edema or acidosis due to low cardiac output (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Pulmonary Embolism due to Pulmonary Vascular Precipitates: If signs of pulmonary distress occur, stop the infusion and initiate a medical evaluation. (5.1)
- Vein Damage and Thrombosis: Solutions with osmolarity of 900 mOsm/L or more must be infused through a central catheter. (2.1, 5.2)
- Increased blood urea nitrogen (BUN): Monitor laboratory parameters and discontinue if exceeds normal postprandial limits and continues to increase. (5.3)
- Acid-Base Imbalance: Monitor laboratory parameters and supplement with electrolytes as needed. (5.4)
- Hepatobiliary Disorders: Monitor liver function parameters and ammonia levels. (5.5)
- Hyperammonemia: Neurocognitive delay possible in infants; monitor blood ammonia levels. (5.6, 8.4)
- Aluminium Toxicity: Increased risk in patients with renal impairment, including preterm infants. (5.7, 8.4)
- Monitoring and Laboratory Tests: Monitor fluid and electrolytes, serum osmolarity, blood glucose, kidney and liver function, blood count and coagulation parameters throughout treatment. (5.8)

---------- ADVERSE REACTIONS ----------
Most common adverse reactions are local reactions (warm sensation, erythema, phlebitis and thrombosis at the infusion site), generalized flushing, fever and nausea (6).

To report SUSPECTED ADVERSE REACTIONS, contact Exela Pharma Sciences, LLC at 1-888-451-4321 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 04/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Important Administration Information
2.2 Preparation and Administration Instructions
2.3 Preparation Instructions for Admixing Using a Parenteral Nutrition (PN) Container
2.4 Dosing Considerations
2.5 Recommended Dosage in Pediatric and Adults
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Pulmonary Embolism due to Pulmonary Vascular Precipitates
5.2 Vein Damage and Thrombosis
5.3 Increased Blood Urea Nitrogen (BUN)
5.4 Acid-Base Imbalance
5.5 Hepatobiliary Disorders
5.6 Hyperammonemia
5.7 Aluminum Toxicity
5.8 Monitoring and Laboratory Tests
6 ADVERSE REACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
8.7 Hepatic Impairment
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ELCYS is indicated for use as an additive to amino acid solutions to meet the nutritional requirements of newborn infants requiring total parenteral nutrition (TPN) and of adult and pediatric patients with severe liver disease who may have impaired enzymatic processes and require TPN. It can also be added to amino acid solutions to provide a more complete profile of amino acids for protein synthesis.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Information

ELCYS is for *admixing use* only. It is *not for direct intravenous infusion*. Prior to administration, ELCYS *must be diluted and used as an admixture* in parenteral nutrition (PN) solutions.

The resulting solution is for intravenous infusion into a central or peripheral vein. The choice of a central or peripheral venous route should depend on the osmolarity of the final infusate. Solutions with osmolarity of 900 mOsm/L or greater must be infused through a central catheter *[see Warnings and Precautions (5.2)]*.

2.2 Preparation and Administration Instructions

- ELCYS is *not for direct intravenous infusion*. Prior to administration, ELCYS *must be diluted and used as an admixture* in PN solutions.
- ELCYS is to be prepared only in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area). The key factor in the preparation is careful aseptic technique to avoid inadvertent touch contamination during mixing of solutions and addition of other nutrients.
- ELCYS is for addition to amino acid solutions prior to further admixing with dextrose injection using a PN container.
- Use a dedicated line for PN solutions.
- Intravenous lipid emulsions can be infused concurrently into the same vein as ELCYS containing amino acid and dextrose solutions by a Y-connector located near the infusion site; flow rates of each solution should be controlled separately by infusion pumps.
- For administration without lipid emulsion, use a 0.22 micron in-line filter.
- To prevent air embolism, use a non-vented infusion set or close the vent on a vented set, avoid multiple connections, do not connect flexible containers in series, fully evacuate residual gas in the container prior to administration, do not pressurize the flexible container to increase flow rates, and if administration is controlled by a pumping device, turn off pump before the container runs dry.
- If infused with lipid emulsion, do not use administration sets and lines that contain di-2-ethylhexyl phthalate (DEHP). Administration sets that contain polyvinyl chloride (PVC) components have DEHP as a plasticizer.
- Visually inspect the diluted PN solution containing ELCYS for particulate matter before admixing, after admixing, and prior to administration. The solution should be clear and there should be no precipitates. A slight yellow color does not alter the quality and efficacy of this product.

2.3 Preparation Instructions for Admixing Using a Parenteral Nutrition (PN) Container

- Remove ELCYS vial from the carton and inspect for particulate matter.
- Transfer the required amount of ELCYS to an amino acid solution using strict aseptic techniques to avoid microbial contamination.
- The amino acid solution containing ELCYS can then be used to prepare admixtures in the PN container using strict aseptic techniques.
- Amino acids solution containing ELCYS may be mixed with dextrose injection. The following proper mixing sequence must be followed to minimize pH related problems:

    1. Transfer dextrose injection to the parental nutrition pooling container
    2. Transfer phosphate salt
    3. Transfer ELCYS-containing amino acid solution
    4. Transfer electrolytes
    5. Transfer trace elements

- Use gentle agitation during admixing to minimize localized concentration effects; shake containers gently after each addition.
- For automated compounding, refer to Instructions for Use of the applicable compounder.
- Because additives may be incompatible, evaluate all additions to the PN container for compatibility and stability of the resulting preparation. Consult with pharmacist, if available. Questions about compatibility may be directed to Exela Pharma Sciences, LLC. If it is deemed advisable to introduce additives to the PN container, use aseptic technique.
- Inspect the final PN solution containing ELCYS to ensure that precipitates have not formed during mixing or addition on additives. Discard if any precipitates are observed.

Stability and Storage

- For single use only. Discard used container of ELCYS.
- Use of ELCYS for admixing should be limited to up to 4 hours at room temperature (25ºC/77ºF) after the container closure has been penetrated. Discard any remaining drug.
- Use PN solution containing ELCYS promptly after mixing. Any storage of the admixture should be under refrigeration and limited to a brief period of time, no longer than 24 hours. After removal from refrigeration, use promptly and complete the infusion within 24 hours. Discard any remaining admixture.
- Protect PN solution from light.

2.4 Dosing Considerations

- The dosage of the final PN solution containing ELCYS must be based on the concentrations of all components in the solution and the recommended nutritional requirements *[see Dosage and Administration (2.5)]*. Consult the prescribing information of all added components to determine the recommended nutritional requirements for dextrose and lipid emulsion, as applicable.

- The dosage of ELCYS should be individualized based on the patient's clinical condition (ability to adequately metabolize amino acids), body weight and nutritional/fluid requirements, as well as additional energy given orally/enterally to the patient. Prior to initiating parenteral nutrition, the following patient information should be reviewed: review of all medications, gastrointestinal function and laboratory data (such as electrolytes (including magnesium, calcium, and phosphorus), glucose, urea/creatinine, liver panel, complete blood count and triglyceride level (if adding lipid emulsion).

- Prior to administration of PN solution containing ELCYS, correct severe fluid, electrolyte and acid-base disorders.

2.5 Recommended Dosage in Pediatric Patients and Adults

The recommended dosage and volume of ELCYS is shown in Table 1 and is based upon the recommended daily protein (amino acids) requirement. For pediatric patients from birth to less than 12 years of age, the recommended dosage of ELCYS is 22 mg/gram of amino acids. For adults and pediatric patients 12 years of age and older, the recommended dosage of ELCYS is 7 mg/gram of amino acids.

Table 1. Recommended Daily Dosage of ELCYS in Pediatric Patients and Adults

Age	Recommended Protein[a] Requirement (g AA/kg/day)[1]	Recommended Dosage (mg ELCYS/g AA)	Recommended Volume (mL ELCYS/g AA)
Preterm and term infants less than 1 month of age	3 to 4	22	0.44
Pediatric patients 1 month to less than 1 year of age	2 to 3	22	0.44
Pediatric patients 1 year to 11 years of age	1 to 2	22	0.44
Pediatric patients 12 years to 17 years of age	0.8 to 1.5	7	0.14
Adults: Stable Patients	0.8 to 1	7	0.14
Adults: Critically Ill Patients[b]	1.5 to 2	7	0.14

AA = Amino Acid

[a] Protein is provided as amino acids (AA).

[b] Includes patients requiring more than 2 to 3 days in the intensive care unit with organ failure, sepsis or postoperative major surgery. Do not use in patients with conditions that are contraindicated *[see Contraindications (4)]*

ELCYS contains 50 mg/mL of cysteine hydrochloride (equivalent to 34.5 mg/mL of cysteine). Therefore, the ELCYS dosages in Table 1 provide:

- 15 mg cysteine/gram of amino acids for pediatric patients less than 12 years of age
- 5 mg cysteine/gram of amino acids for adults and pediatric patients 12 years of age and older

3 DOSAGE FORMS AND STRENGTHS

Injection: 500 mg/10 mL (50 mg/mL) cysteine hydrochloride, USP as a clear, colorless, sterile solution in a 10 mL single-dose vial.

4 CONTRAINDICATIONS

ELCYS is contraindicated in:

- Patients with known hypersensitivity to one or more amino acids.
- Patients with inborn errors of amino acid metabolism due to risk of severe metabolic or neurologic complications.
- Patients with pulmonary edema or acidosis due to low cardiac output.

5 WARNINGS AND PRECAUTIONS

5.1 Pulmonary Embolism due to Pulmonary Vascular Precipitates

Pulmonary vascular precipitates causing pulmonary vascular emboli and pulmonary distress have been reported in patients receiving PN. In some fatal cases, pulmonary embolism occurred as a result of calcium phosphate precipitates. Precipitation following passage through an in-line filter and suspected in vivo precipitate formation has also been reported. If signs of pulmonary distress occur, stop the PN infusion and initiate a medical evaluation. In addition to inspection of the solution *[see Dosage and Administration (2.1, 2.2)]*, the infusion set and catheter should also periodically be checked for precipitates.

5.2 Vein Damage and Thrombosis

ELCYS must be diluted and used as an admixture in PN solutions. It is not for direct intravenous infusion. Solutions with an osmolarity of 900 mOsm/L or greater must be infused through a central catheter *[see Dosage and Administration (2.1)]*. The infusion of hypertonic nutrient injections into a peripheral vein may result in vein irritation, vein damage, and/or thrombosis. The primary complication of peripheral access is venous thrombophlebitis, which manifests as pain, erythema, tenderness or a palpable cord. Remove the catheter as soon as possible, if thrombophlebitis develops.

5.3 Increased Blood Urea Nitrogen (BUN)

Intravenous infusion of amino acids may induce a rise in blood urea nitrogen (BUN), especially in patients with impaired hepatic or renal function. Appropriate laboratory tests should be performed periodically and infusion discontinued if BUN levels exceed normal postprandial limits and continue to rise. It should be noted that a modest rise in BUN normally occurs as a result of increased protein intake.

Administration of amino acid solutions in the presence of impaired renal function may augment an increasing BUN, as does any protein dietary component.

5.4 Acid-Base Imbalance

Administration of ELCYS may result in metabolic acidosis in preterm infants.

Administration of amino acid solutions to a patient with hepatic impairment may result in serum amino acid imbalances, metabolic alkalosis, prerenal azotemia, hyperammonemia, stupor and coma.

Frequent clinical evaluation and laboratory determinations are necessary for proper monitoring of acid-base balance during parenteral nutrition therapy. Significant deviations from normal concentrations may require the use of additional electrolyte supplements.

5.5 Hepatobiliary Disorders

Hepatobiliary disorders are known to develop in some patients without preexisting liver disease who receive PN, including cholecystitis, cholelithiasis, cholestasis, hepatic steatosis, fibrosis and cirrhosis, possibly leading to hepatic failure. The etiology of these disorders is thought to be multifactorial and may differ between patients.

Monitor liver function parameters and ammonia levels. Patients developing signs of hepatobiliary disorders should be assessed early by a clinician knowledgeable in liver diseases in order to identify possible causative and contributory factors, and possible therapeutic and prophylactic interventions.

5.6 Hyperammonemia

Hyperammonemia is of special significance in infants, as it can result in neurocognitive delays. Therefore, it is essential that blood ammonia levels be measured frequently in infants.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.