Alpha\textsubscript{1}-proteinase Inhibitor Prior Approval
January 2018

Prolastin\textsuperscript{®}-C (alpha\textsubscript{1}-proteinase inhibitor [human] lyophilized powder and solution)
Aralast NP\textsuperscript{™} (alpha\textsubscript{1}-proteinase inhibitor [human] lyophilized)
Zemaira\textsuperscript{™} (alpha\textsubscript{1}-proteinase inhibitor [human] lyophilized powder)
Glassia\textsuperscript{™} (alpha\textsubscript{1}-proteinase inhibitor [human] solution)

OVERVIEW
Alpha\textsubscript{1}-proteinase inhibitor (also known as alpha\textsubscript{1}-antitrypsin [AAT]), is indicated for use as chronic replacement or augmentation therapy in individuals who have a congenital deficiency of AAT with clinically demonstrable emphysema. In the scientific literature, the disorder is referred to as AAT deficiency whereas the deficiency or replacement protein is referred to as alpha\textsubscript{1}-proteinase inhibitor. Four products are available commercially in the US: Prolastin-C, Aralast NP, Zemaira, and Glassia. The products vary in availability and in some purification and viral inactivation processes. Aralast NP was modified from Aralast, which was approved by the FDA in 2002. Aralast NP contains significantly less truncated C-terminal lysine (removal of LYS394) compared with Aralast (2% vs. 67%).\textsuperscript{2,6} Clinical studies have demonstrated Aralast and Prolastin bioequivalence; a study involving 28 patients with congenital alpha\textsubscript{1}-antitrypsin deficiency who were given both agents at a dose of 60 mg/kg intravenously (IV) once per week showed similar effects in maintaining target serum AAT levels and increasing antigenic levels of AAT. Aralast NP is derived from pooled human plasma and undergoes manufacturing processes which include solvent detergent and nanofiltration in order to reduce risk of viral transmission. Zemaira was approved by the FDA in 2003 and is also prepared from pooled human plasma. Viral reduction steps used in the manufacturing process for Zemaira include pasteurization (60\degree C for 10 hours) and ultrafiltration.\textsuperscript{3} A study of 44 patients with congenital AAT deficiency compared 60 mg/kg IV of Zemaira to the same dose of Prolastin once per week. No clinically significant differences were seen in serum AAT levels or antigenic AAT levels between the two treatments. Prolastin-C powder for reconstitution was approved in 2009 and has improved product purity and a higher concentration of alpha\textsubscript{1}-proteinase inhibitor when reconstituted compared to Prolastin. Prolastin-C solution was recently approved in September 2017 and is expected to become available in early 2018. A comparative study has demonstrated bioequivalence of Prolastin-C and Prolastin at equipotent doses.\textsuperscript{7} Glassia, approved in 2010, is the only product, in addition to Prolastin-C liquid, available as a solution which does not require reconstitution. Studies have shown Glassia to be similar to Prolastin.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of an alpha\textsubscript{1}-proteinase inhibitor.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Prolastin-C, Aralast NP, Zemaira, or Glassia is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. Alpha\textsubscript{1}-antitrypsin deficiency with emphysema (or COPD), initial therapy. Patient must meet all criteria:
a) Patient must not be a current smoker; AND
b) Patient must have a baseline (pretreatment) AAT serum concentration < 80 mg/dL or 11 μM (11 μmol/L); AND
c) Patient must meet ONE of the following (i or ii):
   i) Moderate airflow obstruction as evidenced by forced expiratory volume (FEV₁) of 30-65% of predicted value, prior to initiation of therapy; OR
   ii) Patient has a rapid decline in lung function as measured by a change in FEV₁ greater than 120ml/year.

2. Alpha₁-antitrypsin deficiency with emphysema (or COPD), continuation therapy. Patient must meet all criteria:
   a) Patient must not be a current smoker; AND
   b) Patient must meet ONE of the following (i or ii):
      i. Elevation of AAT levels to a clinically significant level above baseline or above protective threshold as determined by the prescriber; OR
      ii. Reduction in rate of deterioration of lung function with a corresponding reduction in FEV₁ rate of decline.

Other Uses with Supportive Evidence


Approval Duration
Approval = 365 days (1 year)

References