EARLY RELEASE

New drugs

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Teduglutide

Approved indication: short bowel syndrome

Revestive (Shire)
vials containing 5 mg powder with diluent in pre-filled syringe

Teduglutide is specifically indicated for patients with short bowel syndrome who are dependent on parenteral nutrition. It is an analogue of glucagon-like peptide-2 (GLP-2), which is a peptide hormone secreted by L cells in the distal bowel. Teduglutide activates GLP-2 receptors in the gut and causes release of insulin-like growth factor, nitric oxide and keratinocyte growth factor. This promotes repair and normal growth of the intestinal mucosa by increasing villi height and crypt depth.

The safety and efficacy of teduglutide (given subcutaneously) has been assessed in two main placebo-controlled trials. The studies enrolled people who had been receiving parenteral support for at least 12 months on at least three days a week. The aim of treatment was to decrease their dependence on parenteral support.

In a 24-week trial of 86 adults, those given teduglutide (0.05 mg/kg/day) were more likely to respond (>20% reduction in parenteral support from baseline) compared with those given a placebo (63% vs 30%). After 24 weeks of treatment, the mean reduction in parenteral support volume was 4.4 L/week with teduglutide compared to 2.3 L/week with placebo. Also, more people receiving teduglutide than placebo had at least a one-day reduction in weekly parenteral support (54% vs 23%).[1]

In patients who completed a two-year, open-label extension of the trial, 93% (28/30) continuing teduglutide responded compared to 55% (16/29) who changed from placebo to teduglutide.[2] After 30 months of daily teduglutide, 10 patients had been weaned off parenteral support.

In another 24-week trial, 83 people were randomised to daily teduglutide 0.05 mg/kg, 0.1 mg/kg or placebo.[3] The responder rate with the 0.05 mg/kg dose was significantly higher than with placebo (46% vs 6%, p=0.005). Although there were also more responders with the 0.1 mg/kg teduglutide dose compared to placebo, this effect did not reach statistical significance (25% vs 6%, p=0.17).[3]

In a 28-week extension of the study, 68% (17/25) of patients who continued the 0.05 mg/kg daily dose had responded. In people who discontinued teduglutide, weekly parenteral support volumes had to be increased after four weeks.[4]

After long-term treatment, almost half of the people receiving teduglutide 0.05 mg/kg had developed antibodies. However, these did not appear to affect the efficacy of the drug.

The common adverse events in the trial with teduglutide were abdominal pain (28%), nausea (26%), injection-site reactions (26%), abdominal distension (17%), stoma complication (16%), headache (16%) and vomiting (14%). These events were all less common with the placebo. Sleep disorders and anxiety were also more common with teduglutide. Other events included intestinal obstruction, biliary effects (cholecystitis, cholangitis, cholelithiasis), pancreatitis, pancreatic duct stenosis and pancreatic infection. Bilirubin, alkaline phosphatase, lipase and amylase should be assessed before teduglutide is started and during treatment.

There was one death in the trials that was considered to be related to teduglutide – this was from metastatic cancer from an adenocarcinoma found in the liver.[2] Teduglutide is contraindicated in people with a gastrointestinal malignancy, or a history of it.

Colonoscopy is recommended before starting teduglutide, after 1–2 years of treatment and then every five years. If detected, colorectal polyps should be removed before a patient starts teduglutide.

Teduglutide could potentially increase the absorption of oral medicines so care should be taken with concomitant drugs that require titration or have a narrow therapeutic index (e.g. benzodiazepines, opioids, digoxin and antihypertensive drugs). In vitro studies suggest that teduglutide does not affect cytochrome P450 enzymes. P-glycoprotein drug interactions are not predicted.

The recommended dose of teduglutide is 0.05 mg/kg a day. It should be given subcutaneously at alternating sites in the abdomen. It can also be given in the thigh or arm. Following injection, maximum plasma concentrations are reached after 3–5 hours. The half-life of teduglutide is 1.1 hours and the drug is thought to be eliminated by the kidneys. The dose should be halved in patients with moderate–severe renal impairment (creatinine clearance below 50 mL/min) and end-stage renal disease. Dose adjustment is not needed in mild–moderate liver impairment. The drug has not been tested in severe liver impairment.

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

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Teduglutide seems to reduce the need for parenteral nutrition in people with short bowel syndrome and intestinal failure. However, continued teduglutide treatment is recommended in those who are able to be weaned off parenteral nutrition. Patients taking this drug need to be monitored for gastrointestinal cancer. The safety and efficacy of teduglutide has not been investigated in children.

REFERENCES

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At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.