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IN BRIEF

Nitisinone Oral Suspension *(Orfadin)* for Hereditary Tyrosinemia

The FDA has approved an oral suspension formulation of nitisinone (*Orfadin* – Sobi) for treatment of hereditary tyrosinemia type 1 (HT-1). *Orfadin* has been available in a capsule formulation in Canada since 1994 and in the US since 2002.

HT-1 is an autosomal recessive genetic disorder (estimated birth prevalence: 1:100,000) caused by mutations in the gene responsible for formation of fumarylacetoacetate hydrolase (FAH), which catalyzes the last step in tyrosine metabolism. FAH deficiency results in accumulation of upstream toxic metabolites, causing liver and kidney failure and developmental delays. Before the advent of liver transplantation, HT-1 was invariably fatal, usually as a result of liver failure or hepatocellular carcinoma. Quebec, Canada, which has a relatively high incidence of HT-1, has screened newborns for the disorder since 1970.[1]

Nitisinone inhibits 4-hydroxyphenylpyruvate dioxygenase, preventing formation of upstream toxic metabolites. Started in infancy in combination with a tyrosine- and phenylalanine-restricted diet, it can prevent development of liver and kidney disease and the need for liver transplantation.[2-4]

The recommended starting dosage of nitisinone is 0.5 mg/kg twice daily. The dosage can be increased after one month to 0.75 mg/kg twice daily (max 1 mg/kg twice daily). A 30-day supply of *Orfadin* suspension for a child weighing 10 kg costs $13,623. *Orfadin* capsules can be opened and the contents can be mixed in a small amount of water, formula, or applesauce. A 30-day supply of *Orfadin* capsules (60 5-mg capsules) costs $12,499.[5] ■

1. M Simoncelli et al. Cost-consequence analysis of nitisinone for treatment of tyrosinemia type 1. Can J Hosp Pharm 2015; 68: 210.
2. PJ McKiernan. Nitisinone in the treatment of hereditary tyrosinaemia type 1. Drugs 2006; 66:743.
3. S Gokay et al. The outcome of seven patients with hereditary tyrosinemia type 1. J Pediatr Endocrinol Metab 2016 September 28 (epub).
4. DC Bartlett et al. Early nitisinone treatment reduces the need for liver transplantation in children with tyrosinaemia type 1 and improves post-transplant renal function. J Inherit Metab Dis 2014; 37:745.
5. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2016. Reprinted with permission by First Databank, Inc. All rights reserved. ©2016. www.fdbhealth.com/policies/drug-pricing-policy.

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