

Drug Formulary Commission

Bureau of Health Care Safety and Quality
Department of Public Health
May 18, 2017

Presentation Agenda

Interchangeable Abuse Deterrent Drug Products Evaluation

- Morphabond ER[®]
- Arymo ER[®]

Chemically Equivalent Substitutions

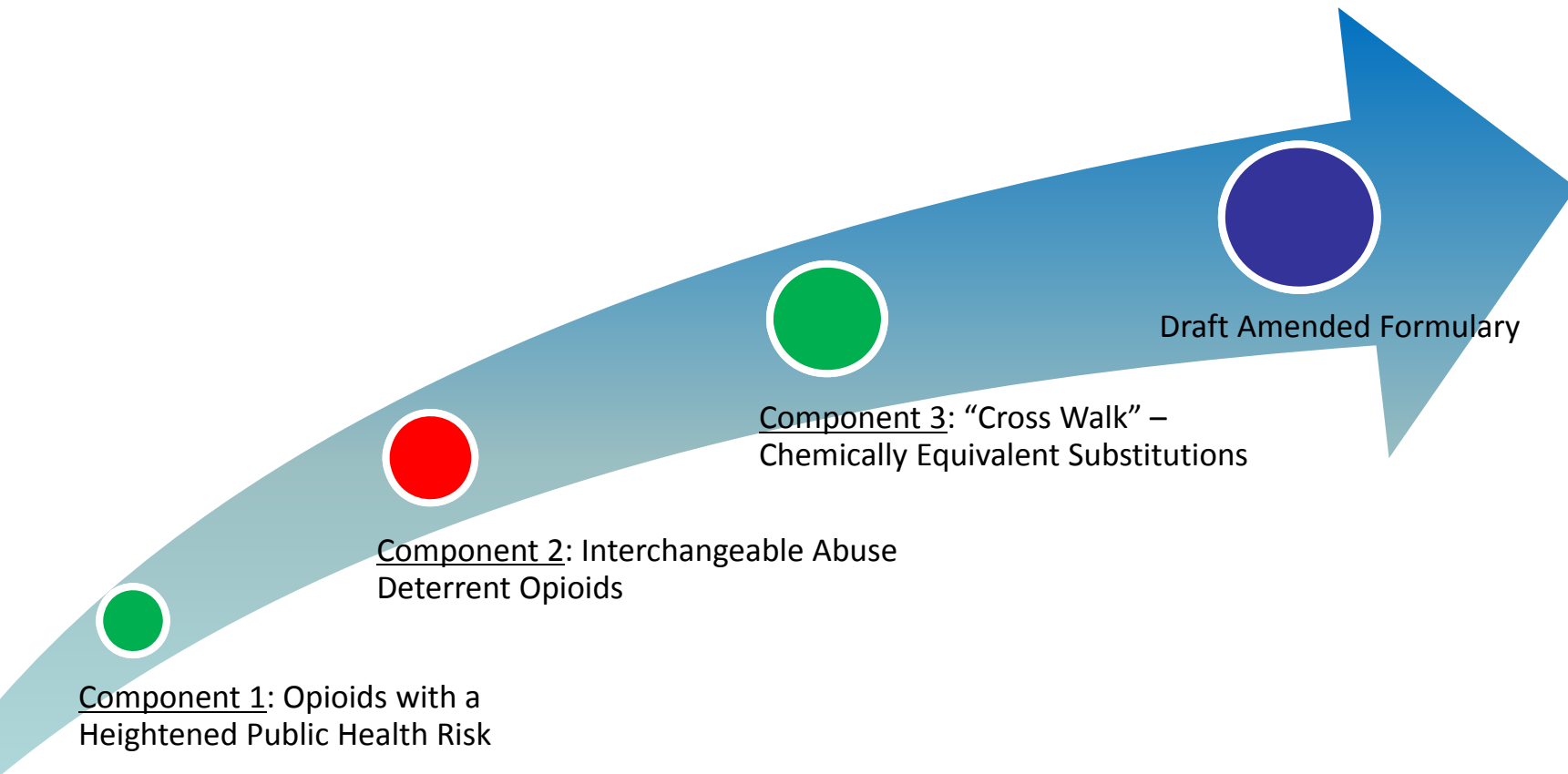
- Morphabond ER[®]
- Arymo ER[®]

Draft Formulary

- 105 CMR 720: *List of Interchangeable Drug Products*
- aka *Drug Formulary Commission*

Next Steps

Formulary Review and Evaluation



MorphaBond ER[®] Monograph Review

Morphine sulfate extended-release

ADF Property

- Physical/Chemical Barrier
- *In vitro* studies indicate intravenous abuse deterrence
- Clinical abuse potential study of the intranasal route

FDA Approval October 2015

FDA ADF labeling approved October 2015

Available Strengths

- 15 mg, 30 mg, 60 mg, 100 mg

Potential IAD Drug Product Evaluation MorphaBond ER[®]

MorphaBond ER[®] is formulated as an extended-release tablet.¹

The abuse-deterrent technology platform is referred to as SentryBond[®].³

In vitro manipulation study data indicates that MorphaBond[®] is difficult to crush or cut using most household tools.²

Attempts to dissolve MorphaBond ER[®] results in formation of a viscous material that is not syringeable.²

Efforts to extract morphine from MorphaBond ER[®] tablets in small volumes generally results in low yields over 30 minutes.²

Extraction of morphine from MorphaBond ER[®] in larger volumes is limited to 30 to 40% over 30 minutes in one household solvent.²

An intranasal clinical abuse potential study indicates that crushed intranasal MorphaBond ER[®] is associated with less drug liking than crushed intranasal MS Contin[®].⁴

Potential IAD Drug Product Evaluation MorphaBond ER[®]

Initial dose (opioid naïve adults): 15 mg every 12 hours.¹

Initial dose (converting from other opioids): 15 mg every 12 hours.¹

Median time to peak plasma concentration (T_{max}) of an intact MorphaBond ER[®] tablet taken orally is approximately 1.6 hours.^{2,9}

Median T_{max} for crushed MorphaBond ER[®] tablets used intranasally is also approximately 1.6 hours; however, the plasma exposure (AUC) to morphine and morphine-6-glucuronide is approximately 37% lower than when taken intact orally.^{2,9}

In vitro data indicates MorphaBond ER[®] does not have a dose-dumping effect; therefore, the FDA did not require an *in vivo* alcohol dose-dumping study.⁹

Administration of MorphaBond ER[®] with a high fat meal resulted in a 33% increase in peak plasma concentration (C_{max}), but no change in AUC compared to fasted state.¹

Potential IAD Drug Product Evaluation MorphaBond ER[®]

MorphaBond ER[®] is subject to the requirements of the Extended-Release and Long-Acting (ER/LA) Risk Evaluation and Mitigation Strategies (REMS) program.²

There was no advisory committee meeting prior to approval of MorphaBond ER[®].

Final report submissions of formal observational studies, intended to determine if the abuse-deterrent properties of Troxyca ER[®] reduce abuse in the community, are due to the FDA in February of 2021.⁹

MorphaBond ER[®] Summary

Chemical name	morphine sulfate
Dosage form	Extended-release tablet
Formulation	SentryBond [®] tablet technology
ADP*	Physical/Chemical Barrier
ADF studies	Intranasal and intravenous (<i>in vitro</i>)
ADF labeling	Intranasal and Intravenous

Arymo ER[®] Monograph Review

Morphine sulfate extended-release

ADF Property

- Physical/Chemical Barrier
- *In vitro* studies indicate intravenous abuse deterrence
- Clinical abuse potential studies of the intranasal and oral routes

FDA Approval

January 2017

FDA ADF labeling approved

January 2017

Available Strengths

- 15 mg, 30 mg, 60 mg

Potential IAD Drug Product Evaluation Arymo ER[®]

Arymo ER[®] is formulated as an extended-release tablet.¹

The abuse-deterrent technology platform is referred to as Guardian[®], which combines a polymer matrix with an injection molding process to make the tablet more difficult to manipulate.²

In vitro manipulation study data indicates that Arymo ER[®] is difficult to crush or cut using household tools, and may require use of multiple tools to obtain 5% of morphine particles smaller than 500 microns.²

Attempts to dissolve Arymo ER[®] results in formation of a viscous material that is only syringeable with an 18 gauge needle, and approximately 16 to 18% of the material can be drawn up.²

Efforts to extract morphine from Arymo ER[®] tablets in large volumes of solvents is limited to less than 60% of morphine over 30 minutes.²

A simulated smoking and free-base isolation study indicates that isolation of free-base morphine was not successful on three attempts, and less than 3% of morphine was released in vapor upon simulating smoking.

Potential IAD Drug Product Evaluation Arymo ER[®]

An oral clinical abuse potential study revealed that manipulated Arymo ER[®] taken orally was associated with less drug liking than manipulated morphine ER tablets (generic MS Contin[®]).⁴

An intranasal clinical abuse potential study revealed that both low volume and high volume manipulated Arymo ER[®] intranasal was associated with less drug liking than manipulated morphine ER tablets (generic MS Contin[®]).⁵

Potential IAD Drug Product Evaluation Arymo ER[®]

Initial dose (opioid naïve adults): 15 mg every 8 or 12 hours.¹

Initial dose (converting from other opioids): 15 mg every 8 or 12 hours.¹

Mean (standard deviation [SD]) time to peak plasma concentration (T_{max}) of an intact Arymo ER[®] tablet taken orally in the oral clinical abuse potential study was 3.6 (1.1) hours.⁴

Mean (SD) T_{max} for manipulated Arymo ER[®] tablets taken orally in the oral clinical abuse potential study was 2.0 (0.7) hours; however, the mean (SD) plasma exposure (AUC) to morphine was slightly lower for the manipulated Arymo ER[®] compared to intact (159.3 [36.8] ng•hr/mL versus 168.0 [53.6] ng•hr/mL, respectively)⁴

In vitro data indicates that as alcohol concentrations increase, the release rate of morphine from Arymo ER[®] is slower.²

There is no clinically significant food effect on Arymo ER[®]; however, T_{max} may be delayed by approximately 2 hours.¹

Arymo ER[®] is subject to the requirements of the Extended-Release and Long-Acting (ER/LA) Risk Evaluation and Mitigation Strategies (REMS) program.²

	Oral ADF	Intranasal ADF	Intravenous ADF
FDA Advisory Committee ⁶	16-3 vote in favor	18-1 vote in favor	18-1 vote in favor
FDA Labeling ⁷	Yes	No	Yes

Final report submissions of formal observational studies, intended to determine if the abuse-deterrent properties of Arymo ER[®] reduce abuse in the community, are due to the FDA in March of 2022.¹³

Arymo ER[®] Summary

Chemical name	morphine sulfate
Dosage form	Extended-release tablet
Formulation	Guardian [®] tablet technology
ADP*	Physical/Chemical Barrier
ADF studies	Intranasal, oral and intravenous (<i>in vitro</i>)
ADF labeling	Oral and Intravenous

Vantrela ER[®] (hydrocodone extended-release)

- FDA approved, launch reportedly planned for 1st Quarter 2017
- Formulary Dossier not yet available
- Monograph to be completed when commercially available

RoxyBond[®] (oxycodone immediate-release)

- FDA approved; however, not commercially available
- Formulary Dossier not yet available
- Monograph to be completed when commercially available

Potential IAD Drug Products – Updates (Pipeline)

Egalet-002 (oxycodone ER)

- Currently in Phase III
- Uses Guardian[®] technology, similar to Arymo ER[®]

KP606/IR (oxycodone prodrug)

- Manufacturer expects human proof-of-concept data this year
- 505(b)(2) New Drug Application (NDA) submission planned this year

NKTR-181

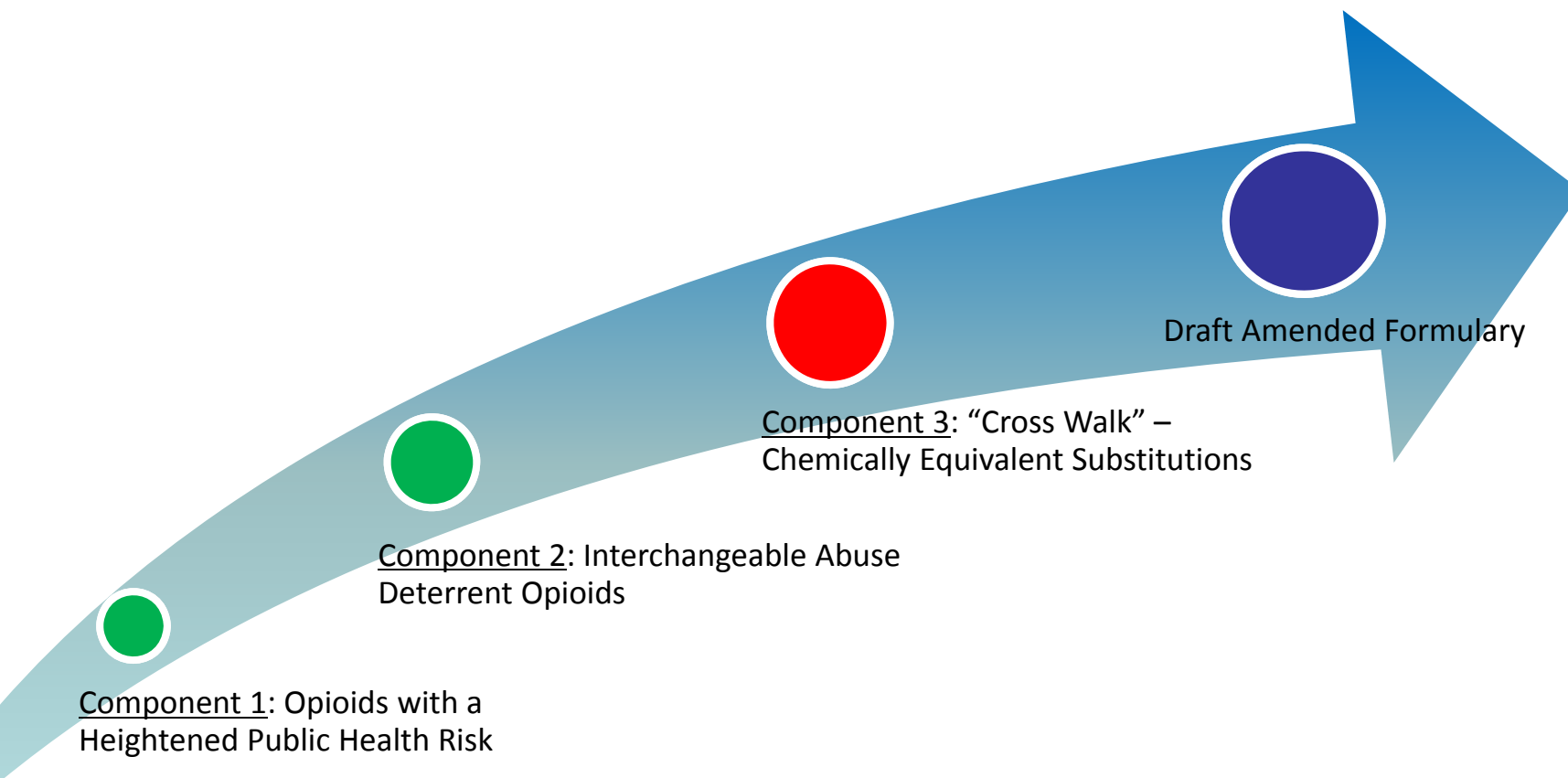
- New chemical entity μ -agonist designed to have reduced level of euphoria
- Phase III: Met primary endpoint of significantly lower average pain intensity scores compared to placebo
- Oral clinical abuse potential study: Significantly lower mean drug liking and drug high scores compared to oxycodone
- FDA granted Fast Track designation

Medication with ADF Claims or FDA Approved ADF Labeling

List of Medications with Abuse-Deterrent Claims or FDA-Approved Labeling

Name	Manufacturer	Ingredient(s)	Dose Form	Method of Abuse Deterrence	DFC Action
Bond®	Inspirion Delivery Sciences/ Daiichi Sankyo	Morphine ER	Tablet	Physical/chemical barrier	PENDING
ER®	Egalet	Morphine ER	Tablet	Physical/chemical barrier	PENDING
a ER®	Teva	Hydrocodone ER	Tablet	Physical/chemical barrier	Not yet commercially available. Launch planned for 1st Quarter 2017
ond®	Inspirion Delivery Sciences	Oxycodone IR	Tablet	Physical/chemical barrier	FDA Approved Not yet commercially available
-002	Egalet	Oxycodone ER	Tablet	Physical/chemical barrier	Currently in Phase III
1/IR	KemPharm, Inc.	Hydrocodone IR	Undisclosed	Prodrug	NDA submission planned 2018 with Priority Review designation
-181	Nektar Therapeutics	New chemical entity	Undisclosed, possibly solution	New Molecular Entity	FDA granted Fast Track designation

“Cross Walk”



Chemically Equivalent Substitution

Chemically Equivalent Substitution”, for the purpose of creating a formulary of drugs with abuse deterrent properties that the Commission has determined may be appropriately substituted for opioids that have been determined to have a heightened public health risk due to the drugs’ potential for abuse and misuse, shall mean drug products which contain the same active ingredients, and are equivalent in strength or concentration, dosage form, and route of administration, and produce a comparable biologic effect. Prodrugs or ingredients without analgesic effect that are used solely for abuse deterrent formulations need not be equivalent.

Drug Product Criteria

In considering whether a drug is a **chemically equivalent substitution** the commission shall consider:

the **accessibility** of the drug and its proposed substitute;

whether the drug's substitute is **cost** prohibitive;

the **effectiveness** of the substitution (FDA approved for pain); and

whether, based upon the current patterns of abuse and misuse, the drug's substitute incorporates abuse deterrent technology that will be an **effective deterrent** to such abuse and misuse.

Cost Impact Methods

Utilization data (units dispensed) was collected from the PMP for 2016 for all Schedule II and III opioids.

Total milligrams dispensed was calculated for each drug product (multiply units dispensed by strength for each strength, add results for each strength per product).

Total cost of each drug product was calculated for 2017 (multiply units dispensed by WAC per strength, add results for each strength per product).

Approximate cost per milligram was calculated for each drug product, in aggregate (divide total cost by total milligrams dispensed for each product).

Cost of substitution was calculated by subtracting approximate cost per milligram of HPHR Opioid (in aggregate) from approximate cost per milligram of the IAD Drug Product (in aggregate), then multiplying the

Cost Impact Methods

Results were provided ranging from 50% to 75% to 100% substitution, and results were also expressed as a percentage increase or decrease in cost.

Tables on the following slides show exact matches in terms of milligram strengths between HPHR Opioid morphine ER products and Morphabond ER[®] or Arymo ER[®]; however, many other combinations exist that contain equivalent amounts of morphine per day and are potentially substitutable.

Cost Impact calculations are based upon milligrams dispensed in attempt to capture cost of substitution for each product that is inclusive of all potential substitutions containing the same amount of morphine per day.

Approximate patient impact is extracted from 2016 PMP data.

Single-Dose Pharmacokinetic Data

Drug	Dose	Peak Concentration (C _{max} , mean [CV%])	Time to Peak Concentration (t _{max} , mean [CV%])	Elimination Half-Life (t _{1/2} , mean [CV%])	Area Under the Curve (AUC _{0-∞} , mean [CV%])
za® (morphine 4 hour capsule)	60 mg	7.2 (45.80%) ng/mL	11.1 (68.47%) hours	21.8 (42.66%) hours	261.9 (31.08%) ng • hr/mL
an® (morphine 2 or 24 hour tablet)	100 mg	13.19 (45.70%) ng/mL	10 (6.00 to 24.00) hours*	33.83 (34.60%) hours	390.98 (25.8%) ng • hr/mL
phaBond ER® (morphine ER tablet)	100 mg	33.39 (23.32%) ng/mL	3.76 (28.91%)	10.32 (24.76%) hours	395.06 (23.23%) ng • hr/mL
phine ER tablet	100 mg	39.3 (42%) ng/mL	2.6 hours†	Not reported	401.6 (31%) ng • hr/mL

CV=coefficient of variation, ER=extended-release

*Values represent median (range)

†CV not reported

Yellow=List A

Green=List B

MorphaBond ER[®] and Morphine Extended-Release 24 Hour Capsule

Product	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
MorphaBond	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
Morphine Extended-Release 24 Hour Capsule	morphine sulfate	30 mg	extended-release capsule	Oral	Q24H	\$4.58	6,509	\$29,835.30	N/A
		60 mg				\$8.90	9,616	\$85,592.02	
		90 mg				\$13.38	3,696	\$49,465.05	
		120 mg				\$15.79	6,446	\$101,788.79	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016
ADP=abuse-deterrent property, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A
Green=List B

Cost of Substitution (100% Conversion): \$380,429

Cost of Substitution (75% Conversion): \$285,322

Cost of Substitution (50% Conversion): \$190,214

Percent Change in Cost: +108.18%

Possible Patient Impact: Approximately 139 Patients

MorphaBond ER® and Kadian®

Product	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
MorphaBond	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
		100 mg				\$28.30	-	-	
Kadian	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$10.63	2,378	\$25,273.38	N/A
		60 mg				\$21.26	8,949	\$190,222.93	
		100 mg				\$34.93	6,384	\$222,976.10	
		200 mg				\$71.76	270	\$19,375.88	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016
ADP=abuse-deterrent property, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A
Green=List B

Cost of Substitution (100% Conversion): -\$108,530 (Cost Avoidance)

Cost of Substitution (75% Conversion): -\$81,397 (Cost Avoidance)

Cost of Substitution (50% Conversion): -\$54,265 (Cost Avoidance)

Percent Change in Cost: -16.60% Decrease in Cost

MorphaBond ER[®]

MorphaBond ER[®] and Morphine Extended-Release 12 or 24 Hour Capsule

Brand Name	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
MorphaBond ER [®]	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
		100 mg				\$28.30	-	-	
Morphine Extended-Release 12 or 24 Hour Capsule	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$4.55	32,122	\$146,142.25	N/A
		60 mg				\$9.10	19,277	\$175,401.42	
		100 mg				\$15.21	19,946	\$303,296.88	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016

ADP=abuse-deterrent property, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A

Green=List B

Cost of Substitution (100% Conversion): \$911,402

Cost of Substitution (75% Conversion): \$683,551

Cost of Substitution (50% Conversion): \$455,700

Percent Change in Cost: 78.34% Increase in Cost

MorphaBond ER[®]

MorphaBond ER[®] and MS Contin[®]

Medication	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
MorphaBond	morphine sulfate	15 mg	extended-release capsule	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
		100 mg				\$28.30	-	-	
MS Contin [®]	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$3.61	10,055	\$36,302.57	N/A
		30 mg				\$6.86	8,590	\$58,931.70	
		60 mg				\$13.39	19,964	\$267,258.07	
		100 mg				\$19.82	10,316	\$204,465.18	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016

ADP=abuse-deterrent property, Q8H=every 8 hours, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A

Green=List B

Cost of Substitution (100% Conversion): \$224,175

Cost of Substitution (75% Conversion): \$168,131

Cost of Substitution (50% Conversion): \$112,087

Percent Change in Cost: 39.54% Increase in Cost

MorphaBond ER[®]

MorphaBond ER[®] and Morphine Extended-Release Tablet

Product	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
MorphaBond	morphine sulfate	15 mg	extended-release capsule	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
		100 mg				\$28.30	-	-	
Morphine ER	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$0.60	3,418,799	\$2,056,407.60	N/A
		30 mg				\$1.14	2,839,373	\$3,245,971.21	
		60 mg				\$2.23	1,336,022	\$2,980,130.67	
		100 mg				\$3.30	470,586	\$1,551,192.63	
		200 mg				\$5.99	44,189	\$264,904.22	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016

ADP=abuse-deterrent property, Q8H=every 8 hours, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A

Green=List B

Cost of Substitution (100% Conversion): \$71,631,075

Cost of Substitution (75% Conversion): \$53,723,306

Cost of Substitution (50% Conversion): \$35,815,537

Percent Change in Cost: 709.32% Increase in Cost

MorphaBond ER® - All Substitutions

Indication	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
MorphaBond	morphine sulfate	15 mg	extended-release capsule	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
		100 mg				\$28.30	-	-	
Morphine extended-release 24	morphine sulfate	30 mg	extended-release capsule	Oral	Q24H	\$4.58	6,509	\$29,835.30	N/A
		60 mg				\$8.90	9,616	\$85,592.02	
		90 mg				\$13.38	3,696	\$49,465.05	
		120 mg				\$15.79	6,446	\$101,788.79	
Morphine ER	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$10.63	2,378	\$25,273.38	N/A
		60 mg				\$21.26	8,949	\$190,222.93	
		100 mg				\$34.93	6,384	\$222,976.10	
		200 mg				\$71.76	270	\$19,375.88	
Morphine extended-release 12 or 8 hour	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$4.55	32,122	\$146,142.25	N/A
		60 mg				\$9.10	19,277	\$175,401.42	
		100 mg				\$15.21	19,946	\$303,296.88	
Morphine ER	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$3.61	10,055	\$36,302.57	N/A
		30 mg				\$6.86	8,590	\$58,931.70	
		60 mg				\$13.39	19,964	\$267,258.07	
		100 mg				\$19.82	10,316	\$204,465.18	
Morphine ER	morphine sulfate	15 mg	extended-release	Oral	Q12H or Q8H	\$0.60	3,418,799	\$2,056,407.60	N/A
		30 mg				\$1.14	2,839,373	\$3,245,971.21	
		60 mg				\$2.23	1,336,022	\$2,980,130.67	

MorphaBond ER[®] and All List A Morphine Extended-Release Products - Continued

Overall Cost of Substitution (100% Conversion): \$73,038,550

Overall Cost of Substitution (75% Conversion): \$54,778,913

Overall Cost of Substitution (50% Conversion): \$36,519,275

Overall Percent Change: 569.08% Increase in Cost

Overall Possible Patient Impact: Approximately 34,574 Patients

Arymo ER® and Morphine Extended-Release 24 Hour Capsule

Drug	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
Arymo ER®	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
Morphine Extended-Release 24 Hour Capsule	morphine sulfate	30 mg	extended-release capsule	Oral	Q24H	\$4.58	6,509	\$29,835.30	N/A
		45 mg				\$6.80	6,482	\$44,054.26	
		60 mg				\$8.90	9,616	\$85,592.02	
		90 mg				\$13.38	3,696	\$49,465.05	
		120 mg				\$15.79	6,446	\$101,788.79	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016
ADP=abuse-deterrent property, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A
Green=List B

Cost of Substitution (100% Conversion): \$352,071

Cost of Substitution (75% Conversion): \$264,053

Cost of Substitution (50% Conversion): \$176,035

Percent Change in Cost: +100.11%

Arymo ER[®] and Kadian[®]

Product	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
Arymo ER [®]	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
Kadian [®]	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$10.63	2,378	\$25,273.38	N/A
		60 mg				\$21.26	8,949	\$190,222.93	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016
 -=abuse-deterrent property, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A
 Green=List B

Cost of Substitution (100% Conversion): -\$129,653 (Cost Avoidance)

Cost of Substitution (75% Conversion): -\$97,240 (Cost Avoidance)

Cost of Substitution (50% Conversion): -\$64,827 (Cost Avoidance)

Percent Change in Cost: -19.83% Decrease in Cost

Arymo ER® and Morphine Extended-Release 12 or 24 Hour Capsule

Drug	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
Arymo ER®	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
Morphine Extended-Release 12 or 24 Hour Capsule	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$4.55	32,122	\$146,142.25	N/A
		60 mg				\$9.10	19,277	\$175,401.42	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016

ADP=abuse-deterrent property, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A

Green=List B

Cost of Substitution (100% Conversion): \$831,034

Cost of Substitution (75% Conversion): \$623,276

Cost of Substitution (50% Conversion): \$415,517

Percent Change in Cost: 71.43% Increase in Cost

Arymo ER[®] and MS Contin[®]

Brand Name	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
Arymo ER [®]	morphine sulfate	15 mg	extended-release capsule	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
MS Contin [®]	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$3.61	10,055	\$36,302.57	N/A
		30 mg				\$6.86	8,590	\$58,931.70	
		60 mg				\$13.39	19,964	\$267,258.07	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016

ADP=abuse-deterrent property, Q8H=every 8 hours, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A

Green=List B

Cost of Substitution (100% Conversion): \$139,530

Cost of Substitution (75% Conversion): \$145,148

Cost of Substitution (50% Conversion): \$96,765

Percent Change in Cost: 34.13% Increase in Cost

Arymo ER[®] and Morphine Extended-Release Tablet

Brand	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
Bond	morphine sulfate	15 mg	extended-release capsule	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
Arymo ER	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$0.60	3,418,799	\$2,056,407.60	N/A
		30 mg				\$1.14	2,839,373	\$3,245,971.21	
		60 mg				\$2.23	1,336,022	\$2,980,130.67	

*Wholesale acquisition cost per Online Red Book as of 3/15/2016

ADP=abuse-deterrent property, Q8H=every 8 hours, Q12H=every 12 hours, Q24H=every 24 hours

Yellow=List A

Green=List B

Cost of Substitution (100% Conversion): \$68,465,275

Cost of Substitution (75% Conversion): \$51,348,956

Cost of Substitution (50% Conversion): \$34,232,637

Percent Change in Cost: 677.97% Increase in Cost

Arymo ER® and All List A Morphine Extended-Release Products

Indication	Active Ingredient	Strengths	Dosage Form	Route of Administration	Dosing Schedule	Cost/unit*	Units Dispensed 2016	Approximate Cost 2016	ADP Efficacy
Arymo ER®	morphine sulfate	15 mg	extended-release capsule	Oral	Q12H	\$5.40	-	-	Category II
		30 mg				\$10.80	-	-	
		60 mg				\$16.98	-	-	
Morphine extended-release 24	morphine sulfate	30 mg	extended-release capsule	Oral	Q24H	\$4.58	6,509	\$29,835.30	N/A
		45 mg							
		60 mg				\$8.90	9,616	\$85,592.02	
		90 mg				\$13.38	3,696	\$49,465.05	
		120 mg				\$15.79	6,446	\$101,788.79	
Morphine ER®	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$10.63	2,378	\$25,273.38	N/A
		60 mg				\$21.26	8,949	\$190,222.93	
Morphine extended-release 12 or 8 hour	morphine sulfate	30 mg	extended-release capsule	Oral	Q12H or Q24H	\$4.55	32,122	\$146,142.25	N/A
		60 mg				\$9.10	19,277	\$175,401.42	
Morphine ER®	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$3.61	10,055	\$36,302.57	N/A
		30 mg				\$6.86	8,590	\$58,931.70	
		60 mg				\$13.39	19,964	\$267,258.07	
Morphine ER®	morphine sulfate	15 mg	extended-release tablet	Oral	Q12H or Q8H	\$0.60	3,418,799	\$2,056,407.60	N/A
		30 mg				\$1.14	2,839,373	\$3,245,971.21	
		60 mg				\$2.23	1,336,022	\$2,980,130.67	

**Arymo ER[®] and All List A Morphine Extended-Release Products -
Continued**

Overall Cost of Substitution (100% Conversion): \$69,712,256

Overall Cost of Substitution (75% Conversion): \$52,284,192

Overall Cost of Substitution (50% Conversion): \$34,856,128

Overall Percent Change: 543.16% Increase in Cost

Overall Possible Patient Impact: Approximately 34,574 Patients

Promulgation of Regulation and Formulary

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Proposed 105 CMR 720, *List of Interchangeable Drug Products*, including draft formulary, as redrafted, to the Public Health Council (11/9/2016)

Public hearing held on proposed changes to regulation (1/19/2017)

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PH staff is reviewing comments and further amending as appropriate.

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PH staff will present the final draft regulation to PHC for promulgation.

Review by Secretary of State → Regulation becomes effective.

Step

Issue guidance, including special substitution considerations, and the requirements and process of substitution.

Conduct prescriber education on abuse deterrent substitutes.

Meeting Summary

Meeting Recap

Review of takeaways

Next steps

Upcoming Meetings

– June 20, 2017

- 9:00AM-12:00PM
- 250 Washington Street