Proposed Regulation: Increase Number of Patients to Which DATA-Waived Physicians Can Prescribe Buprenorphine

White House Office of Management and Budget, Office of Information and Regulatory Affairs

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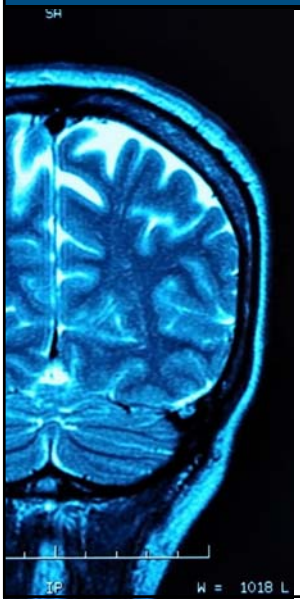
Braeburn pharmaceuticals

Braeburn Pharmaceuticals



- **Pill-free neuropharmaceutical company**
- **Focus on long-acting medicines in neuroscience**
  - Opioid addiction (buprenorphine)
    - Probuphine®
    - CAM2038
  - Pain (buprenorphine)
  - Schizophrenia (risperidone 6-month, ATI-9242)
- **Objectives**
  - Improve patient outcomes
  - Improve public health
  - Decrease social costs associated with drug diversion, misuse and non-adherence

2

Opioid Abuse Crisis

- **4.7 million Americans abuse opioids or heroin each year** (SAMHSA, 2015)
- **2.4 million Americans are dependent on opioids and/or heroin** (SAMHSA, 2015)
  - 311,718 patients taking methadone (Jones, et al., 2015)
  - 709,000 patients taking buprenorphine (Jones, et al., 2015)
  - 1.4 million patients in the "treatment gap" (Jones, et al., 2015)
- **Over 29,000 Americans died from opioid-related overdoses in 2014** (CDC, 2015)
- **Prescription opioid- and heroin-related deaths in the U.S. increased by 9% and 26%, respectively, between 2013 and 2014** (CDC, 2016)

3

Key Considerations in Increasing Buprenorphine Treatment Access

- **31,862 buprenorphine prescribers (10,281 at 100 limit)** (SAMHSA, 2016)
- **30/100 patient limit results in wait lists (e.g., ~50% of ASAM Members)** (ASAM, 2014)
- **Patient limit creates demand for diverted buprenorphine**
- **Risks of diversion, misuse, and abuse must be addressed in expanding MAT access**

By opening the door to a new generation of innovative medicines that *minimize diversion, abuse, misuse, accidental exposure, and non-compliance with doctor's directions*, the proposed regulation can *expand access* while *protecting public health*.

4

Braeburn Letter to HHS Secretary Burwell

- **Recommended increasing patient limit in manner that reflects healthcare providers' capacity to provide high-quality treatment**
- **Recommended promoting best practices in addiction treatment in manner that meets demand, provides appropriate reimbursement, and includes access in criminal justice system**
- **Recommended exemption for lower-risk patient populations:**
  - Stable patients
  - Pregnant women
  - Patients treated with implantables and injectables

5

Development of Implantable & Injectable Buprenorphine Products

Multiple implantable and injectable buprenorphine products under development; expected to account for significant percentage of patients treated over next decade.

- **Probuphine® buprenorphine subdermal implant under FDA review (FDA action expected February 27, 2016)**
- **Monthly injectable buprenorphine (Indivior) in Phase III development (anticipated commercialization by 2018)**
- **CAM2038 weekly and monthly subcutaneous buprenorphine injection products (Braeburn) in Phase III development (anticipated commercialization by 2018)**

6

Probuphine® Implant: What It Is, How It Works

- **Each implant contains 80 mg of buprenorphine**
- **Administered directly to patients**
- **Requires office-based sterile procedure**
  - 4 implants inserted sub-dermally in the upper arm

- **Continuous delivery over 6 months**
- **Implants removed after six months; new implants can be administered in other arm**

7

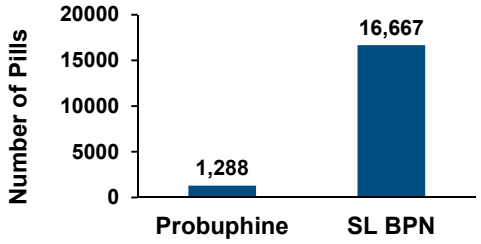
Probuphine® Implant: FDA Review, Trials, Advisory Committee

- **Granted priority review by FDA**
- **Studied in 647 subjects over the last 12 years**
  - Probuphine safety comparable to approved products
  - Insertion/removal procedures generally well-tolerated
- **Study PRO-814**
  - Head-to-head study with sublingual buprenorphine as active comparator
  - Probuphine "non-inferior" to sublingual buprenorphine
  - Totality of evidence supports the benefit of Probuphine for clinically stable patients
- **FDA advisory committee voted 12 to 5 in favor of approval**

8

Buprenorphine Diversion and Accidental Exposure: PRO 814 Study

- **Two cases of alleged theft of active sublingual buprenorphine and placebo tablets**
- **Hospitalization of subject's 2-year-old child accidentally exposed to sublingual buprenorphine**
- **Patients treated with Probuphine had fewer tablets available for diversion, misuse, abuse, and accidental exposure than patients treated with sublingual**



9

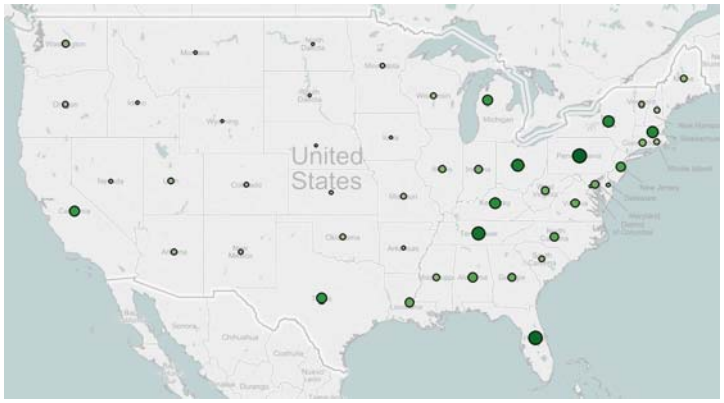
Probuphine Marketing Implementation Plan

- **Risk Evaluation and Mitigation Strategies (REMS)**
  - Educate and certify prescribers and implanters
    - Didactic
    - Live practicum
  - Inform patients of risks related to insertion, removal, and accidental overdose, misuse, and abuse
- **Training sessions targeted to physician interest and states accounting for 90% of current buprenorphine prescriptions**
- **Closed Distribution System –** Engaging DEA
- **Reimbursement** – Engaging CMS
  - Temporary G-Codes for both the medication and the procedures
  - Permanent codes using CPT procedure process

10

Buprenorphine Treatment by State

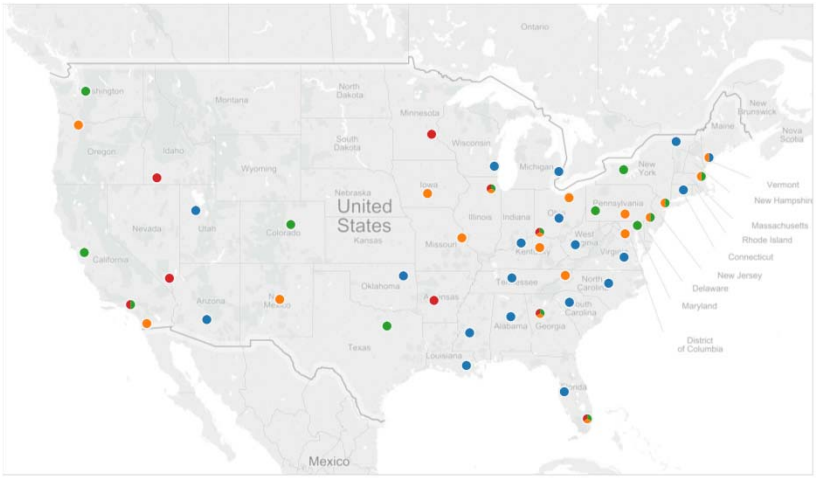
STATE	TRx	%	Cum.
PA	939,236	7.9%	7.9%
FL	874,939	7.4%	15.3%
TN	799,758	6.7%	22.0%
OH	684,261	5.8%	27.8%
MA	598,552	5.0%	32.8%
NY	577,429	4.9%	37.7%
KY	558,461	4.7%	42.4%
TX	462,475	3.9%	46.3%
MI	448,294	3.8%	50.1%
CA	446,564	3.8%	53.8%
NJ	382,296	3.2%	57.1%
AL	360,604	3.0%	60.1%
NC	333,574	2.8%	62.9%
LA	309,875	2.6%	65.5%
VA	303,083	2.6%	68.1%
GA	276,866	2.3%	70.4%
MD	268,495	2.3%	72.7%
IN	253,753	2.1%	74.8%
WV	250,008	2.1%	76.9%
IL	201,079	1.7%	78.6%
CT	200,778	1.7%	80.3%
WA	197,025	1.7%	82.0%
MS	174,514	1.5%	83.4%
ME	151,033	1.3%	84.7%
SC	149,544	1.3%	86.0%
AZ	133,836	1.1%	87.1%
UT	125,585	1.1%	88.2%
WI	123,125	1.0%	89.2%
OK	121,554	1.0%	90.2%



Source: Symphony Health Solutions. Data from period May 2014-April 2015

11

Meeting the Public Health Need: Scheduled Probuphine Trainings



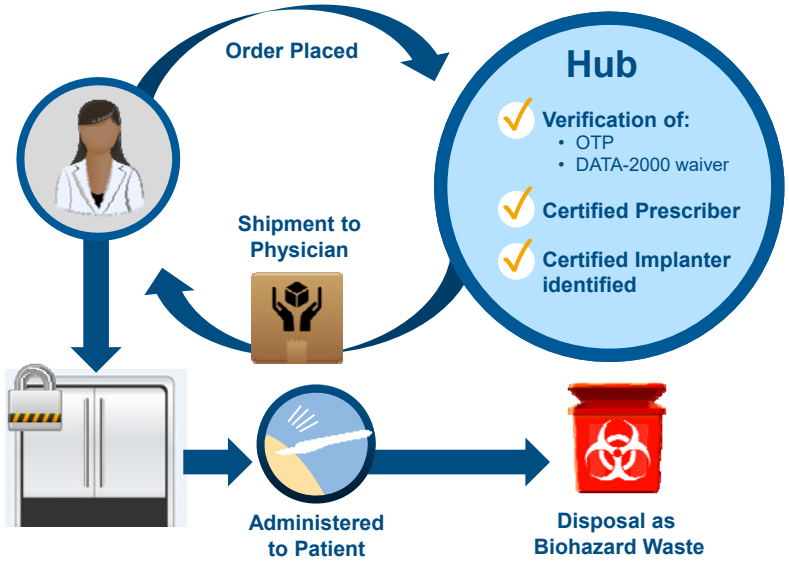
Status

Scheduled	S-March-April 2016
Plan-1	1-April-September 2016
Plan-2	2-October-March 2017
Pan-3	3-April-September 2017

Additional meetings will take place in customer locations based on demand

12

Probuphine® Closed Distribution System



13

Patient and Public Health Benefits of Implantables and Injectables

- Expected to reduce diversion, misuse, abuse, and accidental exposure
- Continuous medication delivery, lower risk of "treatment holidays" (return to illicit opioids)
- Reduced patient anxiety, lower risk of return to illicit opioids
- Improved convenience, greater compliance
- Reduced stigma
- Restored normalcy facilitates comprehensive and high-quality treatment

14

Secretary Burwell Has Authority to Create Exemptions from the Patient Limit

- **"The Secretary may by regulation change such total number." 21 U.S.C. § 823(g)(2)(B)(iii)**
- **"(T)he Secretary shall issue regulations … to address the following . . .**

  (II) Additional exemptions from the requirements of this paragraph and any regulations under this paragraph." **21 U.S.C. § 823(g)(2)(H)(ii)**

15

Exemption of Implantables and Injectables Consistent with DATA 2000 Policy

- **Proposed Exemption: patients treated with injectable or implantable buprenorphine administered by a qualifying practitioner directly to the patient**
- **Policy Rationale:**
  - DATA 2000 was designed to enable community-based use of buprenorphine while limiting risk of diversion and abuse of products prescribed for dispensing through retail pharmacy and self-administered in community
  - Implantables and injectables are not dispensed to patients for self-administration
  - By their method of drug delivery, implantables and injectables offer resistance to diversion, misuse, abuse, accidental exposure

16

Health System Costs Related to Opioid Abuse

- **U.S. prescription opioid abuse costs = +/- $55.7B (2007)**
  - 46% workplace (e.g., lost productivity)
  - 45% healthcare (e.g., abuse treatment)
  - 9% criminal justice (Birnbaum, 2011)
- **Substance use disorder treatment = $24B (2009)** (The Pew Charitable Trusts, 2015)
  - 69% from public sources (The Pew Charitable Trusts, 2015)
- **Opioid Use Disorder (OUD) patients have greater co-morbidities (e.g., hepatitis, opioid poisoning)** (McAdam-Marx, 2010)
- **Annual Medicaid population cost of patients with opioid use disorder: $23,556 versus $8,436 in control population** (McAdam-Marx, 2010)

17

Buprenorphine Treatment Expenditures

- **$2 billion annual U.S. buprenorphine market**
- **Average wholesale monthly costs per patient:**
  - $443/mo for transmucosal buprenorphine
  - $1,309/mo for monthly injectable naltrexone
- **CMS reimbursement rates for non-buprenorphine implant insertion and removal procedures (for single implant)**
  - Insertion : $143.31
  - Removal : $162.66
  - Removal and new insertion : $226.07
- **Medicaid, Medicare, VA & DOD pay for +/- 40% of all expenditures for buprenorphine for OUD** (2015 IMS PlanTrak)

18

Exempting Injectables and Implantables: Benefits Exceed Costs

- **Greater access to treatment**
  - More prescribers would be able to treat more patients under the existing patient limits
- **Expanded treatment reduces societal costs of untreated addiction**
  - Health care (e.g., overdoses, emergency room visits)
  - Productivity (e.g., disability, death, lost wages)
  - Criminal justice (e.g., drug-seeking crimes, recidivism)
- **Overall treatment costs may increase, but per patient costs may not**
  - Savings on other medications, office/pharmacy visits for prescription refills
  - Patients may dedicate saved time and effort to comprehensive treatment (e.g., psychosocial recovery) and other activities (e.g., work productivity)
- **No added costs from diversion, misuse, abuse, and accidental exposure**
- **Provider education/certification adds annual/bi-annual costs to drug companies**

19

Regulatory Flexibility Analysis: Small Businesses Will Benefit

- **Three categories of small business are potentially affected**
  - DATA-2000 waived addiction treatment providers
  - Pharmacies
  - Small businesses with employees who have OUD
- **Addiction treatment providers may accept new patients without discharging stable patients**
- **Pharmacies will not likely be affected: decrease in oral buprenorphine dispensing is unlikely**
- **Small employers will benefit from reduction in untreated OUD among employees**

20

Summary and Conclusion

- **The proposed rule should:**
  - Increase access to buprenorphine treatment
  - Create a specific exemption for a new generation of innovative implantable and injectable opioid addiction treatments that are not dispensed to patients for self-administration
- **Promulgation of rule**
  - Braeburn will provide detailed written comments
  - Public hearing could increase exposure
- **Questions?**
- **Thank you**

21

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22