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Atlas Shrugged:
Fact vs Fiction Regarding ADF Opioids

Mark Garofoli, PharmD, MBA, BCGP, CPE

Faculty

GAROFOLI

Antica Casa Vinicola

- Family of 8 Pharmacists
  - *Wife, In-Laws, & Cousins*
- Family Vineyard in the Marche Region of Italy

Disclosures

- Expert Witness: U.S. Department of Justice, Consumer Protection Branch
- Expert Witness: Cardinal Health

This presentation was not a part of the presenter's official duties at the WVU and does not represent the opinion of WVU

Opinions…

I have personal and professional opinions on pain management. However, some things are better left NSAID.

Learning Objectives

- Identify the seven current types of abuse-deterrent formulations.
- Recall all of the available abuse-deterrent formulation (ADF) opioid medications, with particular attention to the select few that are both FDA approved specifically as ADF opioid medications and available on the U.S. market.
- Discuss common methods of manipulation of abuse-deterrent formulation (ADF) opioid medications.

CDC MME Thresholds & Driving Speed Limits

Avoid Increasing >/= 90 MEDD

Speed Limits

Caution 50 MEDD

CDC MME Thresholds & Driving Speed Limits

Caution
50 MEDD

Avoid
ncreasing
90 MEDD

Driving & Opioid Risk Reduction

PDMP Review
Physical Exam
Urine Drug Screening
Use Caution with Methadone
Short Duration of Initial Opioid
Avoid Sedative Co-Prescribing
Patient & Provider Agreement/Contract
MEDD Cautionary Threshold
Gradual Tapering Plan
Abuse-Deterrent Formulations

Adapted from https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

Opioid Abuse Transition

Research

Original Investigation

The Changing Face of Heroin Use in the United States
A Retrospective Analysis of the Past 50 Years

Theodore J. Cicero, PhD; Matthew S. Ellis, MPE; Hilary L. Surratt, PhD; Steven P. Kurtz, PhD

75% of Heroin Users Started with Prescription Opioids

TJ Cicero, e. a. (2014). The Changing Face of Heroin Use in the United States. *JAMA Psychiatry*, 821-826.

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75% of Heroin Users Started with Prescription Opioids

Family, Friends, Theft ???

Healthcare Professional(s)

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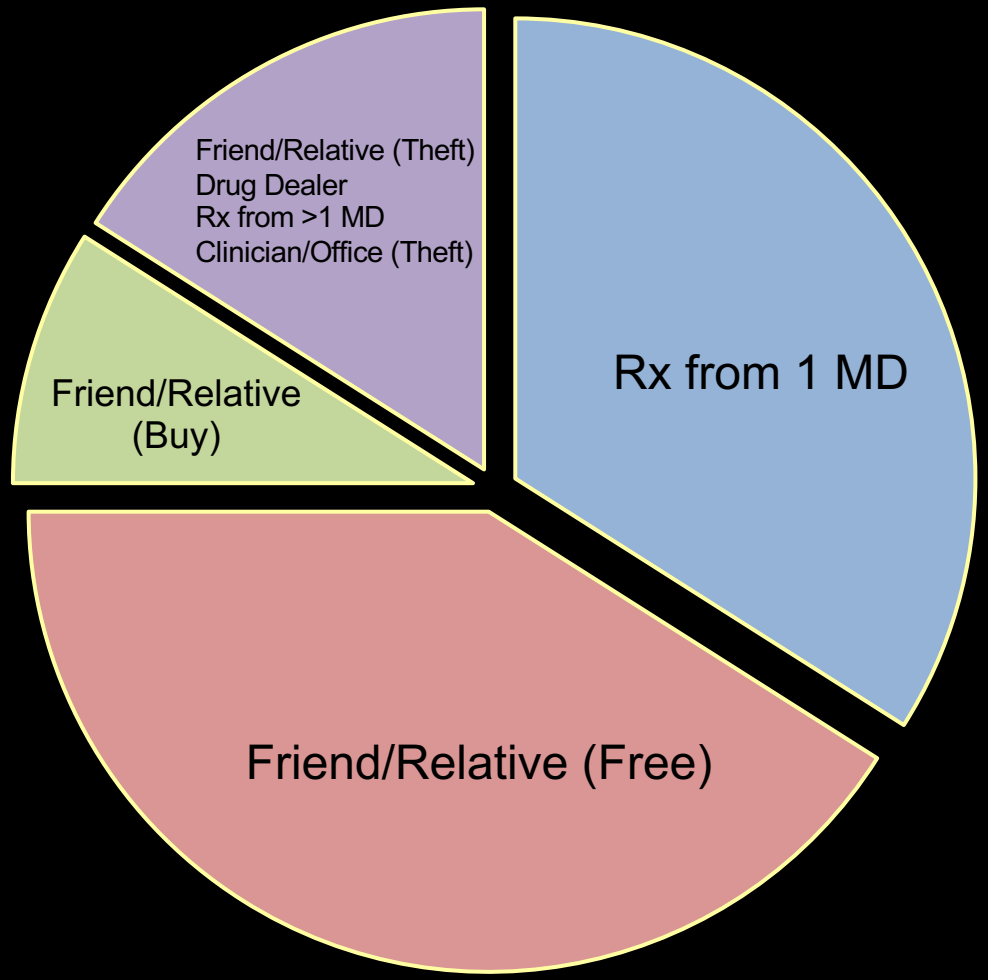
TJ Cicero, e. a. (2014). The Changing Face of Heroin Use in the United States. *JAMA Psychiatry*, 821-826.

Where are these opioids coming from…



HEALTHCARE PROFESSIONAL

~1/3rd

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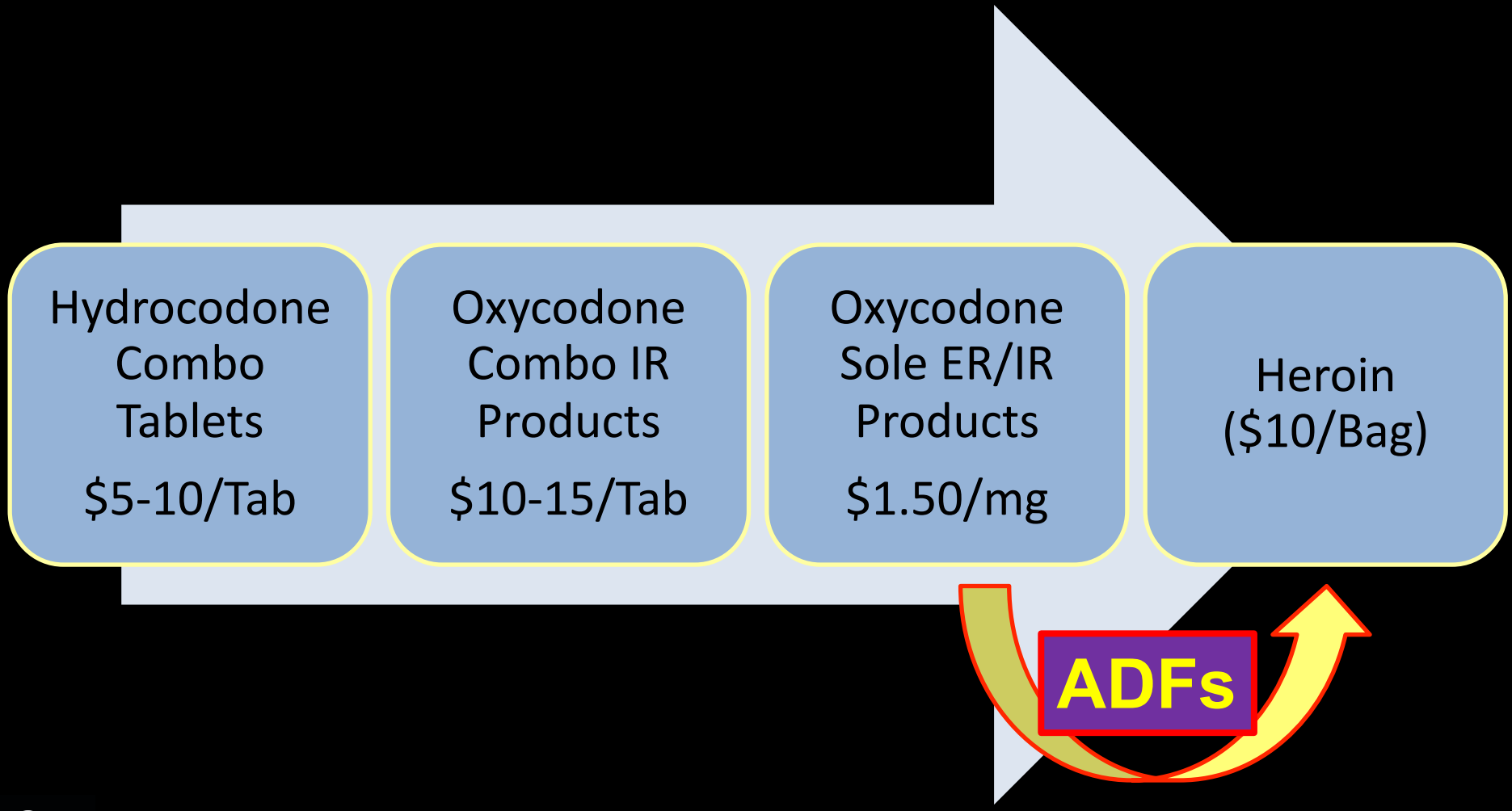
2017 DEA National Drug Threat Assessment. https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf

Opioid Abuse Transition



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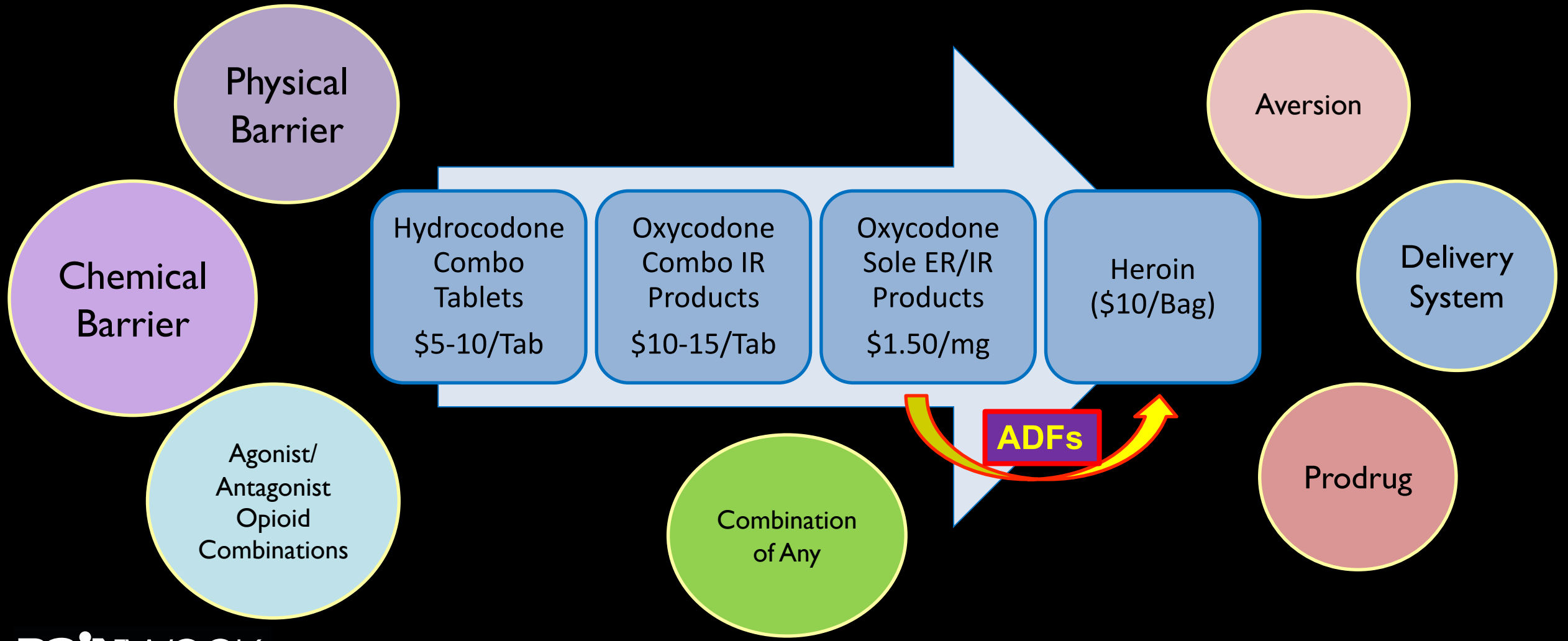
Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use – United States, 2006-2015. *Weekly* / March 17, 2017 / 66(10); 265–269.
www.bluelight.org

Opioid Abuse Transition
ADF Opioid Formulations



Types of Abuse-Deterrent Formulations (ADFs)

ADF Type	Description
1. **Physical Barrier**	Prevent chewing, crushing, cutting, grating, or grinding
2. **Chemical Barrier**	Resist extraction of the opioid through use of common solvents including water, alcohol or other organic solvents
3. **Agonist/Antagonist Opioid Combinations**	Antagonist is added to the formulation to interfere with release if taken in any other way than it was intended
4. **Aversion**	Substances are added to the dosage form to produce an unpleasant effect if the dosage form is manipulated prior to ingestion or if a higher dosage than directed is used
5. **Delivery System**	Alternative delivery systems that are more difficult to manipulate (such as a depot injectable, an implant, or transdermal application)
6. **Prodrug**	Medication contains a prodrug that lacks opioid activity until it has been transformed in the gastrointestinal tract
7. **Combination of the above**	


An Employee-Owned Company
Bob's Red Mill
GF
PREMIUM
ACTIVE DRY YEAST
QUALITY
Great for bread baking!
YOU CAN SEE OUR QUALITY
NET WT 8 OZ (227g)


Fleischmann's
ActiveDry
All Natural Yeast
YEAST
EQUALS 16 ENVELOPES
4 OZ (113 g)


Fleischmann's
ActiveDry
Yeast
ORIGINAL
Fleischmann's
ActiveDry
Yeast
ORIGINAL
Fleischmann's
ActiveDry
Yeast
ORIGINAL
THREE 1/4 OZ PACKETS • NET WT 3/4 OZ (21 g)


ACTIVE DRY YEAST
RED STAR
RED STAR
ACTIVE DRY YEAST
GMO
GLUTEN FREE

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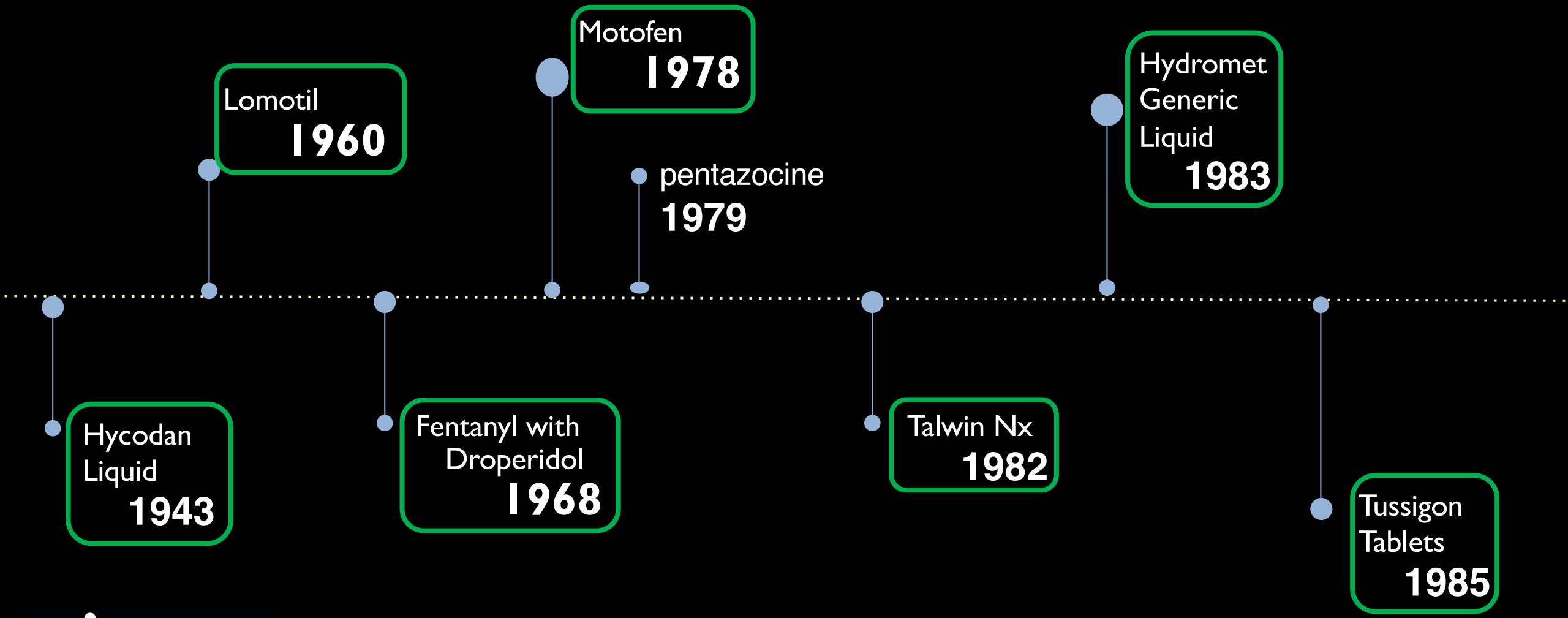
FDA Opioid Timeline



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https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

The Early "ADFs"

Hydrocodone & homatropine

- –Tussigon tablets 5mg/1.5mg (FDA 1985)
- –Hydromet liquid 5mg/1.5mg per 5mL (FDA 1943, generic 1983)
- –Homatropine
  - Anticholinergic similar to atropine (aversion)

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

The Early "ADFs"

Phenylpiperidine opioids (diarrhea treatment)

- –Lomotil® (diphenoxylate & atropine, 1960)
- –Motofen® (difenoxin & atropine, 1978): metabolite of diphenoxylate

- Atropine
  - Produces *dysphoria* in large doses (aversion)
  - Anticholinergic: blurred vision, constipation, visual disturbances

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

The Early "ADF's"

- Fentanyl with droperidol
- Dr. Robert Dripps (U of Penn) strong opponent due to abuse concerns
- Dr. Janssen (Janssen Pharmaceuticals) & Dr. Dripps developed the combination product of droperidol to fentanyl in a 50:1 ratio (FDA approved 1968)
- Dr. de Castro (Europe) recommended ratio based on his patient treatments including the droperidol to produce dysphoria if abused
- FDA later approved fentanyl as solo products

Stanley, T. The Fentany Story. The Journal of Pain, Vol 15, No 12 (December), 2014: pp 1215-1226.

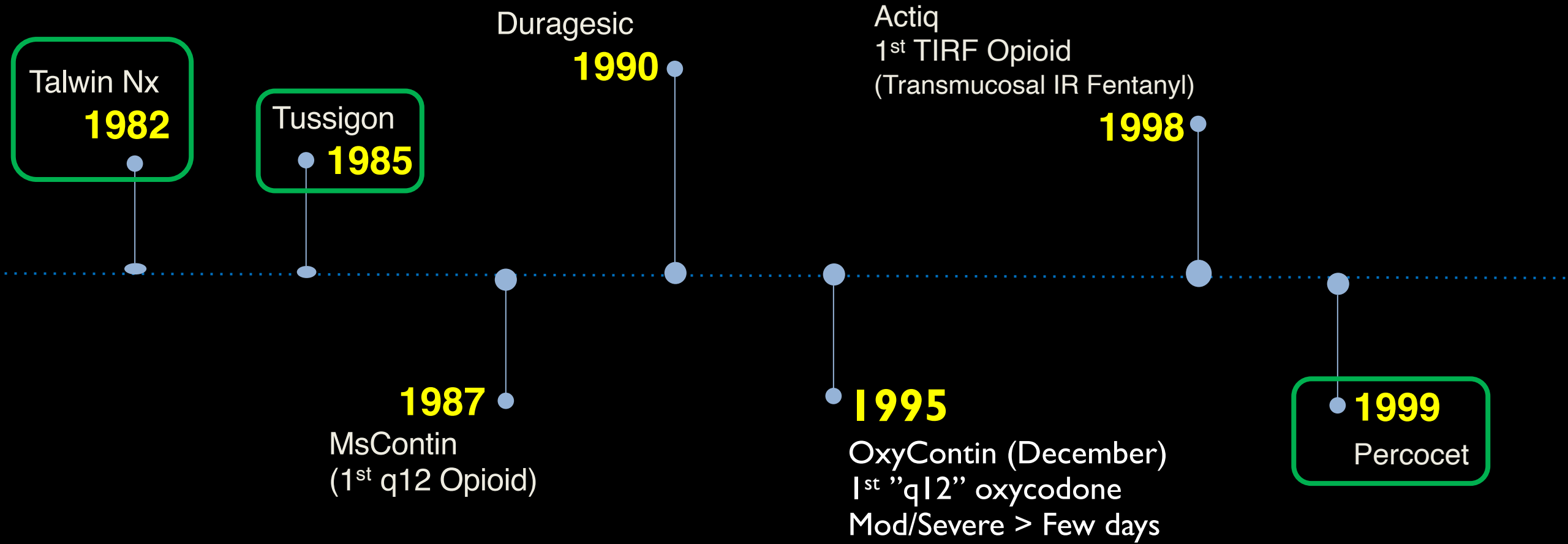
The Early "ADFs"

Pentazocine and naloxone (FDA approved in 1982)

- –Pentazocine single product
  - Kappa agonist, mu antagonist
  - Single product pentazocine FDA approved 1967
  - Observed to be crushed, mixed w/ antihistamine pyribenzamine, & injected
    - –"Pinks & Blues"
  - 1st DEA reclassification: pentazocine (single product) to CIV in 1979

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

FDA Opioid Timeline



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https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

FDA Opioid Timeline

OxyContin Label Changes
Mod/Severe ATC Several Days
Abuse/Dependence Info

2001

2002
Suboxone
2nd Naloxone Agent

FDA Amendments Act
REMS: Risk Evaluation & Mitigation Strategies

2007

2006
Opana ER
*Failed 2003
*2006: Enriched Enrollment

2009
1. Embeda: 3rd Naloxone Agent
2. Fentora: 2nd TIRF, Not Extended to Non-Cancer Pain

PainWeek

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

FDA Opioid Timeline

Reformulation of Opana ER (2006)

2011

2010

1. Reformulation of OxyContin (OP)
2. Propoxyphene Voluntary Withdrawal Recommended

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https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

The Opana Story

2011

- FDA approved Opana ER reformulation from Endo Pharmaceuticals, but without ADF Labeling

2012

- Endo submitted a citizen's petition to the FDA to remove original formulation generic oxymorphone products from the market. The petition was denied, and the FDA noted that the rate of IV abuse of the newly designed opioid had been increasing in the months after its introduction to the market

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

The Opana Story

2017 (March)

- Endo presented post-marketing data to the FDA that contained evidence of serious health concerns with IV abuse of the reformulated product, such as thrombotic thrombocytopenic purpura and an outbreak of HIV infections in Indiana
  - High molecular weight of the polyethylene oxide (PEO) coating that became lodged in the arterioles of the kidneys of IV abusers

2017 (July)

- FDA recommended Endo remove Opana ER from market, and Endo did so

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

FDA Opioid Timeline

Reformulation of Opana ER (2006)

2011

2010

1. Reformulation of OxyContin (OP)
2. Propoxyphene Voluntary Withdrawal Recommended

1. All ER/LA Opioids REMS: Prescriber Voluntary CE
2. Opana ER reformulated to avoid IN Abuse (IV Spiked)

2012

2013

1. FDA ADF Opioid Extra ADF Studies "Category 3"
2. Original Opana ER Allowed to Stay on Market
3. Recommended HCP be CII

https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

FDA Opioid Timeline

2014
Evzio
Embeda (ADF)
Hysingla (ADF)

2015
Zohydro ER
OxyContin >11yo Opioid Tolerant
MorphaBond ER
Narcan Nasal Spray

2016
Xtampza ER
Probuphine (Bup Implant)

2017
1. Arymo ER
2. RoxyBond IR
3. Sublocade (Bup QM)
4. Reformulated Opana ER Removed from Market (FDA Recommended, Endo Volunteered)
5. FDA ADF Studies Guidance
   PO, IV, IN, Sublimation (Smoking)

2018
1. Loperamide Blister/Single-Dose Packs
2. Evaluated Hydexor (Hydrocodone/APAP/Promethazine)
3. Targeted Online Opioids
4. Apadaz

2019
Dsuvia (sufentanil)
Support Act (Disposal Bags)
OTC Naloxone Discussions

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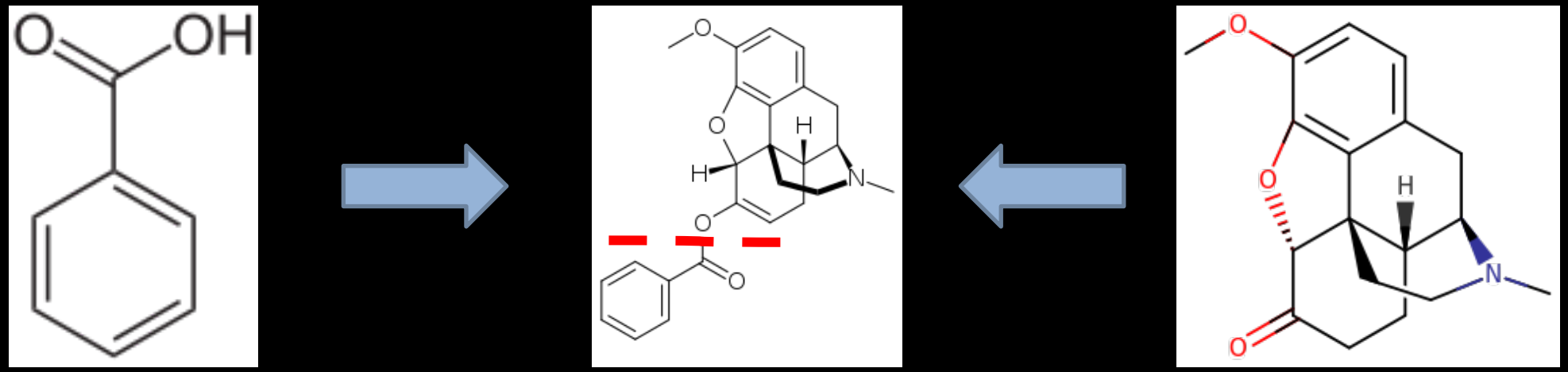
https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

Benzhydrocodone/APAP

- Prodrug of hydrocodone (+APAP) covalently bonded with benzoic acid
  - –Benzoic acid: typical food preservative
  - –Ligand-activated technology (LAT®): GI tract activation
  - –Also being studied with a methylphenidate prodrug



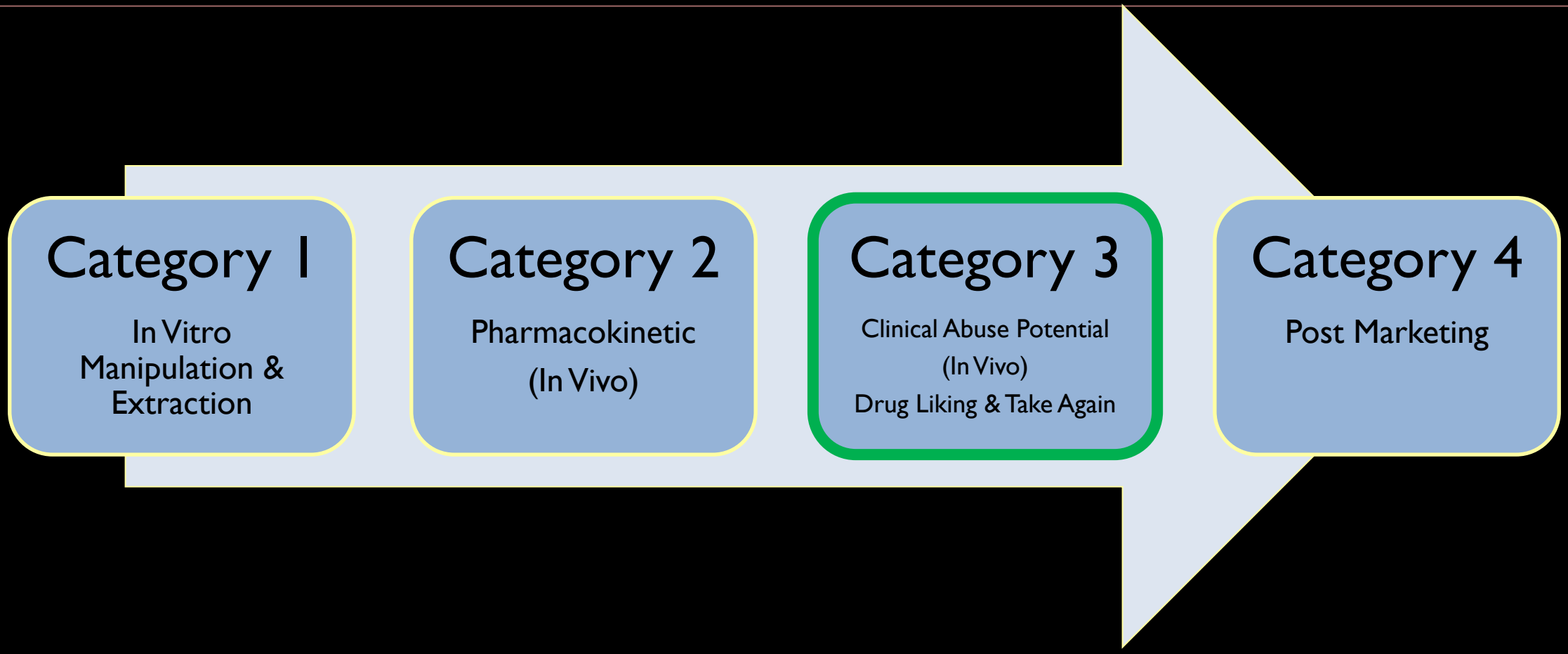
Clinical Pharmacology Online Database. 2018
Apadaz Package Insert. 2018

Benzhydrocodone/APAP

- Controlled Substance Class 2 (just as hydrocodone/apap)
- Indicated for the short-term (*no more than 14 days*) management of *acute* pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate
- NOT FDA approved as an abuse-deterrent formulation (ADF) opioid
- Benzhydrocodone/APAP 6.12/325mg = hydrocodone/APAP 7.5/325mg

Clinical Pharmacology Online Database. 2018
Apadaz Package Insert. 2018

FDA ADF Studies



https://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm338566.htm

Category 3: Abuse Potential Studies

Physically manipulated products compared to regular product

- Cutting
- Grafting
- Milling
- Chewing
- +/- Heat

Routes of Administration

–Ingestion (Oral Route)

- Oral bioavailability

–Injection (Parenteral Route)

- Extractability and Syringeability

–Insufflation (Nasal Route)

- Nasal bioavailability & PD effects

–Smoking (Inhalation Route)

- Ability to sublimate

https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

Category 3: Abuse Potential Studies

In Vitro Studies	In Vivo Studies
Extractability Studies	Nasal & Oral PK
Performed at Both Room Temp & Elevated Temp	Multiple Strengths Tested
Solvents • Level 1: deionized water • Level 2: vinegar, 0.2% baking soda solution, 40% ethanol, & carbonated drink • Level 3: 100% ethanol, 100% isopropyl alcohol, acetone, 0.1 N HCl, & 0.1N NaOH	Agonist/Antagonist Levels

https://www.fda.gov/downloads/Drugs/.../Guidances/UCM492172.pdf

So who made the cut…pun intended

FDA Approved ADF Opioids available on US Market
(July 2020)

Abuse Deterrent Formulation (ADF) Opioids

Active Ingredient	Product	FDA ADF Approval	Formulation
oxycodone	**Xtampza ER®**	IN, IV, & PO Chew	ER Capsule
	Xartemis ER® (+APAP)	-	IR/ER Tablet
	OxyContin®	IN & IV	ER Tablet
	Troxyca®	IN, IV, PO Crush	ER Capsule
	Oxaydo®	-	IR Tablet
	RoxyBond®	IN & IV	IR Tablet
tapentadol	Nucynta ER®	-	ER Tablet
hydromorphone	Exalgo®	-	ER Tablet
morphine	**Embeda®**	IN & PO Crush	ER Tablet
	Arymo®	IV	
	MorphaBond®	IN & IV	
hydrocodone	**Hysingla®**	IN, IV, & PO Chew	ER Tablet
	Zohydro ER®	-	ER Capsule
	Vantrela ER®	IV	ER Tablet
	Hydromet®	-	Liquid
	Tussigon®	-	Tablet
benzhydrocodone	Apadaz®	-	Tablet
pentazocine	Talwin NX®	-	Tablet

Targiniq (oxycodone) & Opana (oxymorphone) are Off Market

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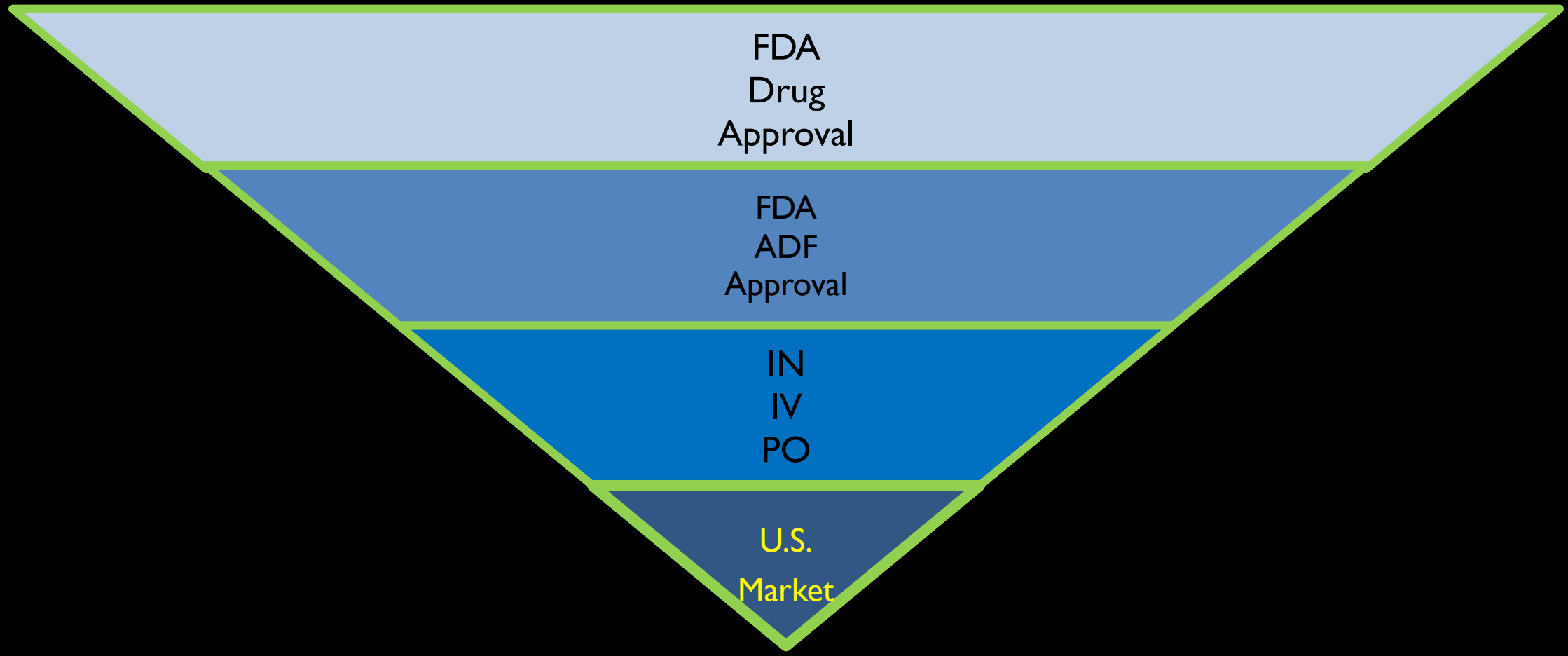
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411218/
https://www.sciencedirect.com/science/article/pii/S0378517316304884
https://www.futuremedicine.com/doi/pdf/10.2217/pmt-2015-0005
https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

ADF Opioid Funnel



FDA Approved ADF Opioids on US Market
(July 2020)

Medicine	Product	FDA ADF Approval			Formulation
oxycodone	Xtampza ER®	IN	IV	PO Chew	ER Capsule
	OxyContin®	IN	IV		ER Tablet
hydrocodone	Hysingla®	IN	IV	PO Chew	ER Tablet
morphine	Embeda®	IN		PO Crush	ER Tablet
	Arymo®		IV		
	MorphaBond®	IN	IV		

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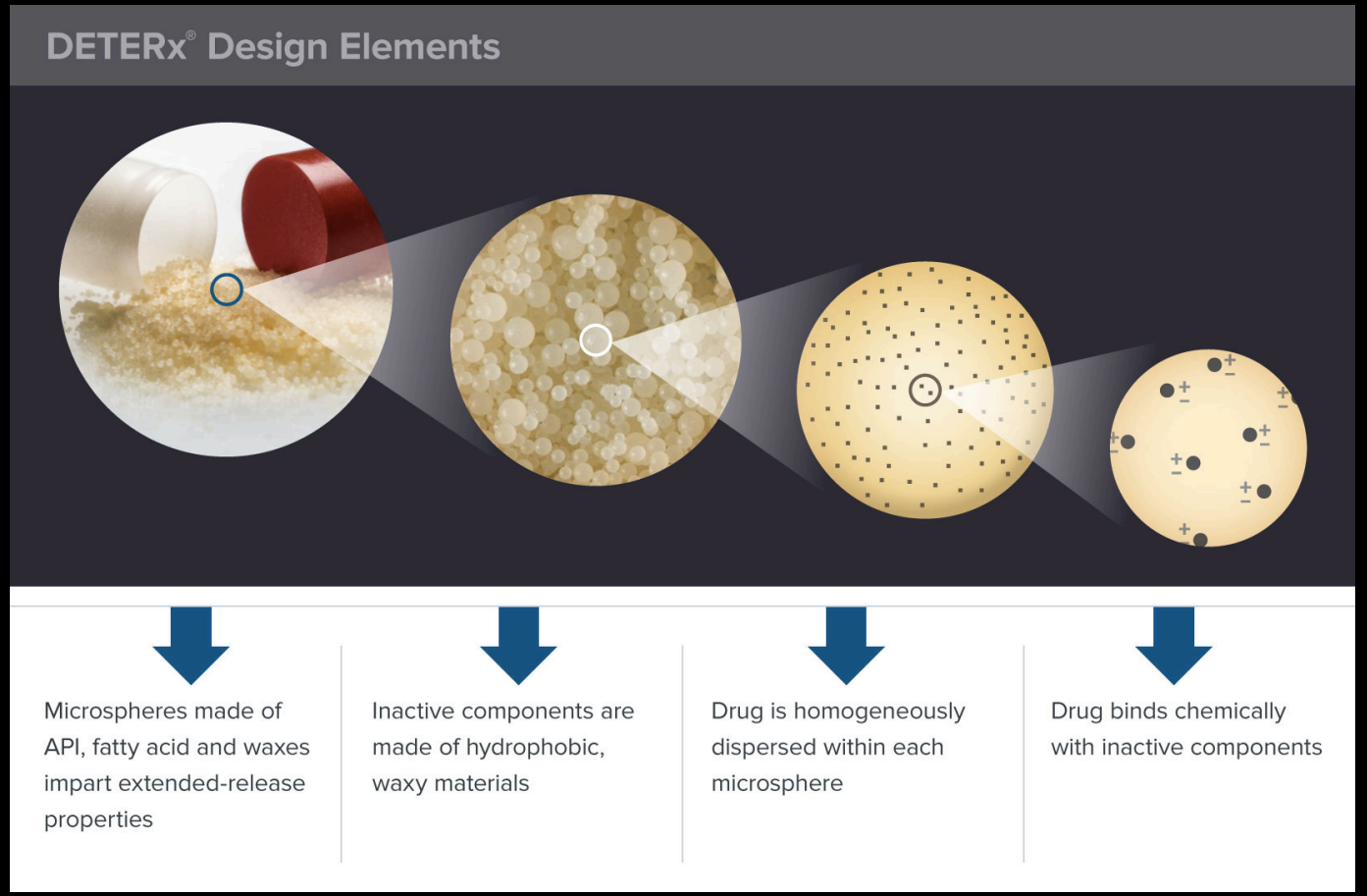
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411218/
https://www.sciencedirect.com/science/article/pii/S0378517316304884
https://www.futuremedicine.com/doi/pdf/10.2217/pmt-2015-0005
https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

Xtampza ER®

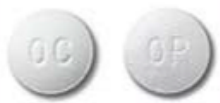
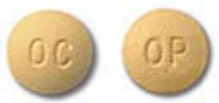
- DETERx technology
  - Waxy microspheres solidify in a needle
- FDA ADF approved
  - IN, IV, & PO
- Take with food
  - GI activated, not pH
- Can be opened and sprinkled into a G-Tube or on food



Xtampza ER (oxycodone) Dosage		Extended-release Oxycodone HCl Dosage
9 mg	Equivalent to	10 mg
13.5 mg		15 mg
18 mg		20 mg
27 mg		30 mg
36 mg		40 mg
27 mg + 27 mg		60 mg
36 mg + 36 mg		80 mg

OxyContin®

- Original formulation (1996-2009): "OC" Imprint
- Newer formulation (2010-present): "OP" Imprint

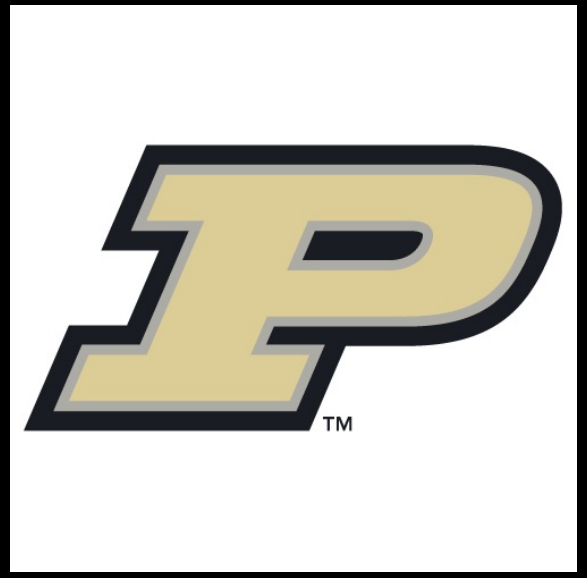
Strength	10 mg	15 mg	20 mg	30 mg	40 mg	80 mg
Comparison of original (first) versus reformulated ***OxyContin®*** tablets (second).						
						

OxyContin®

- RESISTEC technology
  - Forms a viscous gel with water
- ADF category 3 study (IN/IV)
  - 57% reduction in drug liking
  - 43% no reduction in drug liking
- Phase 4
  - ~50% decrease in doctor chopping, overdoses, & poison center calls (heroin replaced?)
- Q12h dosing ???

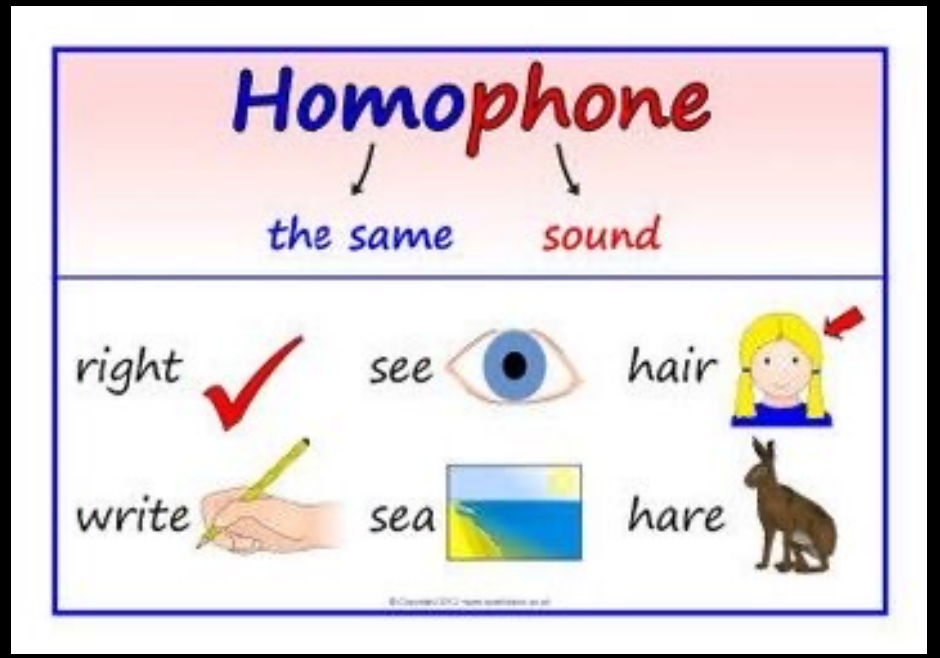
Original OxyContin®

New abuse-deterrent OxyContin®




PURDUE


PERDUE®


Homophone
the same
sound
right
see
hair
write
sea
hare

PAINWEEK®

Oxy-Crisping

Tools of the Trade

- Grater (PediEgg)
- Ceramic/glass plate
- Paper towel
- Microwave
- Fridge/freezer

Oxy-Crisping

Tools of the Trade

- Grater (~~PediEgg~~) (lemon zester)
- Ceramic/glass plate
- Paper towel
- Microwave
- Fridge/freezer

FDA Approved ADF Opioids on US Market

(July 2020)

Medicine	Product	FDA ADF Approval			Formulation
oxycodone	Xtampza ER®	IN	IV	PO Chew	ER Capsule
	OxyContin®	IN	IV		ER Tablet
hydrocodone	Hysingla®	IN	IV	PO Chew	ER Tablet
morphine	Embeda®	IN		PO Crush	ER Tablet
	Arymo®		IV		
	MorphaBond®	IN	IV		

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411218/
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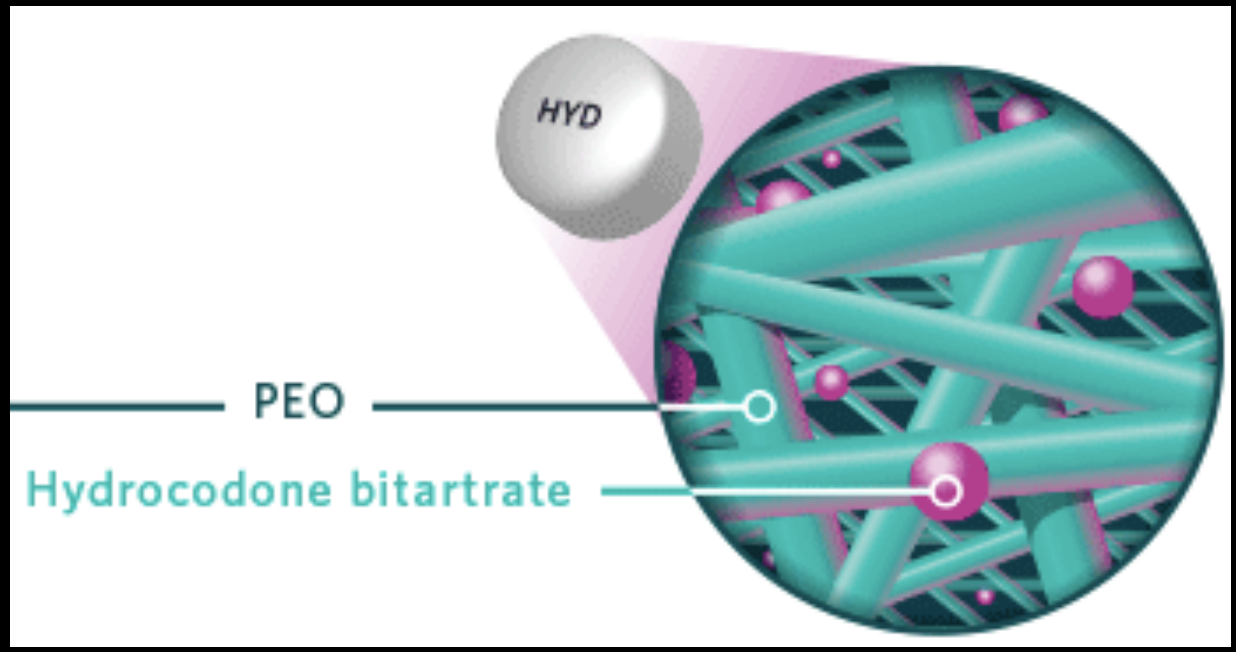
https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

Hysingla®

- RESISTEC technology (*Same as OxyContin)
  - –Forms a viscous gel around water
- ADF Category 3 Studies (IN, IV, & PO): ~80% reduction in drug liking

HYdrocodone
SINGle dose
Long Acting



Hysingla®

Hydrocodone/apap
10mg/325mg
1 T q 4 to 6 h
???

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(July 2020)

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	Arymo®		IV		
	MorphaBond®	IN	IV		

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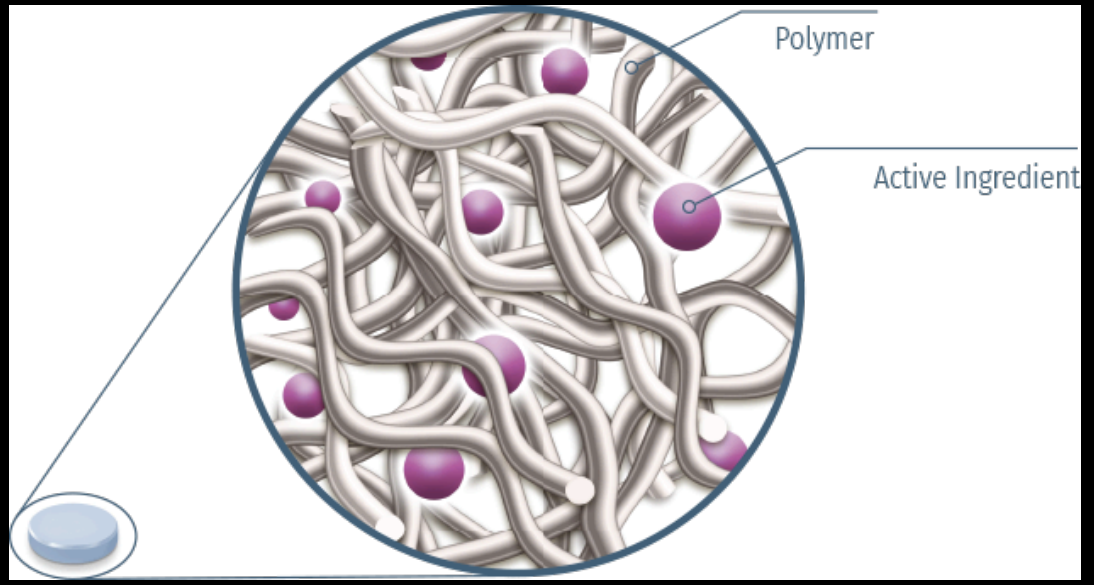
https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

Arymo®

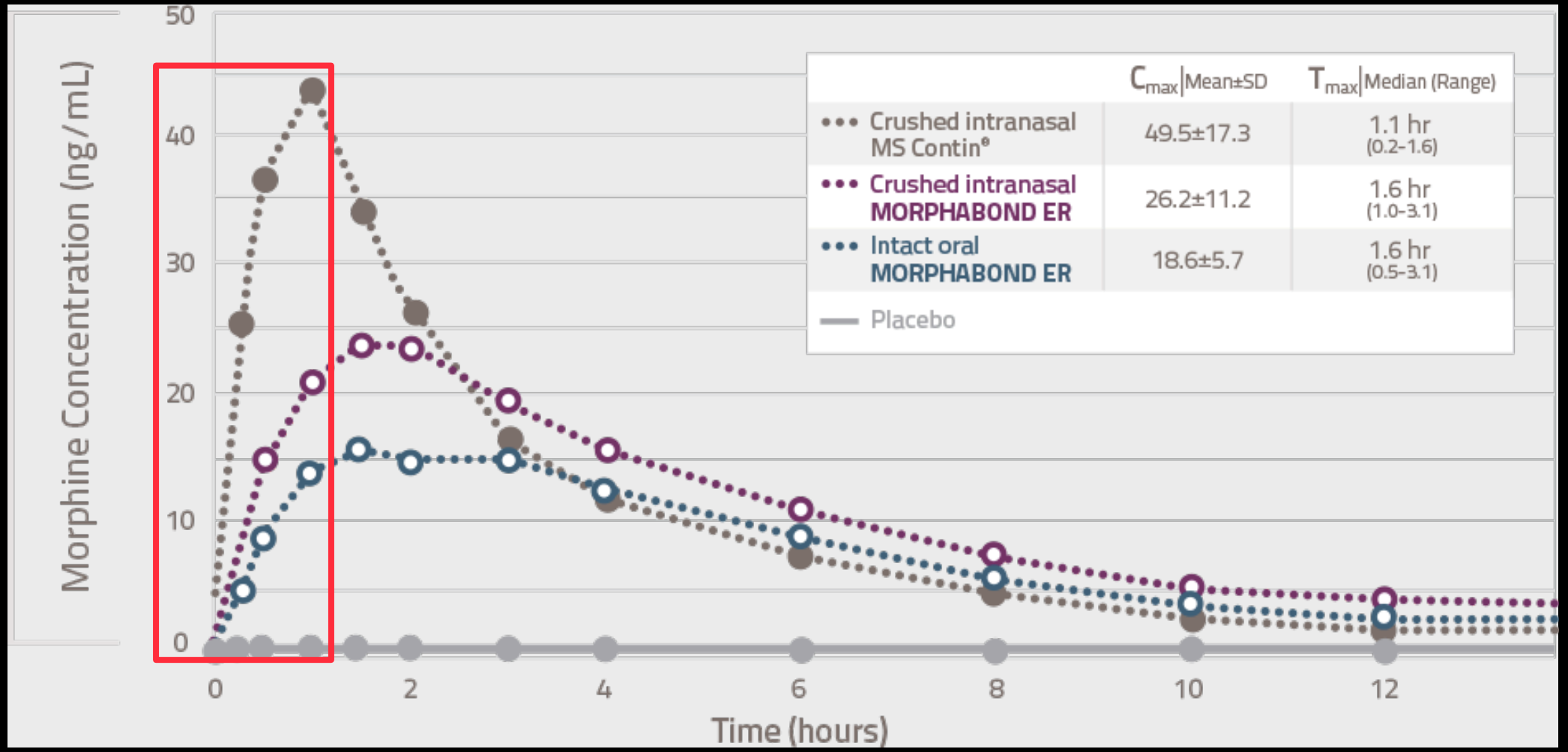
- Guardian technology (polymer matrix)
  - Physical & chemical barrier
- FDA ADF approved for IV
- Oxycodone product in pipeline

MorphaBond®

- Sentry bond technology
- Dose every 8 to 12 hours
- Can be taken +/- food
- FDA ADF approved for IV & IN



MorphaBond®



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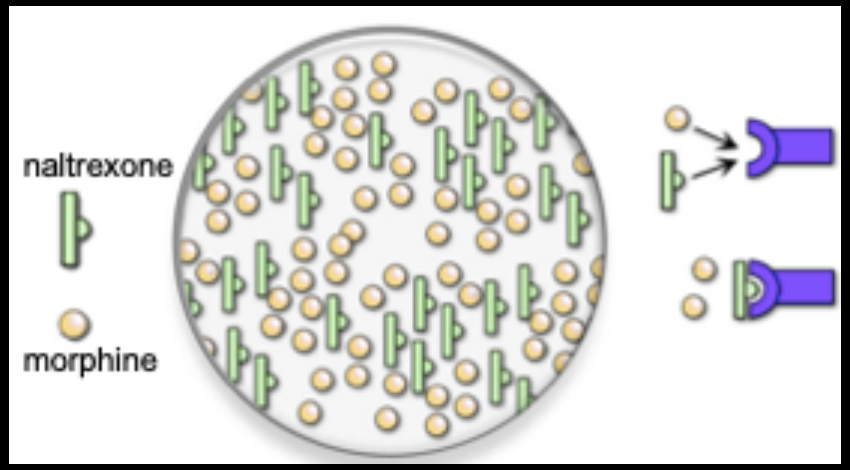
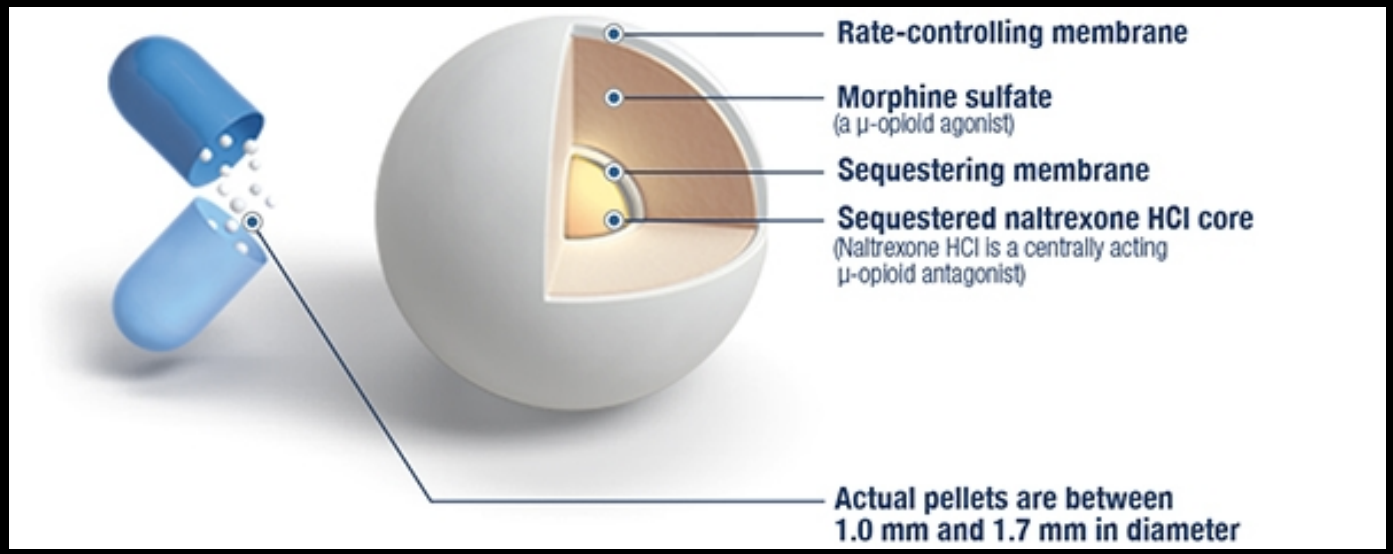
https://morphabondhcp.com/clinical-studies-intranasal-pk-data

Embeda®

- Sequestered naltrexone induces withdrawal if abused and ingested
- FDA ADF approved IN & PO
  - Only FDA ADF opioid originally w/o IV
- Morphine:naltrexone ratio 100:4



EMBEDA vs IR MORPHINE *Oral IR (Study 1)*[1,2]	EMBEDA vs ER MORPHINE *Oral ER (Study 2)*[1,3]	EMBEDA vs ER MORPHINE *Intranasal (Study 3)*[1,4]
EMBEDA intact vs EMBEDA crushed in solution vs IR morphine in solution vs placebo	EMBEDA crushed in solution vs ER morphine crushed in solution vs placebo	Crushed EMBEDA vs crushed ER morphine vs placebo



Embeda®

EMBEDA is available in 6 dosage strengths[1]

 20 mg/0.8 mg	 30 mg/1.2 mg	 50 mg/2 mg
 60 mg/2.4 mg	 80 mg/3.2 mg	 100 mg/4 mg*

MAT Buprenorphine Products with Naloxone…

FORMULATION	STRENGTH			
Sublingual Tablet	2mg BUP 0.5mg NX	-	8mg BUP 2mg NX	-
Sublingual Film	2mg BUP 0.5mg NX	4mg BUP 1mg NX	8mg BUP 2mg NX	12mg BUP 3mg NX

Buprenorphine vs Naloxone

Bluelight

Lazylazyjoe (9/1/2010, 5:57am)

As someone who regularly injects Suboxone, I prefer injecting Suboxone instead of using sublingual mainly because of the efficacy. I can inject 1 to 2mg and be good for an entire day, compared to 4mg sublingual. It also takes affect in 15 minutes instead of 90 minutes.

You do have to be careful though, it is much easier to precipitate withdrawal this way. Wait a little longer for your induction, even longer if coming down off methadone.

The other thing that gets me is that I buy my Suboxone on the street, because between the doc and the pharmacy I'd be paying $150/month & $7.50/pill. If the doc would just prescribe Subtex, I could get it generic and do it legit for about the same cost. It drives me nuts as Suboxone is just as easy to abuse as the Subutex. Not to mention the whole pain management specialist thing is a big scam. There's no reason why a regular doc can't prescribe this schedule 3 drug.

Dread (10/1/2010, 2:08am)
Naloxone was put in there to trick the FDA, and it worked!
It was put in to extend the patent, they had to come up with a "new" product to keep the big bucks coming in.

Buprenorphine vs Naloxone

Package Insert

5.2 Risk of Respiratory and Central Nervous System (CNS) Depression

Buprenorphine has been associated with life-threatening respiratory depression and death. Many, but not all, post-marketing reports regarding coma and death involved misuse by self-injection or were associated with the concomitant use of buprenorphine and benzodiazepines or other CNS depressants, including alcohol. Warn patients of the potential danger of self-administration of benzodiazepines or other CNS depressants while under treatment with SUBOXONE sublingual film *[see Warnings and Precautions (5.3), Drug Interactions (7)]*.

active substantial heroin or other full mu-opioid dependence. However, clinicians should be aware that some opioid-dependent persons, particularly those with a low level of full mu-opioid physical dependence or those whose opioid physical dependence is predominantly to buprenorphine, abuse buprenorphine/naloxone combinations by the intravenous or intranasal route. In methadone-maintained patients and heroin-

PainWeek

Suboxone Full Prescribing Information. February 27, 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022410s000lbl.pdf

Buprenorphine Battles…

THE UNITED STATES DEPARTMENT of JUSTICE

FOR IMMEDIATE RELEASE

Tuesday, April 9, 2019

Indivior Inc. Indicted for Fraudulently Marketing Prescription Opioid

Company Allegedly Lied to Doctors and Public Health Care Benefit Programs About the Safety and Diversion Risks of Suboxone Film

CLERK'S OFFICE U.S. DISTRICT COURT
AT ABINGDON, VA
FILED

APR 09 2019

JULIA C. DUDLEY, CLERK
BY: J. Clark
DEPUTY CLERK

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF VIRGINIA
ABINGDON

UNITED STATES OF AMERICA	)	
	)	
v.	)	**Case No.** 1:19CR00016
	)	
INDIVIOR INC. (a/k/a Reckitt Benckiser Pharmaceuticals Inc.) and INDIVIOR PLC	)	**Violations:** **18 U.S.C. §§ 2, 1341, 1343, 1347, 1349**

PAINWEEK

https://www.justice.gov/opa/pr/indivior-inc-indicted-fraudulently-marketing-prescription-opioid
https://www.justice.gov/opa/press-release/file/1153066/download

Buprenorphine Battles…but the War???

BUSINESS NEWS JULY 11, 2019 / 2:11 AM / UPDATED 2 HOURS AGO

Reckitt to pay $1.4 billion to end opioid addiction treatment probes

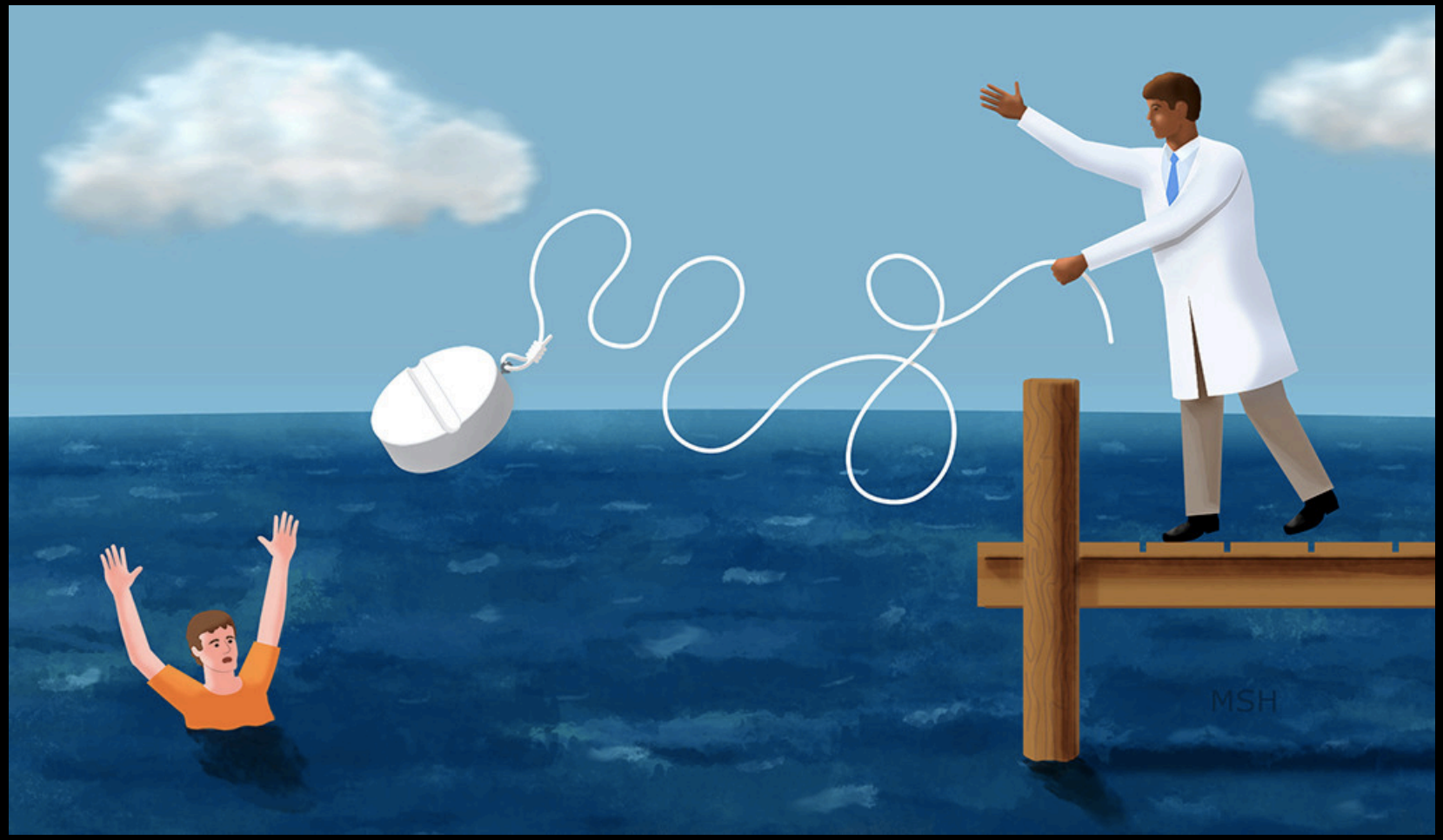
Noor Zainab Hussain, Pushkala Aripaka 4 MIN READ

(Reuters) - Reckitt Benckiser (RB.L) has agreed to pay up to $1.4 billion (£1.1 billion) to end U.S. federal investigations into the marketing of an opioid addiction treatment by its former business Indivior, lifting a cloud that has been hanging over the British company for years.

Separately on Thursday, Indivior raised its full-year profit and revenue guidance after Suboxone lost market share at a slower pace than expected, sending its shares 35% higher.

https://uk.reuters.com/article/uk-reckitt-benc-grp-probe-indivior/reckitt-benckiser-to-pay-up-to-1-4-billion-to-end-indivior-probe-idUKKCN1U60LT

Buprenorphine Improves & Saves Lives
When Utilized as Approved by the FDA



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FDA Approved ADF Opioids on US Market
(July 2020)

Medicine	Product	FDA ADF Approval			Formulation
oxycodone	Xtampza ER®	IN	IV	PO Chew	ER Capsule
	OxyContin®	IN	IV		ER Tablet
hydrocodone	Hysingla®	IN	IV	PO Chew	ER Tablet
morphine	Embeda®	IN		PO Crush	ER Tablet
	Arymo®		IV		
	MorphaBond®	IN	IV		

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411218/
https://www.sciencedirect.com/science/article/pii/S0378517316304884
https://www.futuremedicine.com/doi/pdf/10.2217/pmt-2015-0005
https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm

ADFs, At What Cost?

Chemical Barrier

Physical Barrier

Aversion

Combination of Any

Agonist/ Antagonist Opioid Combinations

Delivery System

Prodrug

Non-ADF Opioids	ADF Opioids
$5.82 Average Cost	$11.60 Average Cost $6.86 Break-Even Cost

Conflicts of Interest

Aetna
Anthem
Blue Cross Blue Shield of Massachusetts
Blue Shield of California
Harvard Pilgrim Health Care
Kaiser Permanente
Partners Healthcare
Premera Blue Cross
United HealthCare
Washington State Health Care Authority

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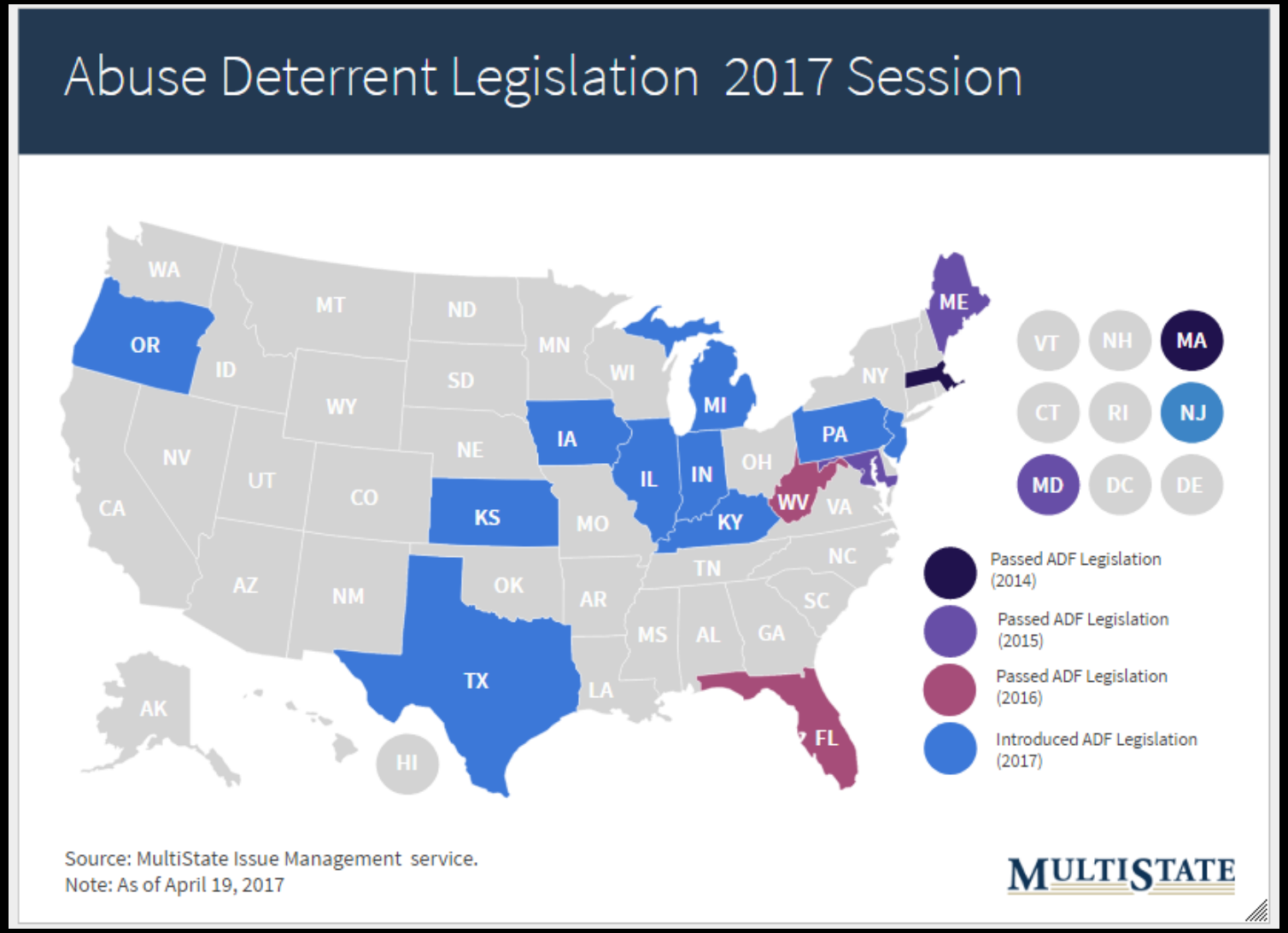
https://icer-review.org/wp-content/uploads/2017/08/ADF_RAAG_080817.pdf

States Mandating (By Law) ADF Opioid Coverage

- Massachusetts (2014)
- Maine (2015)
- Maryland (2015)
- Florida (2016)
- West Virginia (2016)



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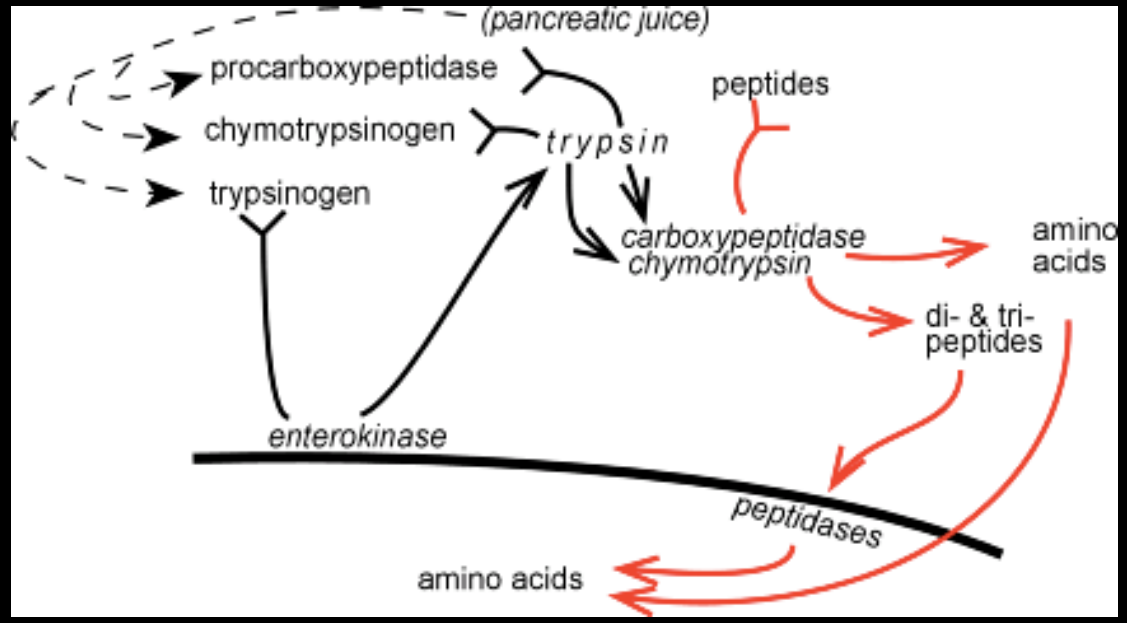
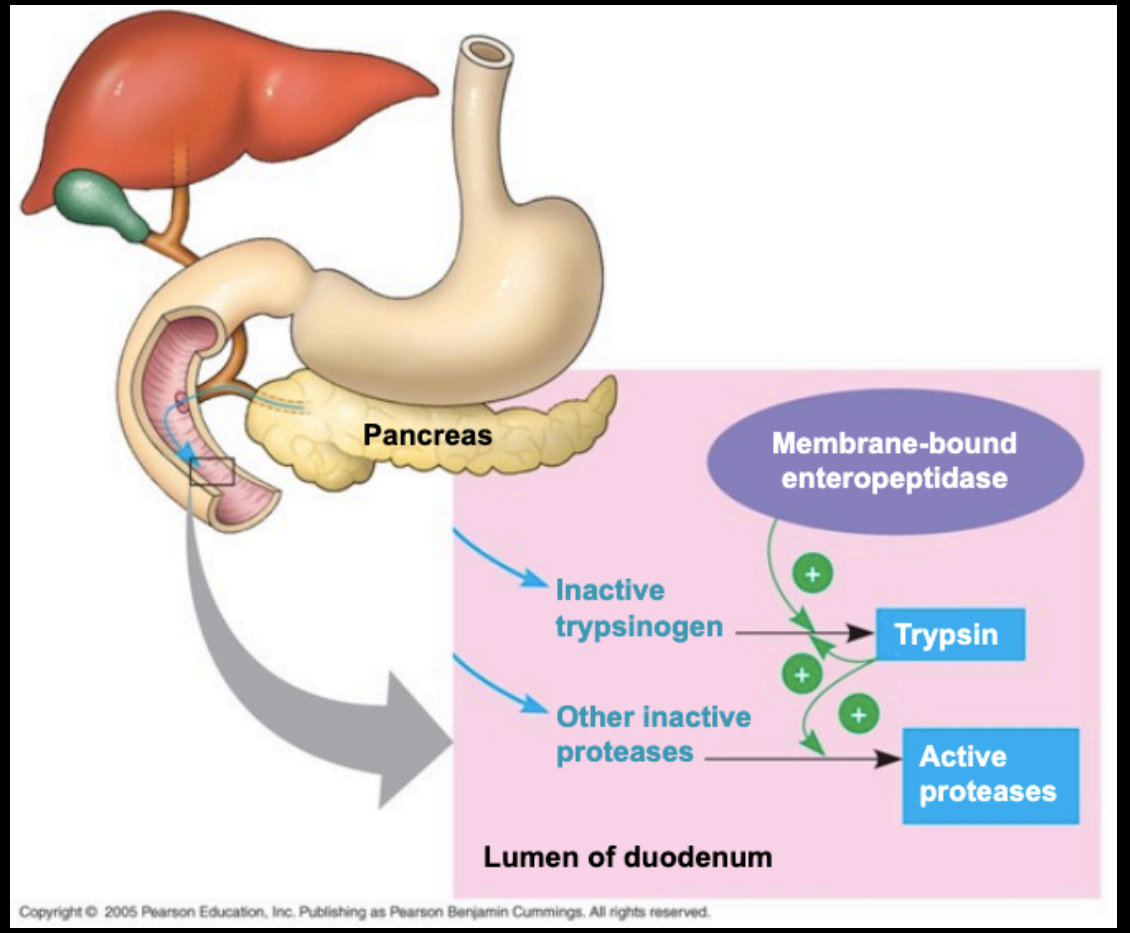
ADF Opioid Pipeline
TAAP

- TAAP (trypsin activated abuse protection)
  - Trypsin is found only in the small intestine
- MPAR (multi-pill abuse resistance)
  - A small amount of trypsin inhibitor (soybeans & egg whites) added to each pill not affecting opioid release
  - If multiple pills are ingested (on purpose or accidentally) the trypsin inhibitor blocks the activation of the opioid prodrug

Trypsin → Protein Breakdown



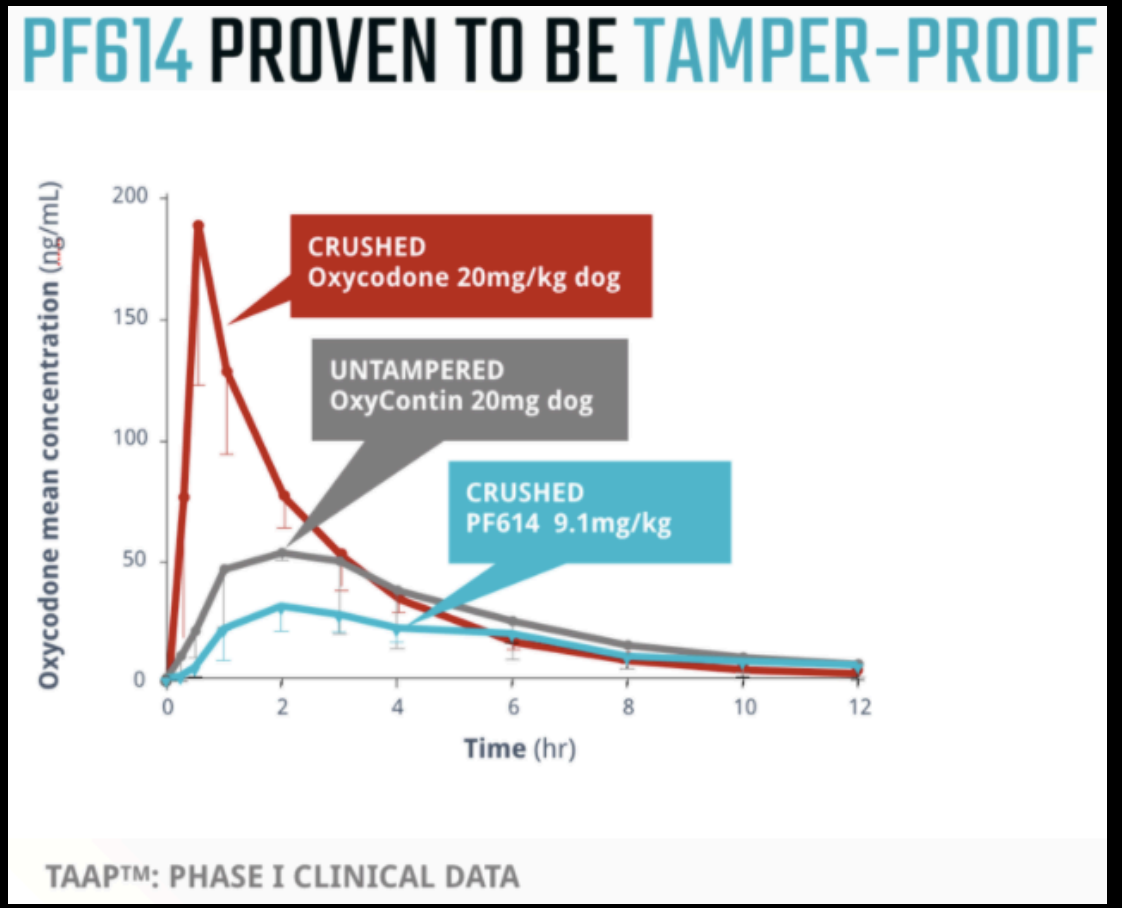


PAINWEEK

http://www.physiologymodels.info/digestion/proteins.htm

ADF Opioid Pipeline
TAAP & MPAR

- Oxycodone (PF614)
  - 12-hour t ½ (true BID dosing)
- Hydromorphone ER (PF329)
- Amphetamine (PF8001/8026)
  - ADHD
- R-Methadone (PF26810)
  - Medication assisted treatment



https://ensysce.com/our-pipeline

PainWeek®

Audience Question #1

A 45yo female patient with chronic lower back pain and hypertension presents to your practice as a new patient already having utilized hydrocodone, for many years. While performing an opioid risk assessment, you find out that she is living in a house with a spouse who has a substance use disorder. You would like to convert the patient's current non-abuse-deterrent formulation (ADF) ER opioid to an FDA approved ADF ER opioid formulation that is readily available on the US market. Which of the following is the most appropriate selection based on this intention?

a) Zohydro ER
b) Hysingla
c) Vantrela
d) Xtampza ER

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a) Zohydro ER
b) HYSINGLA [CORRECT ANSWER]
c) Vantrela
d) Xtampza ER

Medicine	Product
oxycodone	Xtampza ER®
	OxyContin®
hydrocodone	Hysingla®
morphine	Embeda®
	Arymo®
	MorphaBond®

Audience Question #2

A 55yo male patient with chronic lower back pain and DM2 presents to your practice as a new patient already having utilized oxycodone, for many years. Upon performing an opioid risk assessment, you find that he is of high risk for opioid abuse. He also states that he would prefer an opioid medication that can be sprinkled on his food instead of swallowing the pill whole. You would like to convert the patient's current non-abuse-deterrent formulation (ADF) ER opioid to an FDA approved ADF ER opioid formulation that is readily available on the US market. Which of the following is the most appropriate selection based on this intention?

a) Embeda
b) Zohydro ER
c) OxyContin
d) Xtampza ER

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a) Embeda
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c) OxyContin
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Medicine	Product
oxycodone	Xtampza ER®
	OxyContin®
hydrocodone	Hysingla®
morphine	Embeda®
	Arymo®
	MorphaBond®

Audience Question #3

Which of the following states have legislation mandating the prescription insurance benefit coverage of abuse-deterrent formulation (ADF) opioid medications in at least some manner?

a) Massachusetts
b) Maryland
c) Florida
d) All of the above

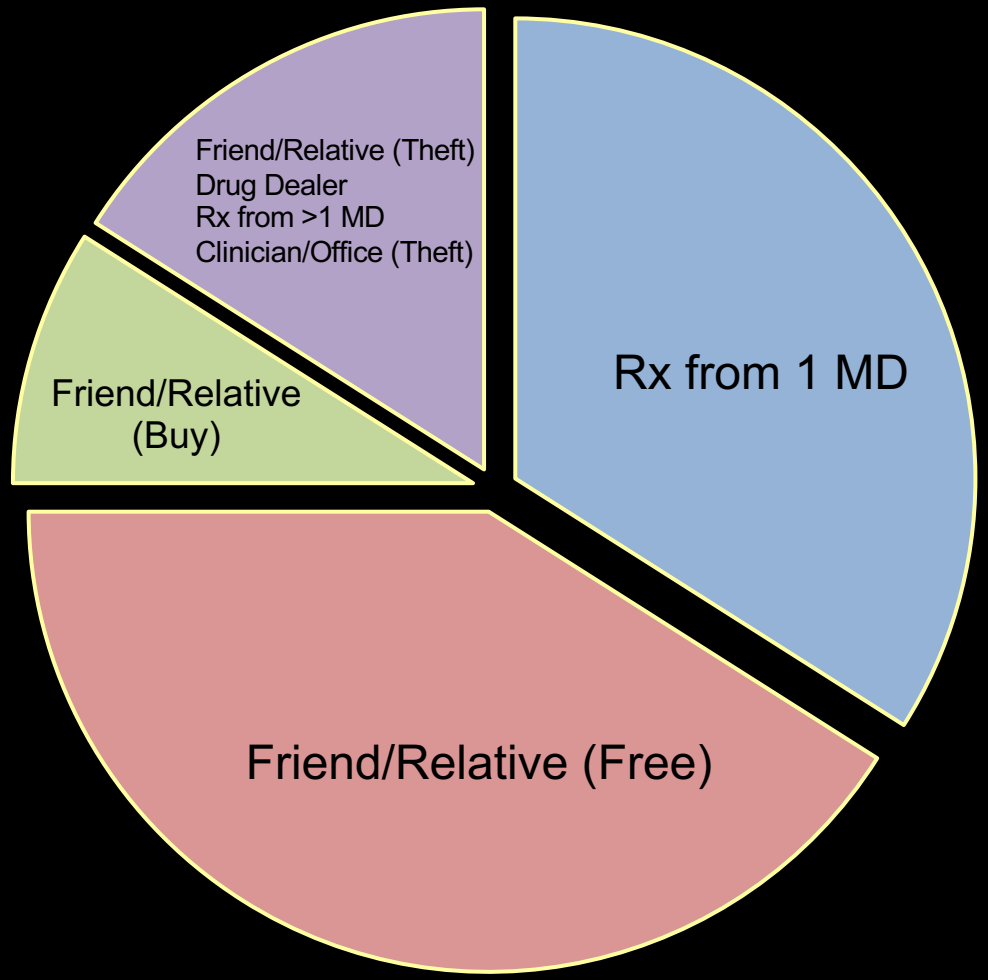
Audience Question #3

Which of the following states have legislation mandating the prescription insurance benefit coverage of abuse-deterrent formulation (ADF) opioid medications in at least some manner?

a) Massachusetts
b) Maryland
c) Florida
d) ALL OF THE ABOVE [CORRECT ANSWER]

- Massachusetts (2014)
- Maine (2015)
- Maryland (2015)
- Florida (2016)
- West Virginia (2016)

Where are these opioids coming from…



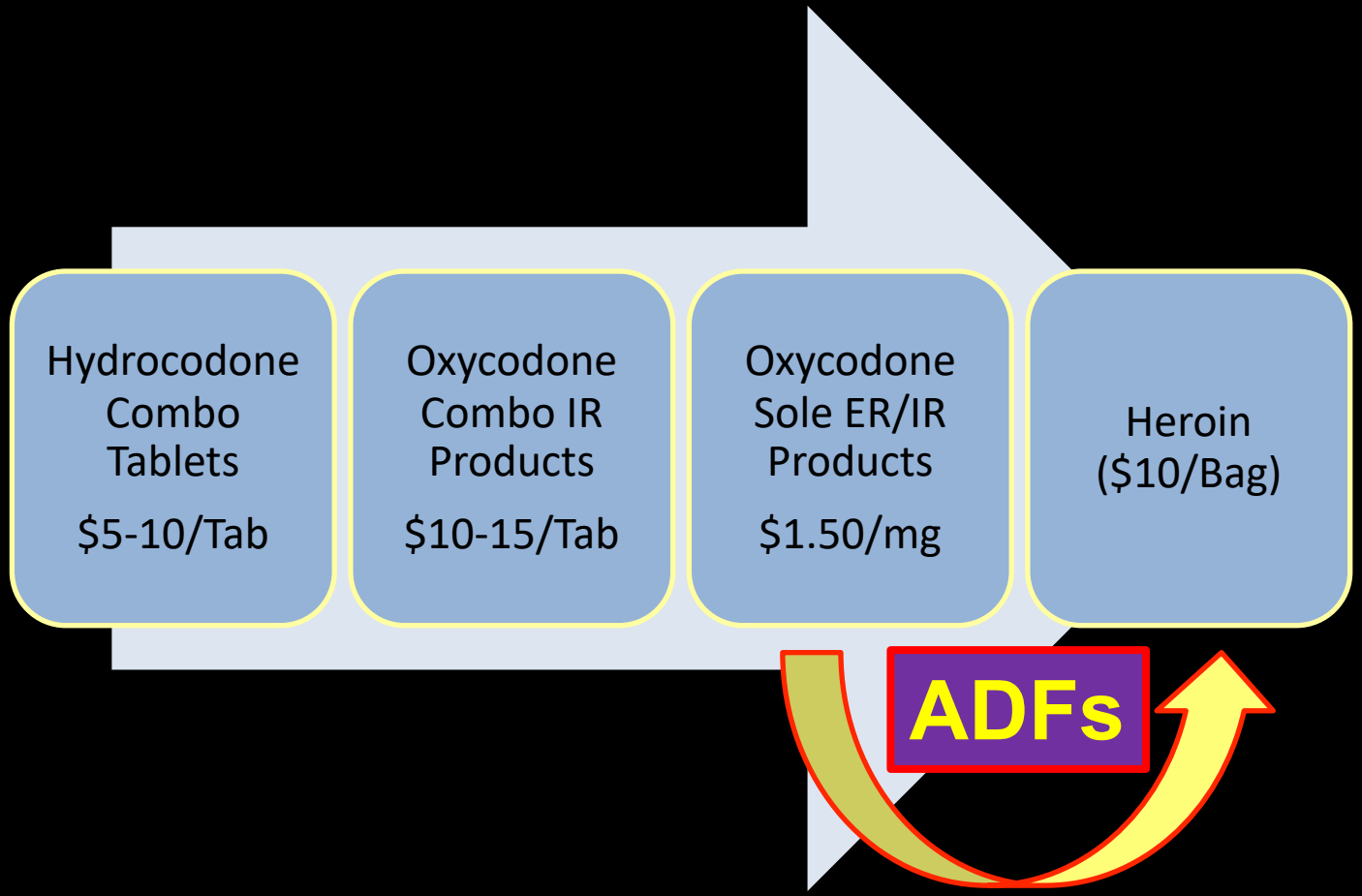
HEALTHCARE PROFESSIONAL

~1/3rd

PAINWEEK®

2017 DEA National Drug Threat Assessment. https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf

Opioid Abuse Transition



Medicine	Product
oxycodone	Xtampza ER®
	OxyContin®
hydrocodone	Hysingla®
morphine	Embeda®
	Arymo®
	MorphaBond®

Shah A, et al. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use – United States, 2006-2015. *Weekly* / March 17, 2017 / 66(10); 265–269.
www.bluelight.org

Discussion

Mark Garofoli, PharmD, MBA, BCGP, CPE
LinkedIn: Mark Garofoli

DIAMORPHINE HYDROCHLORIDE 5 mg, 10 mg, 30 mg, 100 mg or 500 mg FOR INJECTION

PACKAGE LEAFLET: INFORMATION FOR THE USER

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

IN THIS LEAFLET:

1 WHAT DIAMORPHINE IS AND WHAT IT IS USED FOR

Diamorphine is a narcotic analgesic.

Diamorphine is used to treat severe pain associated with:

- terminal illness
- heart attack
- fluid on the lungs.