



Infantile hemangioma: New therapy approved

- Before 2014, there were no FDA approved drugs for the treatment of infantile hemangioma.
- The efficacy of propranolol in the treatment of infantile hemangioma (IH) was first discovered in 2007 by a team of doctors from the Children's University Hospital of Bordeaux.
- While propranolol has long been known and used in cardiology, its use in infants with IH had never been properly studied and there was no pharmaceutical form approved for pediatric use.
- In 2009, **Pierre Fabre Dermatologie** undertook the pharmaceutical, toxicological and clinical development required to make the Bordeaux University Hospital discovery accessible to infants with IH, with proven clinical safety and efficacy.

In March 2014, a new major milestone was reached: Hemangeol™ (propranolol hydrochloride oral solution) became the first and only FDA approved treatment for "proliferating infantile hemangioma requiring systemic therapy". It will be available June 2014 in the United States. Marketing authorization with the name Hemangiolo® in Europe is expected for April 28th, 2014.

Hemangeol™ has proven safety and efficacy with twice a day dosing in a pediatric formulation.

The first global randomized controlled clinical trial for IH treatment:

- A randomized, double-blind, placebo-controlled, multi-dose, and multi-center adaptive phase II/III trial
- 65 centers, 15 countries, 460 infants aged 5 weeks to 5 months old (at therapy initiation)
- 60% of patients on Hemangeol™ 3.4mg/kg/day (divided into twice daily dosing) had complete or nearly complete resolution of IH lesion at 6 months with 10% requiring retreatment for recurrence
- The most common adverse reactions to HEMANGEOL (occurring \geq 10% of patients) were sleep disorders, aggravated respiratory tract infections, diarrhea, and vomiting
- Adverse reactions led to treatment discontinuation in fewer than 2% of patients

The only approved pediatric propranolol formulation

Hemangeol™ oral solution was specifically developed for use in the pediatric population and follows the guidelines of health regulatory agencies:

- No unnecessary excipients such as sugar, alcohol, paraben, preservatives
- Strawberry and vanilla flavors adapted to infant's taste
- Ease of administration which includes oral dosing syringe and syringe adapter
- Suitable for mixing with a small amount of milk or juice for administration

For important safety information see accompanying highlights of full prescribing information.

Pierre Fabre Laboratories is the second largest independent pharmaceutical group in France, with products distributed in more than 130 countries. Through its two branches, Pierre Fabre Pharmaceuticals and Pierre Fabre Dermo-cosmetics, Pierre Fabre's activities cover all areas of healthcare from prescription and nonprescription drugs to dermo-cosmetic treatments and natural health products. Pierre Fabre Laboratories are held in majority by the Pierre Fabre Foundation, a recognized public utility foundation since 1999, with the mission of improving access to drugs and quality healthcare in less advanced countries. The subsidiary **Pierre Fabre Dermatologie** has become a major player in dermatology over the last 30 years with a product portfolio that covers the management of major dermatological disorders including acne, psoriasis, inflammatory dermatitis, fungal infections, and alopecia. Pierre Fabre Dermatologie is committed to the absolute requirement of quality, efficacy and safety of its drugs, research into the pharmaceutical forms best suited to dermatology, and partnering in particular with pediatric dermatologists.

Infantile hemangioma: New therapy approved



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HEMANGEOL safely and effectively. See full prescribing information for HEMANGEOL.

HEMANGEOL™ (propranolol hydrochloride oral solution)
Initial U.S. Approval: 1967

INDICATIONS AND USAGE

HEMANGEOL oral solution is a beta-adrenergic blocker indicated for the treatment of proliferating infantile hemangioma requiring systemic therapy.

DOSAGE AND ADMINISTRATION

- Initiate treatment at ages 5 weeks to 5 months.
- Starting dose is 0.15 mL/kg (0.6 mg/kg) twice daily. After 1 week, increase dose to 0.3 mL/kg (1.1 mg/kg) twice daily. After 2 weeks, increase to a maintenance dose of 0.4 mL/kg (1.7 mg/kg) twice daily.
- Administer doses at least 9 hours apart during or after feeding.
- Readjust dose for changes in the child's weight.
- Monitor heart rate and blood pressure for 2 hours after the first dose or increasing dose.

DOSAGE FORMS AND STRENGTHS

Oral solution: 4.28 mg/mL propranolol hydrochloride

CONTRAINDICATIONS

- Premature infants with corrected age <5 weeks
- Infants weighing less than 2 kg
- Known hypersensitivity to propranolol or excipients
- Asthma or history of bronchospasm
- Bradycardia (<80 beats per minute), greater than first degree heart block, decompensated heart failure
- Blood pressure <50/30 mmHg
- Pheochromocytoma

WARNINGS AND PRECAUTIONS

- Hypoglycemia: Administer during or after feeding. Do not use in patients who are not able to feed or are vomiting.
- Bradycardia and hypotension.
- Bronchospasm: Avoid use in patients with asthma or lower respiratory infection.
- Increased risk of stroke in PHACE syndrome.

ADVERSE REACTIONS

The most common adverse reactions to HEMANGEOL (occurring $\geq 10\%$ of patients) were sleep disorders, aggravated respiratory tract infections, diarrhea, and vomiting.

To report SUSPECTED ADVERSE REACTIONS, contact Pierre Fabre Pharmaceuticals, Inc. at 1-855-PFPHARM (737-4276) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- The drug interactions with propranolol are those known in adults. Consider both the infant's medications and those of a nursing mother.
- CYP2D6, CYP1A2 or CYP2C19 inhibitors increase propranolol plasma concentration. CYP1A2 inducers (phenytoin, phenobarbital) or CYP2C19 inducers (rifampin) decrease propranolol plasma concentration when co-administered.
- Patients on corticosteroids may be at increased risk of hypoglycemia because of loss of the counter-regulatory cortisol response; monitor patients for signs of hypoglycemia.

USE IN SPECIFIC POPULATIONS

- HEMANGEOL is not intended to be prescribed to pregnant or nursing women. HEMANGEOL is excreted in human milk.
- Safety and effectiveness for infantile hemangioma have not been established in pediatric patients greater than 1 year of age.

For more information call 1-855-PFPHARM (737-4276) or visit www.hemangeol for full prescribing information.

Revised: 4/2014