- Transthyretin (TTR), a 55 kDa tetramer also known as prealbumin, is a transporter of the retinol-binding protein–vitamin A complex and thyroxine that circulates in the blood; TTR can undergo rate-limiting dissociation and monomer misfolding, leading to aggregation, including the formation of amyloid fibrils.
- Mutations in the TTR gene generally destabilize the tetramer and accelerate tetramer dissociation, promoting amyloidogenesis.
- TTR-related amyloidosis is a rare, fatal, protein-misfolding disorder characterized by the formation and tissue deposition of TTR aggregates, including amyloid fibrils; TTR amyloidosis is associated with a broad spectrum of clinical symptoms, encompassing progressive neuropathy and cardiomyopathy.
- Tafamidis meglumine, the first pharmacotherapy approved to slow the progression of peripheral neurologic impairment in TTR familial amyloid polyneuropathy, is a rationally-designed, non-NSAID benzoxazole derivative that binds with high affinity and selectivity to TTR and kinetically stabilizes the tetramer, slowing tetramer dissociation and subsequent monomer formation, misfolding, and amyloidogenesis.
- Tafamidis is generally well-tolerated for the treatment of early-stage TTR amyloidosis, and it effectively stabilizes TTR across a number of amyloidogenic TTR genotypes, including wild-type TTR, and may thereby slow disease progression.
- In patients with early-stage Val30Met amyloid polyneuropathy, treatment with tafamidis results in reduced neurological deterioration, preserved nutritional status, and quality of life.

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