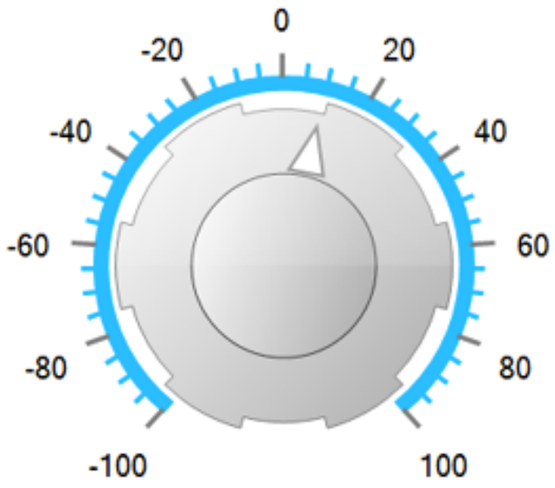
Brandogesic® (meunkephalin)

Fine-tune your control



Brandogesic

Brandogesic® (muenkephalin) Prescribing Information

INDICATION

Brandogesic® is indicated for the management of moderate to severe chronic pain when analgesia is needed for an extended period of time.

CONTRAINDICATIONS

Brandogesic® is contraindicated in patients with a known hypersensitivity to muenkephalin or any of the ingredients of Brandogesic®.

Brandogesic® is contraindicated in patients with respiratory depression (unless monitored in a setting with resuscitative equipment), asthma, head injury or ileus.

Brandogesic® is not indicated for pain in the pre- or post-operative period.

WARNINGS

Respiratory depression that does not respond to hypercapnia is the most significant risk associated with Brandogesic®. Brandogesic® should be administered cautiously to patients with conditions accompanied by hypercapnia, hypoxia or impaired respiratory reserve.

Many medications, including alcohol, other analgesics or anesthetics, tranquilizers and sedatives, or other CNS depressants can potentiate the effects of Brandogesic®, resulting in respiratory or circulatory collapse, coma or death.

In the presence of closed head injury, the hypercapnic effects of Brandogesic® may elevate intracranial pressure.

Brandogesic® may exacerbate gastrointestinal obstruction, particularly in the setting of ileus.

Brandogesic® may cause spasm at the Sphincter of Oddi.

Brandogesic® is not recommended for women who are or may become pregnant, during labor and delivery, or while nursing.

Patients should not perform activities such as driving a car or operating machinery until they understand the effects of Brandogesic® on mental and physical abilities.

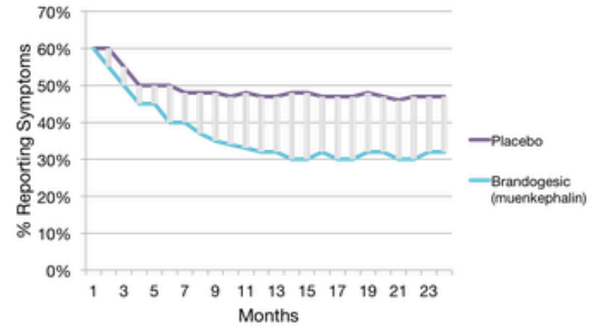
ADVERSE REACTIONS

Adverse reactions reported at (≥5%) in placebo-controlled trials were: sedation and somnolence or insomnia, nausea and/or vomiting, constipation or diarrhea, dizziness, pruritus and headache.

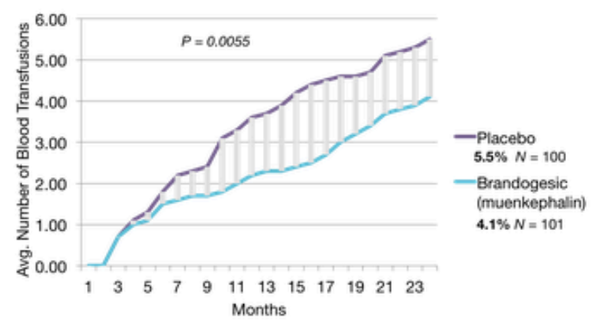
Dizziness, somnolence and confusion were seen more frequently in patients 65 years of age and over.

Meaningful Efficacy Across Multiple Endpoints

47% Reduction versus placebo in reported symptoms[1,2]



14% Reduction versus placebo in average number of blood transfusions[1,3,4]



[1]2-year, randomized, double-blind, placebo-controlled study in 201 patients with Paroxysmal nocturnal hemoglobulinuria (PNH). *N*= 201 patients.

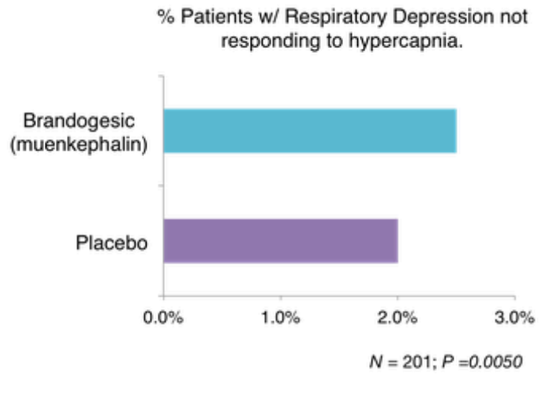
[2]Symptoms were thrombosis, smooth muscle spasm, difficulty swallowing, and pain while urinating. Patients had not experienced thrombosis in 6 months prior to trial start.

[3]Patients had not received blood transfusion in 6 months prior to trial start.

[4]All patients DAT$^-$, total bilirubin > 1.9 mg/dL, lactate dehydrogenase > 330 IU/L at baseline, with follow-up measurements at 2, 4, 8, 12, and 24 months.

Respiratory depression that does not respond to hypercapnia is the most significant risk associated with Brandogesic®. Brandogesic® should be administered cautiously to patients with conditions accompanied by hypercapnia, hypoxia or impaired respiratory reserve.

In a 2-year RCT of Brandogesic, 2.5% of patients experienced respiratory depression, vs. 2% on placebo.[1]



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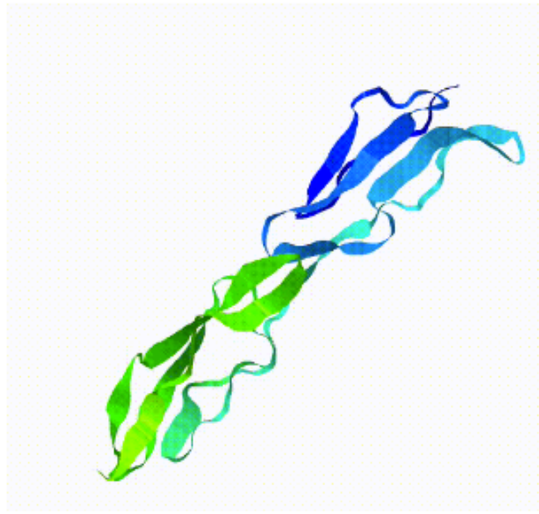
- sedation and somnolence or insomnia
- nausea and/or vomiting
- constipation or diarrhea
- dizziness
- pruritus
- headache

[1]2-year, randomized, double-blind, placebo-controlled study in 201 patients with Paroxysmal nocturnal hemoglobulinuria (PNH). *N*= 201 patients.

[2]Sedation and somnolence or insomnia: 13% (*N*= 201 *P*= 0.0050) vs. 4% on placebo Nausea and/or vomiting: 7% vs. 6% on placebo Constipation or diarrhea: 5% vs. 5% on placebo Priuritus: 5% vs. 4% on placebo Headace: 5% vs. 8% on placebo

A unique mechanism of action[1]



Brandogesic works by binding to CD55 and inhibits hemolysis specifically under conditions where blood CO_2 exceeds 25mEq/L,[1] controlling hemolysis only when blood nitrates are low and symptoms thought to be most evident.[2] CO_2 levels are thought to be higher during the day than at night, adding a further level of control.[3,4]

[1]Derk AJ, Rado CF, Pugnisans EA *AJ Gen Mut* 2014;367:1020-1036. Data on file.

[2]Cicsea M et al. *Geneticiae* 2014;12:2030-2031 and n.

[3]Matakishi ZR et al. *Sleep* 2009;1:20-41.