



ATryn® (Antithrombin [Recombinant])

Facts

ATryn® (Antithrombin [Recombinant]), is approved by the U.S. Food and Drug Administration (FDA) for the prevention of peri-operative and peri-partum thromboembolic events in patients with hereditary antithrombin deficiency. It is not indicated for treatment of thromboembolic events in hereditary antithrombin deficient patients. Administered by intravenous infusion, ATryn is developed through recombinant technology. GTC has granted Lundbeck Inc. the right to market ATryn in the U.S.¹ and pursue further clinical development.

About ATryn

- ATryn was developed to provide a safe and reliable recombinant antithrombin that is readily available.³
- Recombinant antithrombin has the same amino acid sequence as antithrombin derived from human plasma.¹⁰ Antithrombin (Recombinant) and plasma-derived antithrombin both contain six cysteine residues forming three disulphide bridges and 3-4 linked carbohydrate moieties. The glycosylation profile of ATryn is different from plasma-derived antithrombin, which results in an increased heparin affinity. When assayed in the presence of excess of heparin the potency of the recombinant product is not difference from that of plasma-derived product.¹⁰
- ATryn is not formulated with human plasma protein.¹⁰

Indications and Usage:

ATryn [Antithrombin (Recombinant)] is indicated for the prevention of peri-operative and peri-partum thromboembolic events in hereditary antithrombin deficient patients.

Important Safety Information:

ATryn is contraindicated in patients with known hypersensitivity to goat and goat milk proteins. Allergic-type hypersensitivity reactions are possible. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period. Patients should be informed of the early signs of hypersensitivity reactions including hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis. If these symptoms occur during administration, treatment must be discontinued immediately. Adding ATryn to or withdrawing ATryn from anticoagulants that use antithrombin to exert their anticoagulative effects may alter this effect. To avoid excessive or insufficient anticoagulation, coagulation tests suitable for the anticoagulant used (e.g., aPTT and anti-Factor Xa activity) are to be performed regularly, at close intervals, and in particular in the first hours following the start or withdrawal of ATryn. In such situations, patients should be monitored for the occurrence of bleeding or thrombosis.

The serious adverse reaction that has been reported in clinical studies is hemorrhage (intra-abdominal, hemarthrosis, and post procedural). The most common adverse events reported in clinical trials at a frequency of $\geq 5\%$ are hemorrhage and infusion site reaction.

For more information, please see full Prescribing Information at www.lundbeckinc.com.

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About Hereditary Antithrombin Deficiency

Antithrombin deficiency may be caused by either a hereditary deficiency (genetic disorder) or an acquired deficiency (for example, impaired synthesis or increased consumption of antithrombin).

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Hereditary deficiency may result in excessive clotting, leading to venous thromboembolic events (VTEs).⁴

Antithrombin is a naturally occurring protein that helps regulate the blood clotting mechanism in the body.⁴ People with hereditary antithrombin deficiency have lower than normal levels of antithrombin and are at increased risk for venous blood clots, including pulmonary embolism, or PE (clots in the lung) and deep vein thrombosis, or DVT (e.g., clots in the leg), particularly in the high-risk situations of surgery or childbirth.⁴ Clots can also appear in veins in other areas of the body, including arms, intestinal tract and around the brain.⁴

Patients with hereditary antithrombin deficiency may be maintained on a blood thinning agent. When these patients undergo the high risk situations of surgery or childbirth, the blood thinning medication may be discontinued to minimize the risk of excessive bleeding. Antithrombin helps restore normal anticoagulation during these high risk periods.

While hereditary antithrombin deficiency may be uncommon, it carries a high risk for thrombosis. The prevalence of hereditary antithrombin deficiency in the general population is approximately one in 2,000 to one in 5,000.^{5,6} By the age of 50, approximately 50 percent of people with hereditary antithrombin deficiency will have experienced a VTE.⁶ The prevalence of VTEs caused by hereditary antithrombin deficiency has been reported in the literature to be from 2 to as high as 8 percent.⁹

About Lundbeck Inc.

Lundbeck Inc. was established in March 2009 following the acquisition of Ovation Pharmaceuticals, Inc. by H. Lundbeck A/S in Copenhagen, Denmark, and has proven success in developing and commercializing high-need treatments. The company is committed to providing innovative therapies that fulfill unmet medical needs of people with severe, and often rare, disorders for which few, if any, effective treatments are available. Lundbeck Inc. has been recognized for excellence in the global pharmaceutical and biotechnology industries with the 2009 North American Frost & Sullivan Award for Entrepreneurial Company of the Year and with the Scrip 2006 and 2007 “Pharma Company of the Year” award for small to mid-sized enterprises. More information about the company, its products and full prescribing information may be found at www.lundbeckinc.com.

About GTC Biotherapeutics

GTC Biotherapeutics (Nasdaq: GTCB) develops, supplies, and commercializes therapeutic proteins produced through transgenic animal technology. In addition to ATryn, GTC is developing a portfolio of recombinant human plasma proteins with known therapeutic properties. These proteins include recombinant forms of human coagulation factors VIIa, VIII, and IX, which are being developed for the treatment of hemophilia, and alpha-1 antitrypsin. GTC also has a monoclonal antibody portfolio that includes a monoclonal antibody to CD20 and a monoclonal antibody to CD137. GTC’s intellectual property includes a patent in the United States through 2021 for the production of any therapeutic protein in the milk of any transgenic mammal. GTC’s transgenic production platform is particularly well suited to enabling cost effective development of proteins that are difficult to express in traditional recombinant production systems as well as proteins that are required in large volumes. Additional information is available on the GTC web site, www.gtc-bio.com.

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