

considered a standard approach for symptomatic treatment of advanced NETs. Lanreotide, another long-acting somatostatin analogue that is also administered monthly, appears to have similar clinical efficacy to octreotide in the treatment of metastatic NETs and the carcinoid syndrome. As described further below, both octreotide and lanreotide also share the ability to slow tumor growth, providing an additional benefit to patients.

Somatostatin analogue side effects are generally mild. Mild nausea, abdominal discomfort, bloating, and loose stools occur in up to one-third of patients during the first month or two of treatment but usually subsequently subside. Patients with persistent symptoms of bloating or loose stools may be experiencing pancreatic insufficiency associated with use of somatostatin analogues; use of pancreatic enzyme supplements can ameliorate these symptoms. Mild glucose intolerance may also occur due to inhibition of insulin secretion. One of the more significant side effects associated with somatostatin analogues is impaired gallbladder contractility, resulting in delayed gallbladder emptying, and long-term administration of somatostatin analogues has been associated with an increased risk of cholelithiasis. For this reason, patients with advanced NETs in whom surgery is planned and for whom somatostatin analogue therapy is being considered should generally also undergo prophylactic cholecystectomy.

Over time, for reasons that remain uncertain, patients receiving somatostatin analogues for symptoms of hormone secretion may become refractory to treatment. Not uncommonly, such patients experience symptom exacerbation toward the final week of each treatment cycle. Such patients may benefit from an increased frequency of administration (i.e., every 3 weeks) or use of additional short-acting octreotide for breakthrough symptoms.

The association between high levels of circulating serotonin and symptoms of the carcinoid syndrome has also led to a strategy aiming to directly inhibit serotonin synthesis ([Fig. 84-6](#)). This approach was first undertaken in the late 1960s with the drug para-chlorophenylalanine, which was reported to reduce symptoms of carcinoid syndrome but also caused significant central nervous system (CNS) side effects. Telotristat ethyl, a tryptophan hydroxylase