PROPRANOLOL TREATMENT FOR INFANTILE HEMANGIOMAS: INPATIENT PROTOCOL

Guideline Number: MMG112.F

Related Policies
None

INSTRUCTIONS FOR USE

This Medical Management Guideline provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Evidence of Coverage (EOC) and Schedule of Benefits (SOB)] may differ greatly from the standard benefit plan upon which this Medical Management Guideline is based. In the event of a conflict, the member specific benefit plan document supersedes this Medical Management Guideline. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Medical Management Guideline. Other Policies and Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Management Guideline is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Member benefit coverage and limitations may vary based on the member’s benefit plan Health Plan coverage provided by or through UnitedHealthcare of California, UnitedHealthcare Benefits Plan of California, UnitedHealthcare of Oklahoma, Inc., UnitedHealthcare of Oregon, Inc., UnitedHealthcare Benefits of Texas, Inc., or UnitedHealthcare of Washington, Inc.

BENEFIT CONSIDERATIONS

Essential Health Benefits for Individual and Small Group
For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits (“EHBs”). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this guideline, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Introduction
This clinical guideline addresses the use of oral propranolol for the treatment of Infantile Hemangiomas (IH) and the potential need for up to a two day inpatient stay to monitor certain patients for heart rate, blood pressure and blood sugar levels.
• Oral propranolol is indicated for treating Infantile Hemangiomas (IH) according to U.S. Food and Drug Administration (FDA) labeled indications.
• An inpatient admission up to two days (48 hours) in a licensed acute care hospital may be indicated for treating IH with oral propranolol in infants 2 months or younger. The purpose of the inpatient admission is to monitor heart rate, blood pressure and blood sugar levels.
• Children over 2 months of age with medical comorbidities that require closer monitoring when initiating oral propranolol (e.g., small for gestational age [SGA], prematurity requiring apnea monitoring, cardiac disease, reactive airways, associated congenital anomalies) may be treated as inpatients for the same 2 day protocol unless the medical issues require longer monitoring. In that event, comorbidities requiring a longer stay must be identified, with an anticipated length of inpatient stay.
  o Medical management is highly individualized and treatment with oral propranolol is considered in the presence of ulceration, impairment, of a vital function, (ocular compromise or airway obstruction), or risk of permanent disfigurement.
  o Any requests for an extension of the inpatient stay beyond two days must be clinically reviewed.

DEFINITIONS

Infantile Hemangioma (IH): A benign neoplasm that commonly develops in neonates within their first few months of life. These vascular tumors are more common in Caucasians, and girls are three to five times more likely than boys to have a hemangioma. Most IHs undergo rapid initial proliferation, beginning in the first few weeks of life and continuing over several months followed by involution that begins in the last few months of the baby's first year. In most cases, involution dramatically decreases after 4 years of age, but significant sequelae of the lesions may persist permanently. (Léauté-Labrèze et al., 2015).

DESCRIPTION OF SERVICES

The treatment of Infantile Hemangioma (IH), the most common childhood vascular tumor with an incidence of 3% to 10%, has undergone a revolution since the observation in 2008 of dramatic regression of IH with oral propranolol, a nonselective β-adrenergic receptor-blocking agent. Although most IHs resolve naturally without treatment, approximately 10% to 15% cause complications requiring intervention, ideally early in the proliferative phase of growth (Léauté-Labrèze et al., 2016).

The mechanism of action of propranolol on IH is yet to be clearly defined. Some of the proposed hypotheses include vasoconstriction, decreased renin production, inhibition of angiogenesis, and stimulation of apoptosis (Drolet et al., 2013).

In April 2014, the U.S. Food and Drug Administration (FDA) approved oral Hemangeol (propranolol hydrochloride) solution for the treatment of proliferating IH requiring systemic therapy. For additional information see the following: https://www.accessdata.fda.gov/scripts/cder/ daf/index.cfm?event=overview.process&apilno=205410. (Accessed December 4, 2017)

CLINICAL EVIDENCE

Léauté-Labrèze et al. (2015) performed a randomized controlled trial of oral propranolol in 460 infants aged 1 to 5 months with infantile hemangiomas (IH). Patients administered a dose of 3.4 mg/kg per day exhibited a 60% rate of successful treatment (complete or nearly complete resolution of the target hemangioma), compared with a 4% rate among those treated with placebo.

Hogeling et al. (2011) conducted a randomized controlled trial in 40 children between the ages of 9 weeks and 5 years with facial IHs. Children younger than 6 months were admitted to the hospital for monitoring after their first dose at weeks 1 and 2. No significant hypoglycemia, hypotension, or bradycardia occurred. IH growth stopped by week 4 in the propranolol group. Significant decrease in IH redness and elevation occurred in the propranolol group at weeks 12 and 24 (P = .01 and .001, respectively). The authors concluded that propranolol hydrochloride administered orally at 2 mg/kg per day reduced the volume, color, and elevation of focal and segmental IH in infants younger than 6 months and children up to 5 years of age.

Georgountzou et al. (2012) evaluated the effectiveness, safety and tolerability of propranolol as single-agent treatment in 28 patients with problematic, proliferative-phase IHs. Oral propranolol was administered at a dose of 2 mg/kg/day. Cardiologic evaluation was performed before treatment initiation. Hemodynamic variables and blood glucose levels were monitored during the first 24 hours of treatment, while the children were hospitalized. Clinical response and tolerance were assessed every month, along with photographic documentation. The authors observed that propranolol as a first-line treatment, yielded excellent results with very good clinical tolerance. The optimal duration of the treatment remains to be defined by long-term observation.
Patel and Bauman (2014) conducted a literature review to evaluate best practices in the management of propranolol in the treatment of IH. Although there is a lack of consensus between routine outpatient or inpatient initial administration, inpatient initiation is suggested for infants who are ≤ 8 weeks (corrected gestational age), lack adequate social support, or have comorbid heart, lung, or blood glucose conditions. For inpatients, propranolol is initiated at 0.33 mg/kg orally three times daily (TID); and blood pressure (BP) and heart rate (HR) are checked 1 and 2 hours after each administration. If three doses are tolerated, propranolol is increased to the target of 0.66 mg/kg TID (2 mg/kg/day) with similar BP and HR monitoring. Once the target dose is tolerated for at least 2 hours, the patient is discharged. If dose initiation or escalation is not tolerated, the dose is reduced and gradually increased until tolerated.

Based on a consensus conference on the use of propranolol for treatment of IH, Drolet et al. (2013) recommend that inpatient initiation be done in infants 8 weeks of gestationally corrected age, or any age infant with inadequate social support, or any age infant with comorbid conditions affecting the cardiovascular system, the respiratory system including symptomatic airway hemangiomas or blood glucose maintenance.

REFERENCES


GUIDELINE HISTORY/REVISION INFORMATION

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<tr>
<td>04/01/2018</td>
<td>Reformatted and reorganized policy; transferred content to new template</td>
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<td>Revised coverage rationale:</td>
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<td>o Replaced language indicating:</td>
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<td>“This clinical guideline addresses the use of oral propranolol for the treatment of infantile hemangiomas (IH) and the need for up to a two day inpatient stay to monitor certain patients for heart rate, blood pressure and glycemic control” with “this clinical guideline addresses the use of oral propranolol for the treatment of infantile hemangiomas (IH) and the potential need for up to a two day inpatient stay to monitor certain patients for heart rate, blood pressure and blood sugar levels”</td>
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<td>“Oral propranolol is proven for the treatment of Infantile Hemangiomas (IH)” with &quot;oral propranolol is indicated for treating Infantile Hemangiomas (IH) according to U.S. Food and Drug Administration (FDA) labeled indications”</td>
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<td>“A two day inpatient length of stay in a licensed acute care hospital is medically necessary for the treatment of patients 2 months or younger; newborns (up 2 months or age) may be admitted to an inpatient setting for 48 hours with oral propranolol&quot; with &quot;an inpatient admission up to two days (48 hours) in a licensed acute care hospital may be indicated for treating IH with oral propranolol in infants 2 months or younger; the purpose of the inpatient admission is to monitor heart rate, blood pressure and blood sugar levels”</td>
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  | o Removed language indicating the physicians and facility providing care must follow a written protocol  
  | o Updated definitions:  
  | o Modified definition of “Infantile Hemangioma (IH)”  
  | o Removed definition of “Propranolol”  
  | o Updated supporting information to reflect the most current description of services, clinical evidence, and references  
  | o Archived previous policy version MMG112.E |