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BARHEMSYS® approved by US FDA www.barhemsys.com

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Overview

- On 26 February, the FDA approved BARHEMSYS® for sale in the US
  - Priority for 2020 is gaining as many hospital formulary approvals as possible

- Current unmet needs in PONV treatment provide large commercial opportunity
  - Initially focussing on ~16m patients each year in need of rescue treatment after failed prophylaxis
  - Opportunity also exists for ~18m higher risk patients each year in need of combination prophylaxis

- BARHEMSYS has a broad and unique label to address these unmet needs
  - It is the first drug approved for rescue treatment following failure of prophylaxis with standard of care
  - And the first drug approved for prophylaxis combination use with a 5-HT_3 antagonist

- Experienced team in place to support the launch that has been working for the last 2 years to prepare the market

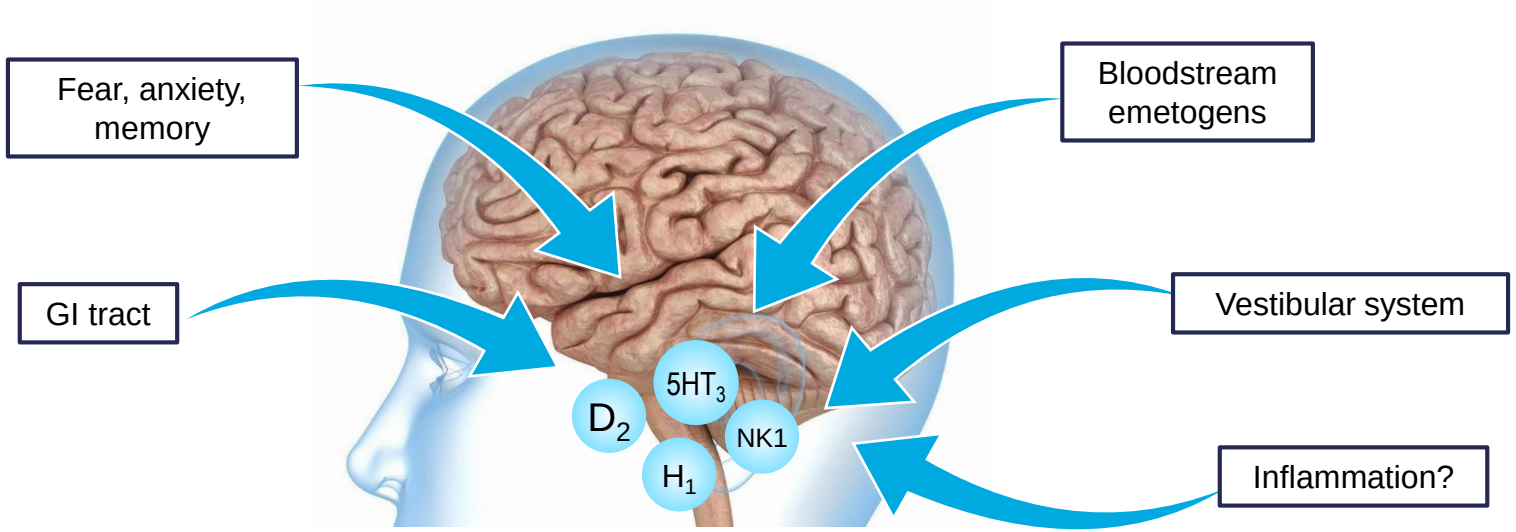
- Financial position strengthened and portfolio expanded through the Cosmo/Byfavo transaction in January 2020
  - €10m ($11.1m) equity injection received from Cosmo and €10m loan facility now available

BARHEMSYS® and the opportunity in PONV

BARHEMSYS A new option in PONV	• BARHEMSYS is the **first drug indicated for rescue treatment of PONV** following failed prophylaxis with standard of care • Differentiated antiemetic mechanism (dopamine D_2/D_3) • Clinically proven in 4 pivotal PONV trials, **demonstrated economic savings** up to ~$670 per patient
Significant US market opportunity in PONV	• ~65m eligible surgeries annually with ~49m patients receiving preventative antiemetics • **~16m of these still develop PONV and need rescue treatment with a different mechanism** • Patients receive on average 2 doses of current rescue treatments • ~18m of these patients are high-risk and eligible for combination prophylaxis
Concentrated market, addressable by small direct sales force	• ~80% of surgeries carried out in ~1,600 hospitals • Plan to launch with 30 sales territories to address the account targets with the greatest opportunity • **Core team in place, field force recruitment underway, planning to launch 2H 2020**

Nausea and vomiting is a complex process

- managed by combinations of antiemetics targeting multiple mechanisms



- Multiple pathways involved, including:
  - Serotonin (5-HT_3)
  - **Dopamine (D_2)**
  - Inflammatory mediators
  - Substance P (NK1)

- Previous drug of choice in PONV was D_2 antagonist droperidol, now rarely used due to safety issues

- Prevailing standard-of-care for PONV prophylaxis: 5-HT_3-RA ± corticosteroid
- NK1-RA added in CINV

- Despite this
  - About one-third of surgical patients still get PONV
  - Up to 50% of cancer patients still get CINV

Options for rescue treatment were unsuitable/ineffective

- "When rescue therapy is required, the antiemetic should be chosen from a **different therapeutic class** than the drugs used for prophylaxis" (Consensus Guidelines)

- 90% of US prophylaxis includes a 5-HT_3 antagonist

And yet…

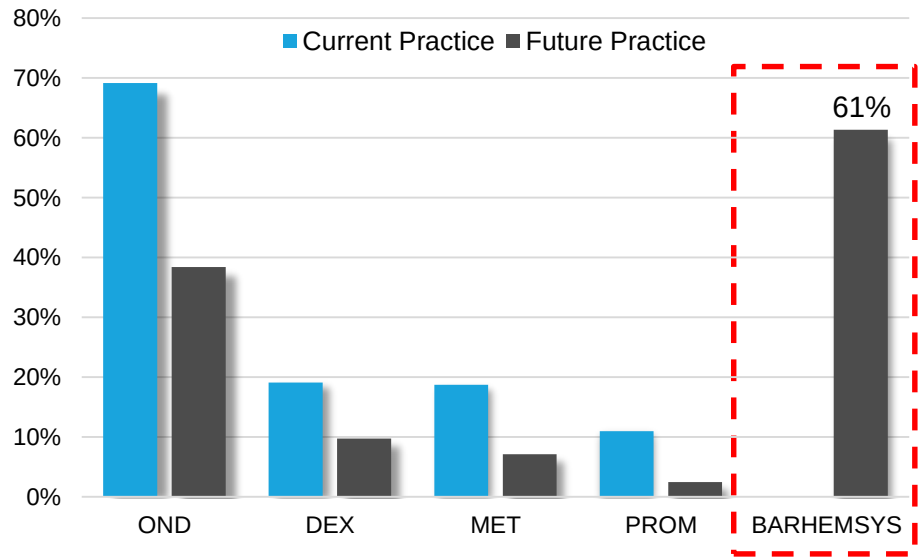
- 69% of rescue patients currently receive a 5-HT_3 (against guidelines, contrary to label)
- ~20% of rescue patients receive a steroid which has slow onset

- **Before approval of BARHEMSYS, no drug was indicated for rescue treatment of PONV**
- **No other drug shown to be effective for rescue in randomised controlled trials**

"Most rescue therapies are ineffective, would be a nice option to try" - OND/MET rescue user

"It seems ideal if we can use it the way we used droperidol before 2001" - Promethazine user

PONV Rescue Utilization



Major unmet need for an effective, safe antiemetic that is not a 5-HT_3 or steroid

BARHEMSYS® – effective for treatment and prevention of PONV demonstrated clinical benefit and significant economic benefits

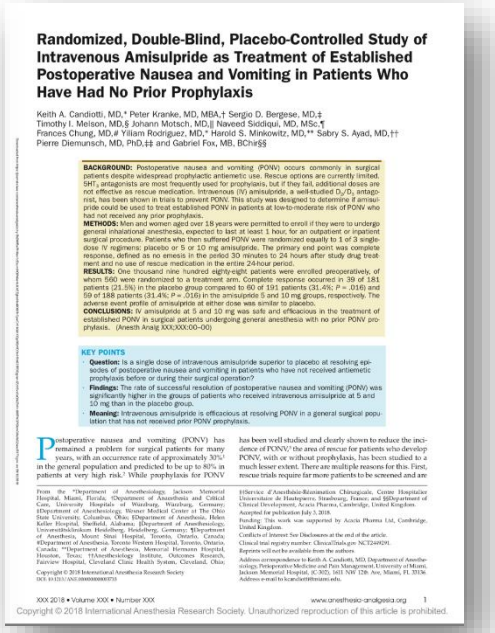
- Comprehensive clinical package of 9 clinical trials – 3,343 subjects enrolled of whom 1,954 received BARHEMSYS
- All 4 pivotal trials are published in the peer-reviewed literature

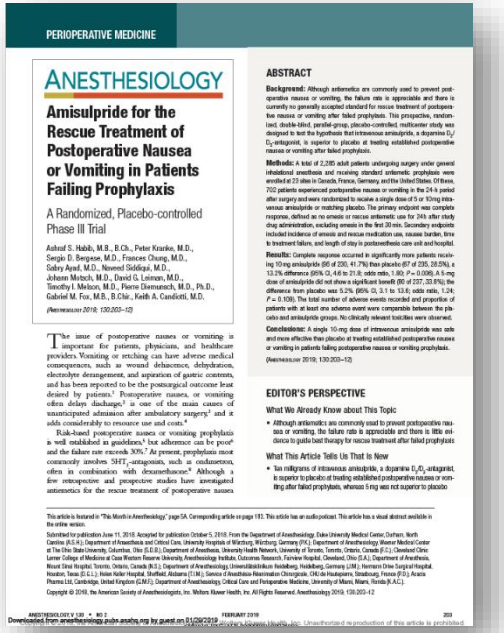

Intravenous Amisulpride for the Prevention of Postoperative Nausea and Vomiting

Two Concurrent, Randomized, Double-blind, Placebo-controlled Trials


Amisulpride Prevents Postoperative Nausea and Vomiting in Patients at High Risk

A Randomized, Double-blind, Placebo-controlled Trial


Randomized, Double-Blind, Placebo-Controlled Study of Intravenous Amisulpride as Treatment of Established Postoperative Nausea and Vomiting in Patients Who Have Had No Prior Prophylaxis


PERIOPERATIVE MEDICINE

ANESTHESIOLOGY

Amisulpride for the Rescue Treatment of Postoperative Nausea or Vomiting in Patients Failing Prophylaxis

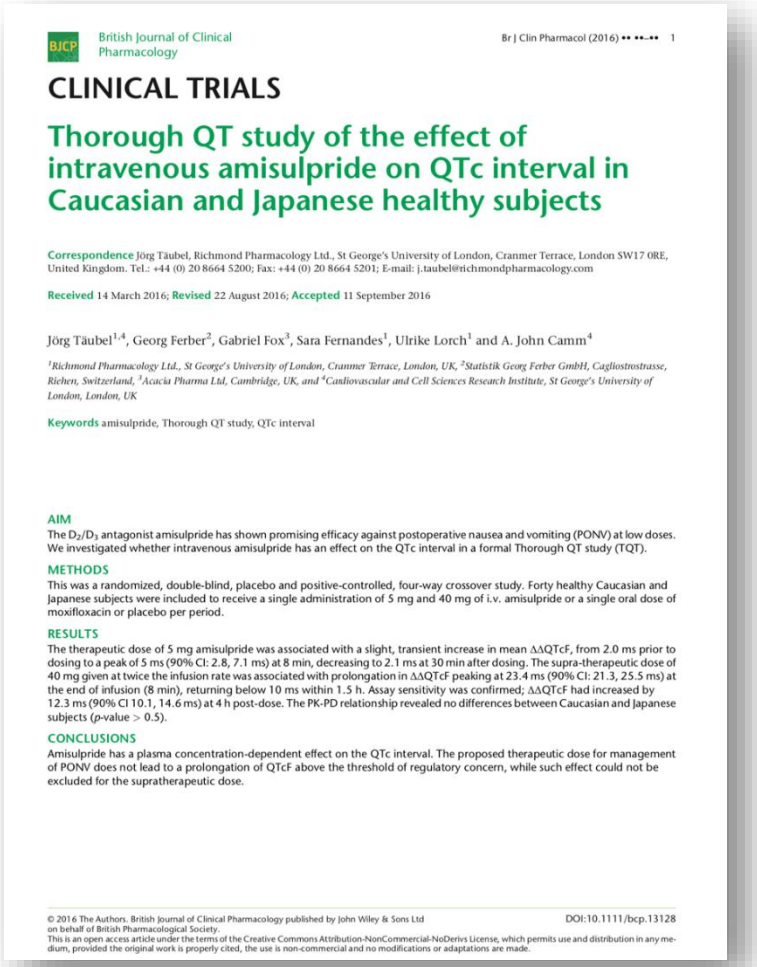
A Randomized, Placebo-controlled Phase III Trial

- First drug to be approved for rescue treatment following failed standard of care prophylaxis
- **Saves time in PACU and overall length of stay delivering potential net saving of ~$670 per rescue patient dosed***

References – 1) Kranke P, et al. (2013) Br J Anaesth 111(6): 938-945; 2) Kranke P, et al. (2018). Anesthesiology 128(6): 1099-1106; 3) Candiotti KA, et al. (2018). Anesth Analg doi: 10.1213/ANE.0000000000003733; 4) Habib AS, et al. (2019). Anesthesiology, 130:203-212

* Assuming a price of $80 per 10 mg rescue dose

BARHEMSYS® - excellent safety profile



British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2016) •• ••–••

CLINICAL TRIALS

Thorough QT study of the effect of intravenous amisulpride on QTc interval in Caucasian and Japanese healthy subjects

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Keywords amisulpride, Thorough QT study, QTc interval

AIM

The D_2/D_3 antagonist amisulpride has shown promising efficacy against postoperative nausea and vomiting (PONV) at low doses. We investigated whether intravenous amisulpride has an effect on the QTc interval in a formal Thorough QT study (TQT).

METHODS

This was a randomized, double-blind, placebo and positive-controlled, four-way crossover study. Forty healthy Caucasian and Japanese subjects were included to receive a single administration of 5 mg and 40 mg of i.v. amisulpride or a single oral dose of moxifloxacin or placebo per period.

RESULTS

The therapeutic dose of 5 mg amisulpride was associated with a slight, transient increase in mean ΔΔQTcF, from 2.0 ms prior to dosing to a peak of 5 ms (90% CI: 2.8, 7.1 ms) at 8 min, decreasing to 2.1 ms at 30 min after dosing. The supra-therapeutic dose of 40 mg given at twice the infusion rate was associated with prolongation in ΔΔQTcF peaking at 23.4 ms (90% CI: 21.3, 25.5 ms) at the end of infusion (8 min), returning below 10 ms within 1.5 h. Assay sensitivity was confirmed; ΔΔQTcF had increased by 12.3 ms (90% CI 10.1, 14.6 ms) at 4 h post-dose. The PK-PD relationship revealed no differences between Caucasian and Japanese subjects (p-value > 0.5).

CONCLUSIONS

Amisulpride has a plasma concentration-dependent effect on the QTc interval. The proposed therapeutic dose for management of PONV does not lead to a prolongation of QTcF above the threshold of regulatory concern, while such effect could not be excluded for the supratherapeutic dose.

DOI:10.1111/bcp.13128

- Excellent safety profile in all clinical trials
  - Number of adverse events generally lower with BARHEMSYS than placebo
  - Consistent with large published literature on high-dose oral amisulpride use
- Unlike droperidol, no boxed warning for QT prolongation
  - BARHEMSYS label contains similar QT language to ondansetron, the most widely used antiemetic
- Approved for use without dose modification in wide range of patients:
  - Elderly
  - Hepatic impairment
  - Mild and moderate renal impairment
- Absence of other key toxicities that limit use of older antiemetics:
  - Extrapyramidal side effects
  - Sedation
  - Tissue damage on infusion
  - Anticholinergic effects

*References – 1) Taubel J, et al. (2017) Br J Clin Pharmacol 83(2): 339-348. 2) Acacia Pharma DP10022 study report on file

BARHEMSYS® prescribing information* - a broad and unique indication

----------INDICATIONS AND USAGE ----------

BARHEMSYS is a dopamine-2 (D_2) antagonist indicated in adults for:

- Prevention of postoperative nausea and vomiting (PONV), either alone or in combination with an antiemetic of a different class. (1)
- Treatment of PONV in patients who have received antiemetic prophylaxis with an agent of a different class or who have not received prophylaxis. (1)

*Full prescribing information can be found at www.barhemsys.com

BARHEMSYS® prescribing information* - no boxed warning

CONTRAINDICATIONS

Known hypersensitivity to amisulpride. (4)

WARNINGS AND PRECAUTIONS

QT Prolongation: Occurs in a dose- and concentration-dependent manner. Avoid use in patients with congenital long QT syndrome and in patients taking droperidol. ECG monitoring is recommended in patients with pre-existing arrhythmias/cardiac conduction disorders; electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia); congestive heart failure; and in patients taking other medicinal products (e.g., ondansetron) or with other medical conditions known to prolong the QT interval. (5.1, 7.2)

ADVERSE REACTIONS

Most common adverse reactions (≥ 2%) are:

- Prevention of PONV: increased blood prolactin concentrations, chills, hypokalemia, procedural hypotension, and abdominal distension. (6.1)
- Treatment of PONV: infusion site pain. (6.1)

*Full prescribing information can be found at www.barhemsys.com

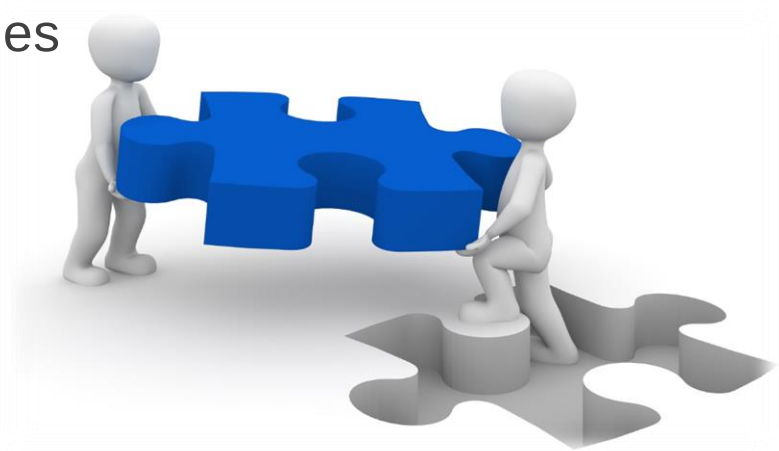
BARHEMSYS®
- stable formulation, convenient presentation

- Single terminally sterilized aqueous solution of 5 mg in a 2 mL glass vial
  - 10 mg 4 mL vial in development
- 5 year shelf life
- No refrigeration required
- No reconstitution required
- Fits in Pyxis™ machines
- Uncomplicated manufacturing process

Education on the current unmet needs in PONV is key to laying a solid foundation for launch

Why?

- No promotion or education in this space in over a decade
- Current medical practice for rescue is contrary to guidelines



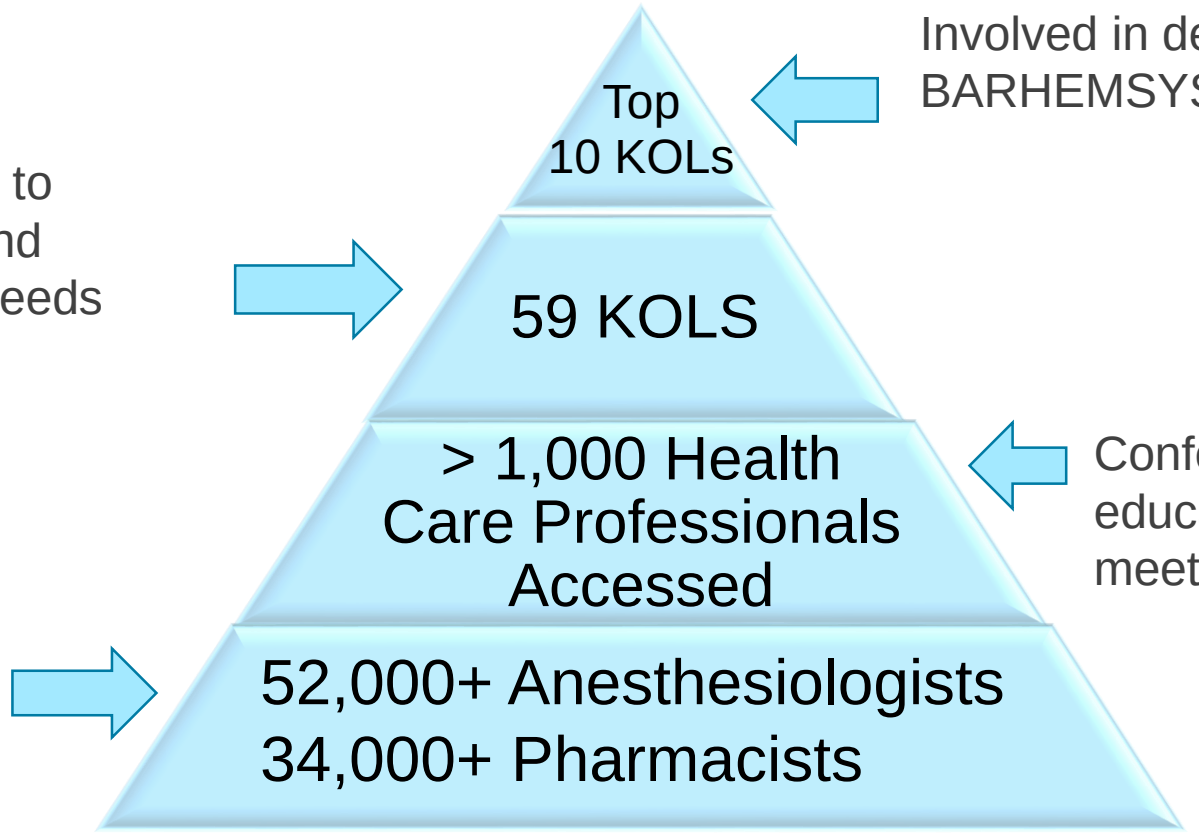
How?

- Disease state campaign that highlights:
  - Current clinical and economic impact
  - Need for different options
  - Need for different mechanism in rescue

How? – leveraged close relationships with key opinion leaders

Involved in Advisory Boards to develop PONV education and raise awareness of unmet needs in PONV

Worse.Than.Pain. print advertising campaign and Special Report on clinical and economic impact of PONV

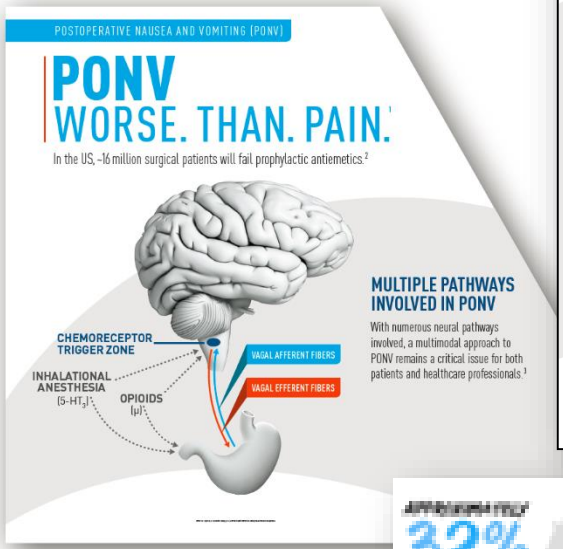


Involved in design & execution of BARHEMSYS clinical trials

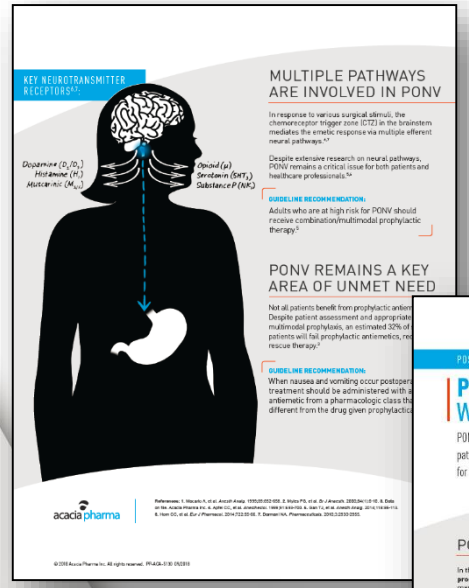
Conference presence and educational symposia at key meetings

How? - disease state awareness materials to educate and prepare the market

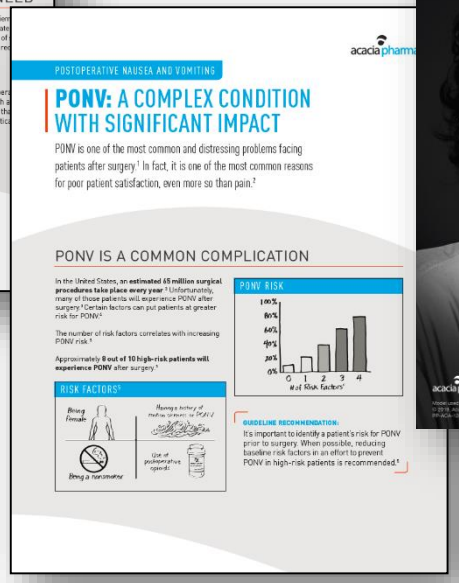
Booth panels

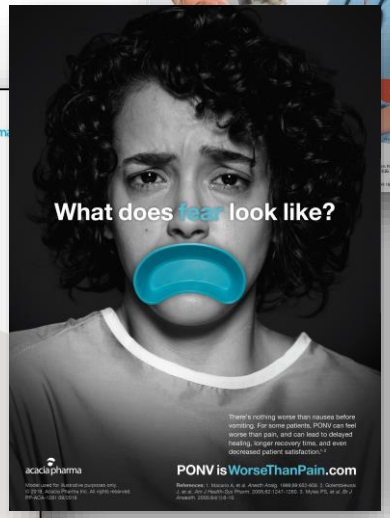


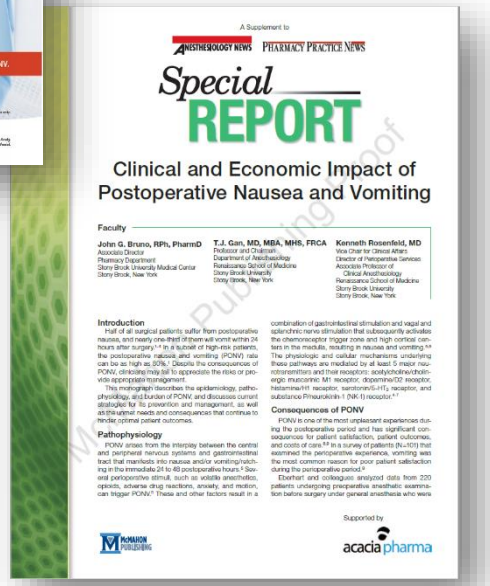
Informational brochure



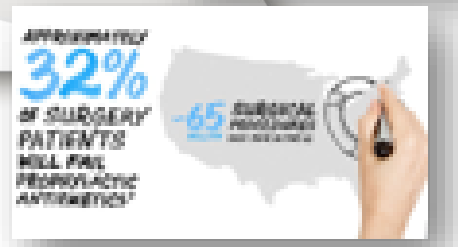
Print advertising







Educational video



Special publication

Supply chain in place to provide access to hospitals

Manufacturing	Contract manufacturing in place and fully operational with plan to make and store API and finished product to de-risk supply chain
3PL	Outsourced 3rd party logistics provider for product importation and distribution to wholesalers/hospitals contracted and ready to launch
Wholesalers	Distribution service agreements negotiated with the major hospital wholesalers plus specialty wholesalers for outpatient surgery centers
GPOs & IDNs	Ready to finalize contracts with the top Group Purchasing Organizations and Integrated Delivery Networks to facilitate ease of product access for hospitals

Experienced team with demonstrated hospital success, aligned to drive efficiencies at launch

Commercial Leadership Team

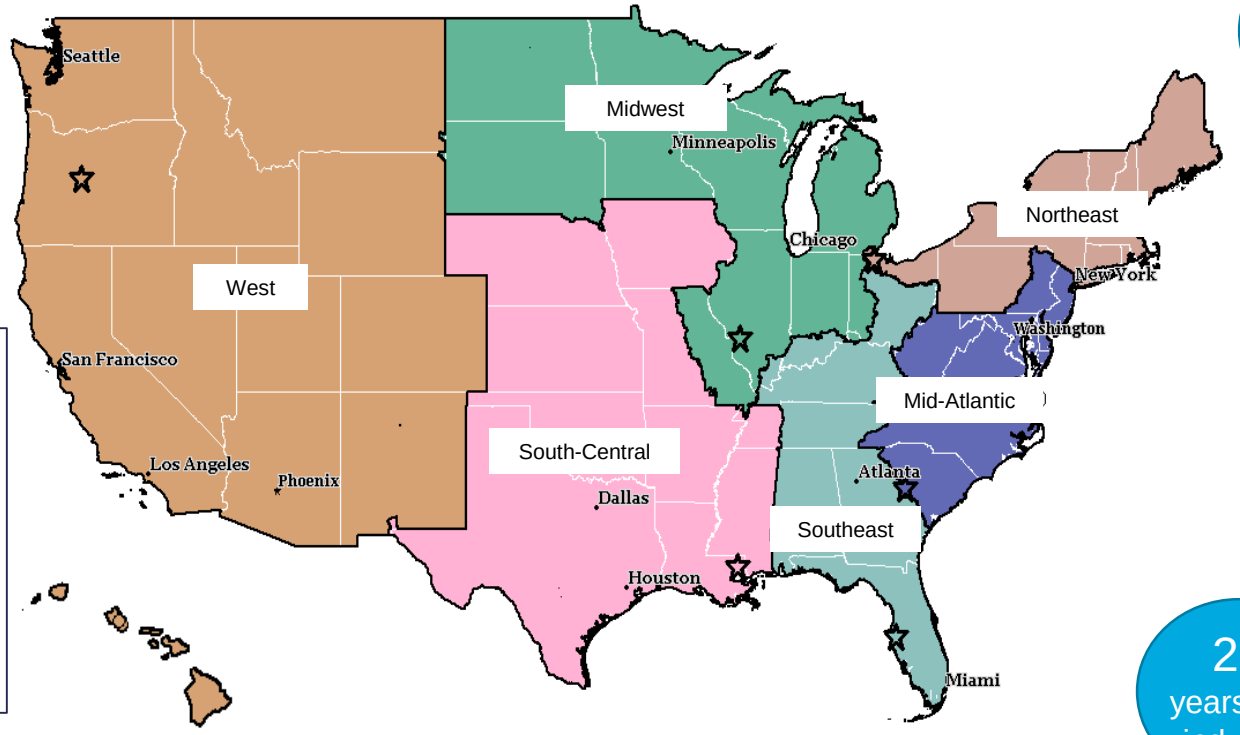
25+ years avg industry

60+ launches

Sales Leadership Team

21 years avg industry

17+ years hospital



National Accounts Team

23 years avg industry

20+ years hospital

Field Force Design

- 1 VP of Sales
- 1 National Accounts Group Leader
- 1 National MSL Group Leader
- 6 Sales Regions each with:
  - 1 RBD
  - 1 MSL
  - 1 National Account Director
  - 5 Hospital Territory Managers

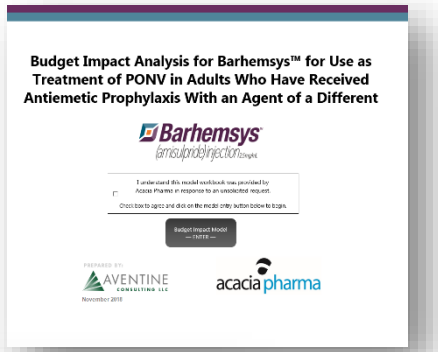
Medical Science Liaison Team

22 years avg industry

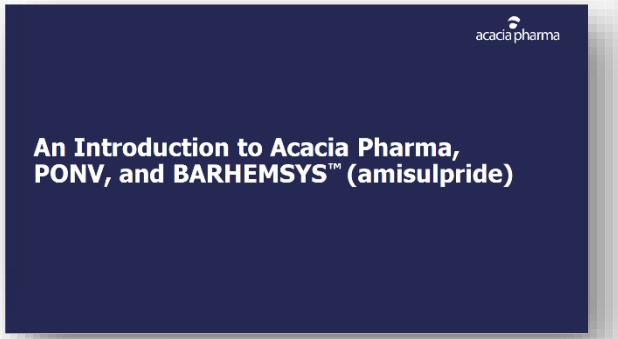
10+ years as MSL

Resources to drive formulary access and point of care availability

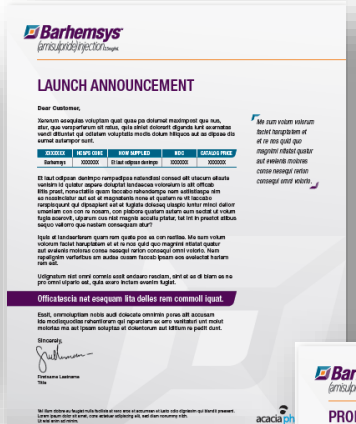
Budget impact model



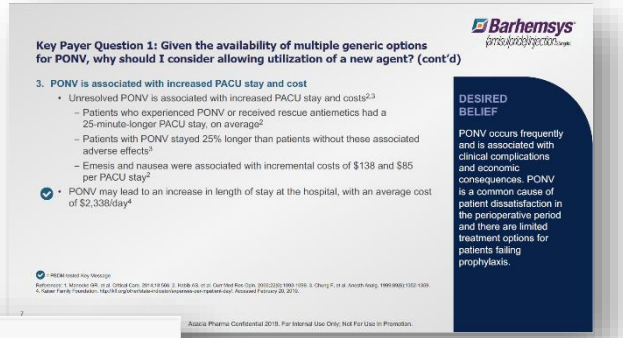
Presentation deck



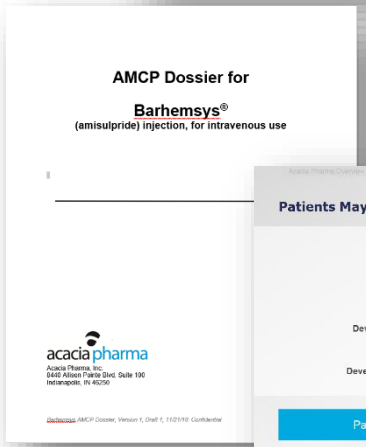
Announcement letter

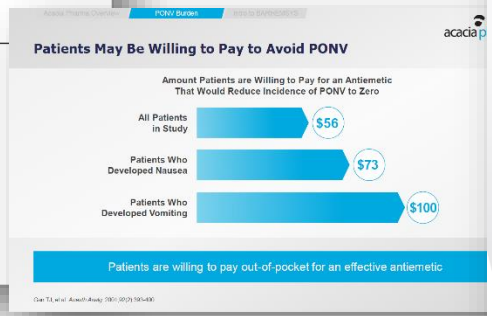


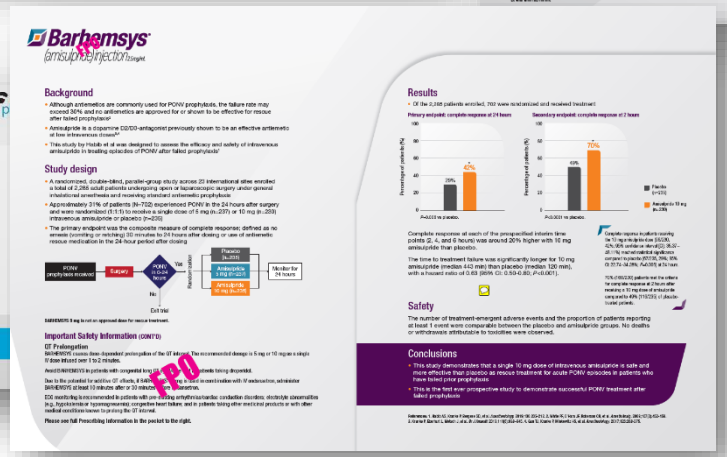
Formulary kit value message



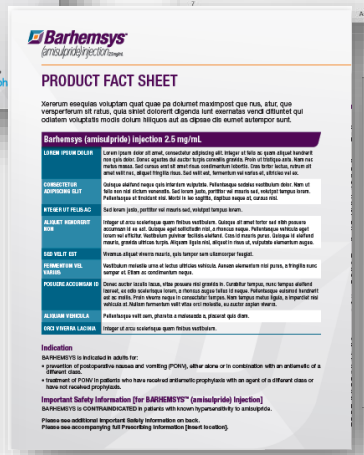
P&T committee dossier

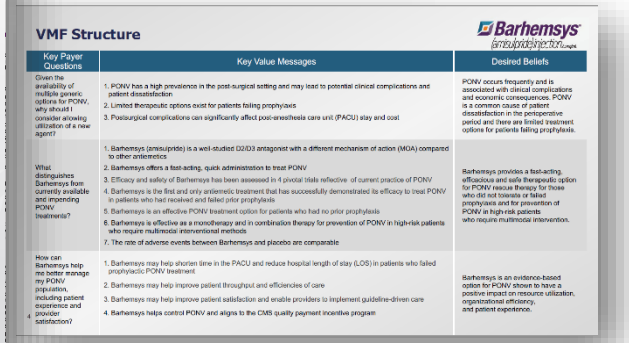






Reprint and carrier

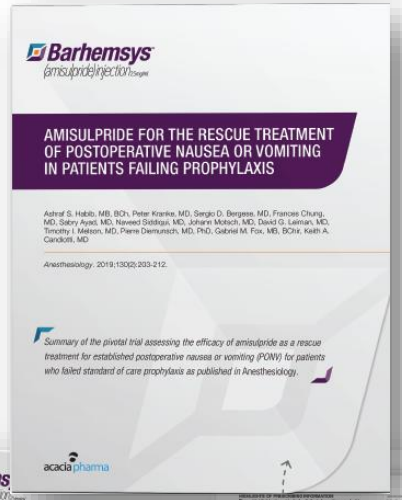




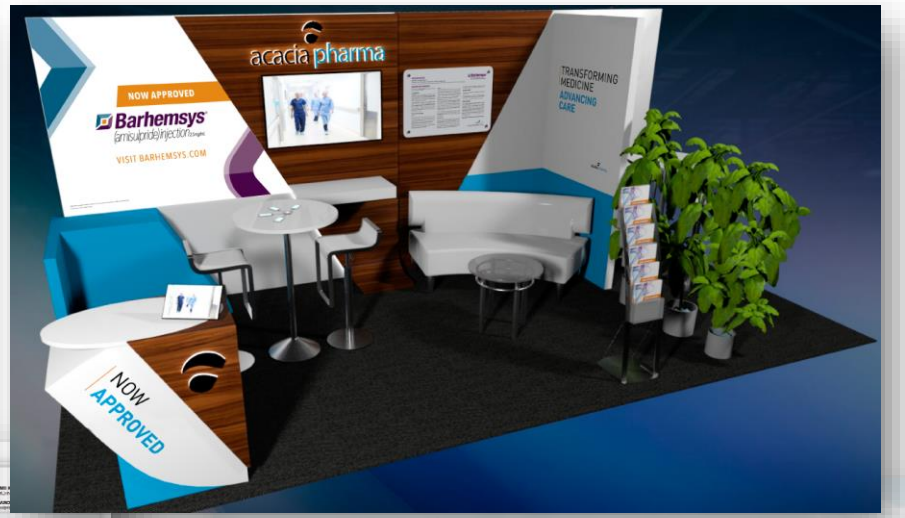
Fact sheet

… and to differentiate BARHEMSYS® and drive utilization

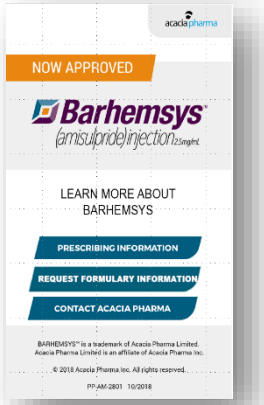
Sales aid



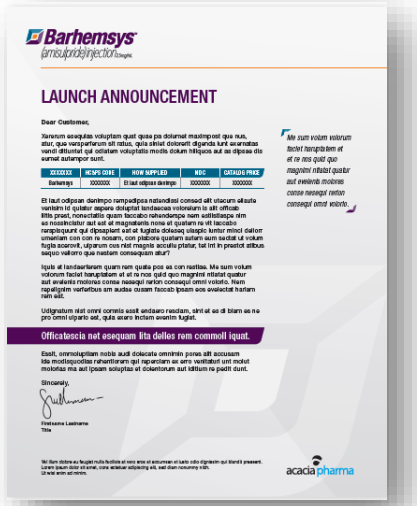
Conference booth



Website

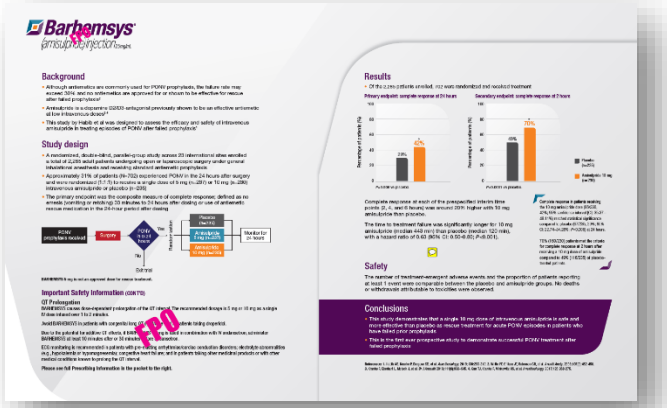


Announcement letter



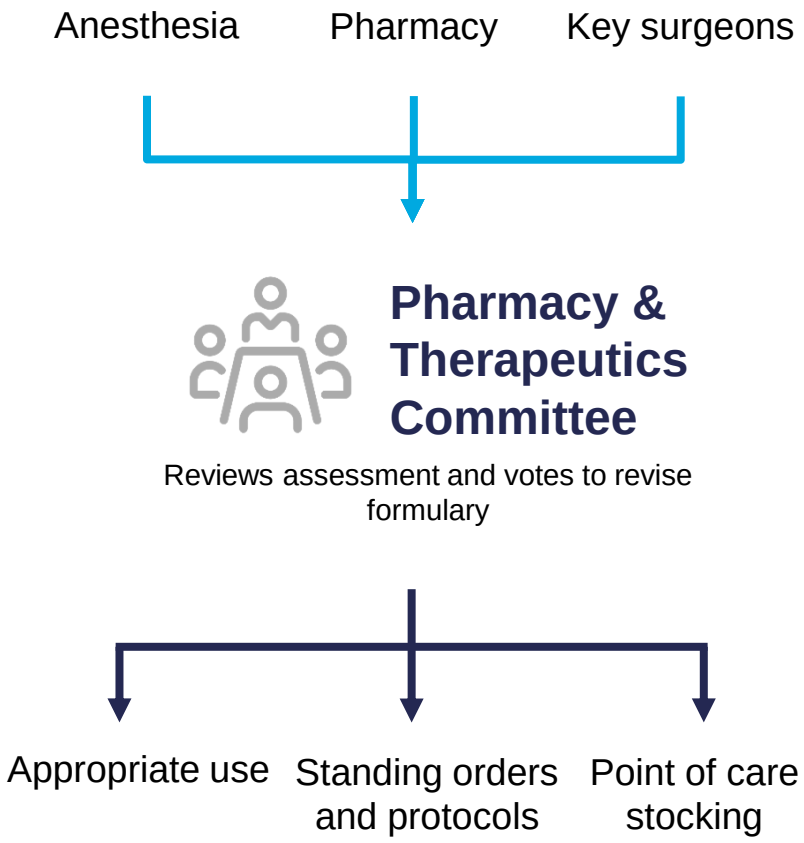
Branded campaign

Reprint and carrier



Formulary access is key:

- initial plan developed for access and pull-through based on rescue treatment

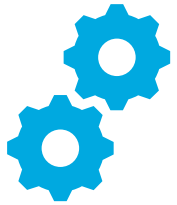


- Demonstrate real unmet need
  - No drug approved for rescue treatment
- Price for broad access on hospital formularies
- Demonstrable pharmacoeconomic benefit
  - ~$670 net saving per rescue patient dosed*
- Paid for through capitated fixed fee for surgical procedure - “the DRG”
- Appropriate restrictions on use in place
  - Use following failed standard of care or in high risk patients

* Assuming a price of $80 per 10 mg rescue dose

Formulary process and timing

- Highly experienced commercial team
  - Many successful hospital launches
  - Knows what to expect
  - Successfully launched a branded product (OFIRMEV®) into a generic post-operative market to same key players (anesthesiologists) with a similar value proposition



- Hospital products require formulary approval before physicians gain access
  - Average formulary process of 9-12 months
  - Leading indicators we will track:
    - Formulary reviews scheduled
    - Positive formulary decisions
    - Initial and repeat product orders by account

Summary

- On 26 February the FDA approved BARHEMSYS® for sale in the US
- Priority for 2020 is to obtain as many hospital formulary approvals as possible
- Current unmet needs in PONV management provide large commercial opportunity
- BARHEMSYS has a broad and unique label to address these unmet needs
- Financial position strengthened and portfolio expanded through the Cosmo/Byfavo transaction in January 2020
- Experienced team in place to support the launch that has been working for the last 2 years to prepare the market

- We look forward to making this medicine available to physicians and patients to help solve an unmet need that:
  - Patients perceive as **Worse.Than.Pain.**
  - And to helping improve outcomes, reduce overall hospital costs and enhance surgical recovery for patients