Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee

NDA 208090

Xtampza

Oxycodone ER Capsules

Food Effect with Xtampza ER

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OTS, CDER

Background

- Xtampza is an extended-release, abuse-deterrent, microsphere-in-capsule oral formulation containing oxycodone.
- Clinical Pharmacology studies
  - Single dose relative bioavailability (BA) study (CP-OXYDET-15)
    - Fasted and Fed BA compared to Oxycontin
    - Food-effect (Fasted vs. Different kinds of food)
  - Effect of physical manipulation on pharmacokinetics (PK) (impact of food on results) (CP-OXYDET-17)
  - Impact of food on PK following oral abuse (CP-OXYDET-24)
  - Alcohol Interaction Study *in vivo* (CP-OXYDET-26)
  - Other studies (Reviewed but not discussed in presentation)

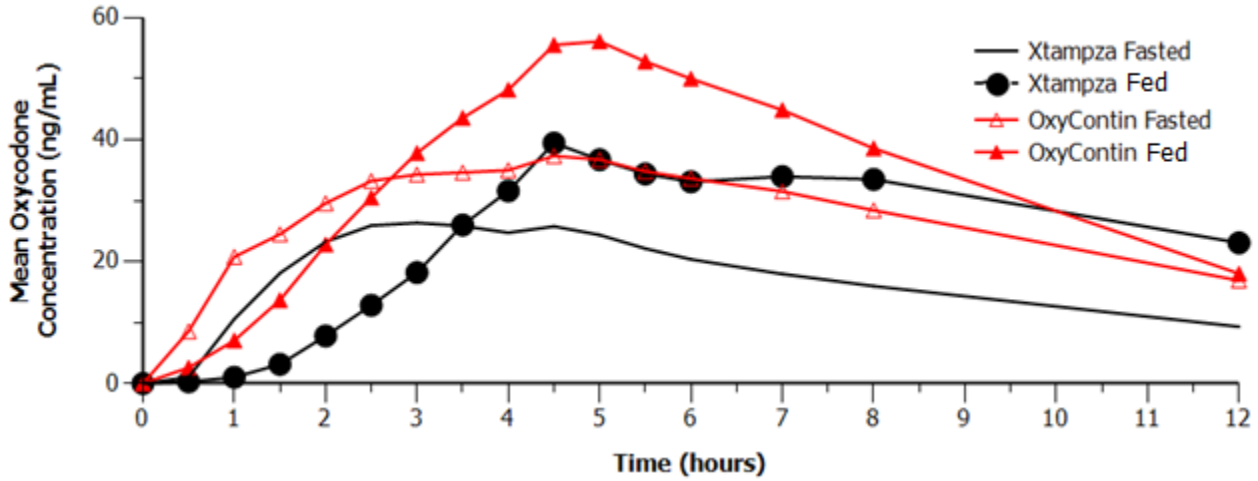
Regulatory Background

- Several developmental formulations were evaluated for PK
  - High variability and low bioavailability of Oxycodone DETERx under fasting state became apparent early on.
  - A two-fold increase in bioavailability was noted when investigational formulations were given with food.
- Agency recommended that the sponsor modify the formulation so that the food-effect is substantially smaller.
- Twelve different developmental formulations were evaluated.
  - Sponsor indicates that the final formulation had the least variability in Cmax compared to three other formulations.
  - The final formulation still had substantial food-effect.
- Agency advised Collegium to include additional clinical studies to document safety and efficacy of Xtampza when taken with food.
  - All relevant clinical studies employed the final formulation.

Effect of Food Type on Xtampza Bioavailability

- Relative bioavailability study CP-OXYDET-15
- Pharmacokinetics of Xtampza 40 mg capsule was determined when taken with
  - high-fat high-calorie (HFHC) meal,
  - medium-fat medium-calorie (MFMC) meal,
  - low-fat low-calorie (LFLC) meal,
  - fasted state,
- Xtampza PK compared with
  - OxyContin 40 mg dosed with an HFHC meal and
  - OxyContin 40 mg dosed in the fasted state.
- Naltrexone-blocked healthy volunteers (n=45)

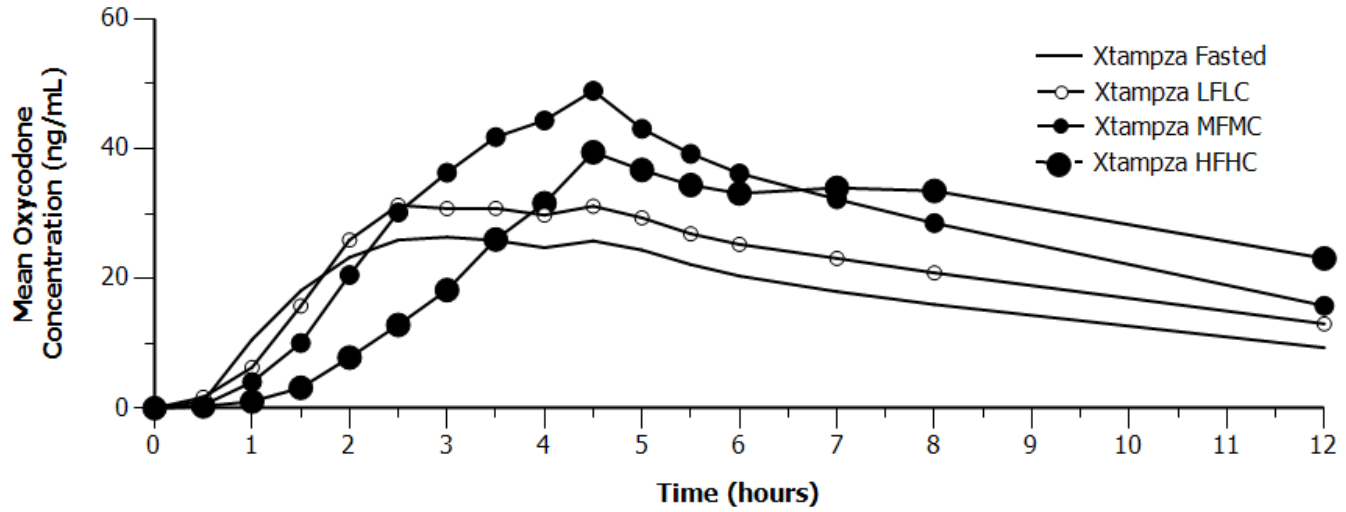
Xtampza Bioavailability is Lower Compared to OxyContin Under Fasting and Fed State



Parameter	Xtampza Fasted	OC Fasted	Ratio Fasted (90% CI)	Xtampza Fed	OC Fed	Ratio Fed (90% CI)	OC Fed/Fast Ratio
Cmax (ng/mL)	29.84	40.3	**74%** (69 – 78)	49.75	61.1	**81.3%** (76 – 87)	**151%** (142 – 161)
AUClast (ng.h/mL)	317.9	444.4	**71%** (68 – 75)	472.6	521.1	90.7% (86 – 95)	117% (111 – 122)

HFHC: High-fat High-calorie; OC: OxyContin

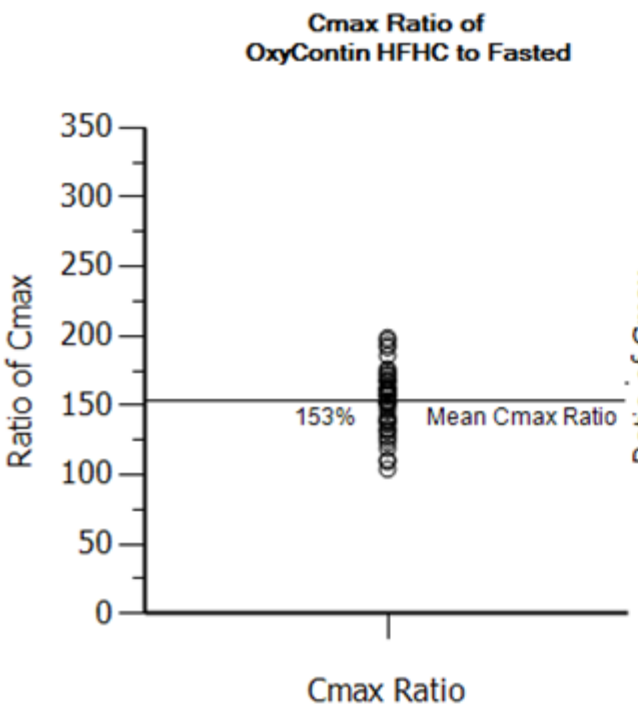
Xtampza Bioavailability Increases with Fat & Calorie Content in Food

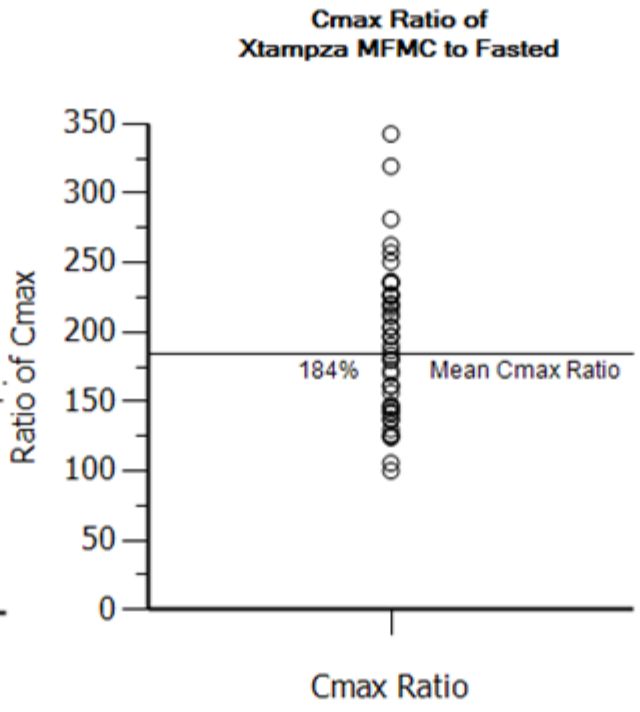


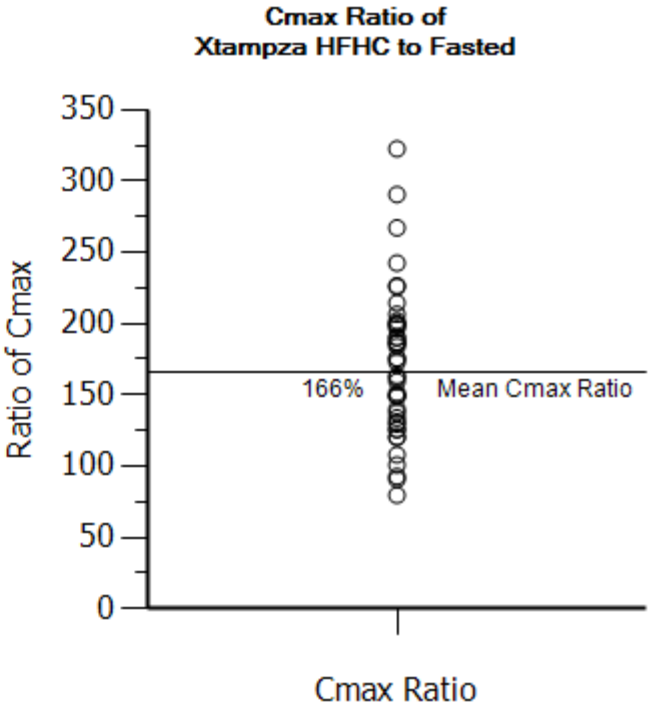
Parameter	Fasted (Ref)	LFLC	LFLC/Fast Ratio (90% CI)	MFMC	MFMC/Fast Ratio (90% CI)	HFHC	HFHC/Fast Ratio (90% CI)
Cmax (ng/mL)	29.84	35.9	**120**% (112 – 128)	54.9	**184.2**% (172 – 196)	49.75	**166.7**% (156 – 177)
AUClast (ng.h/mL)	317.9	372.6	117% (111 – 123)	440.7	**138**% (132 -145)	472.6	**148.6**% (141 – 156)

LFLC: Low-fat Low-calorie; MFMC: Medium-fat Medium calorie; HFHC: High-fat High-calorie

Higher Variability in Cmax Ratio of Fed/Fasted Noted for Xtampza







MFMC: Medium-fat Medium calorie;
HFHC: High-fat High-calorie

Impact of Food-effect on Physical Manipulation of Xtampza

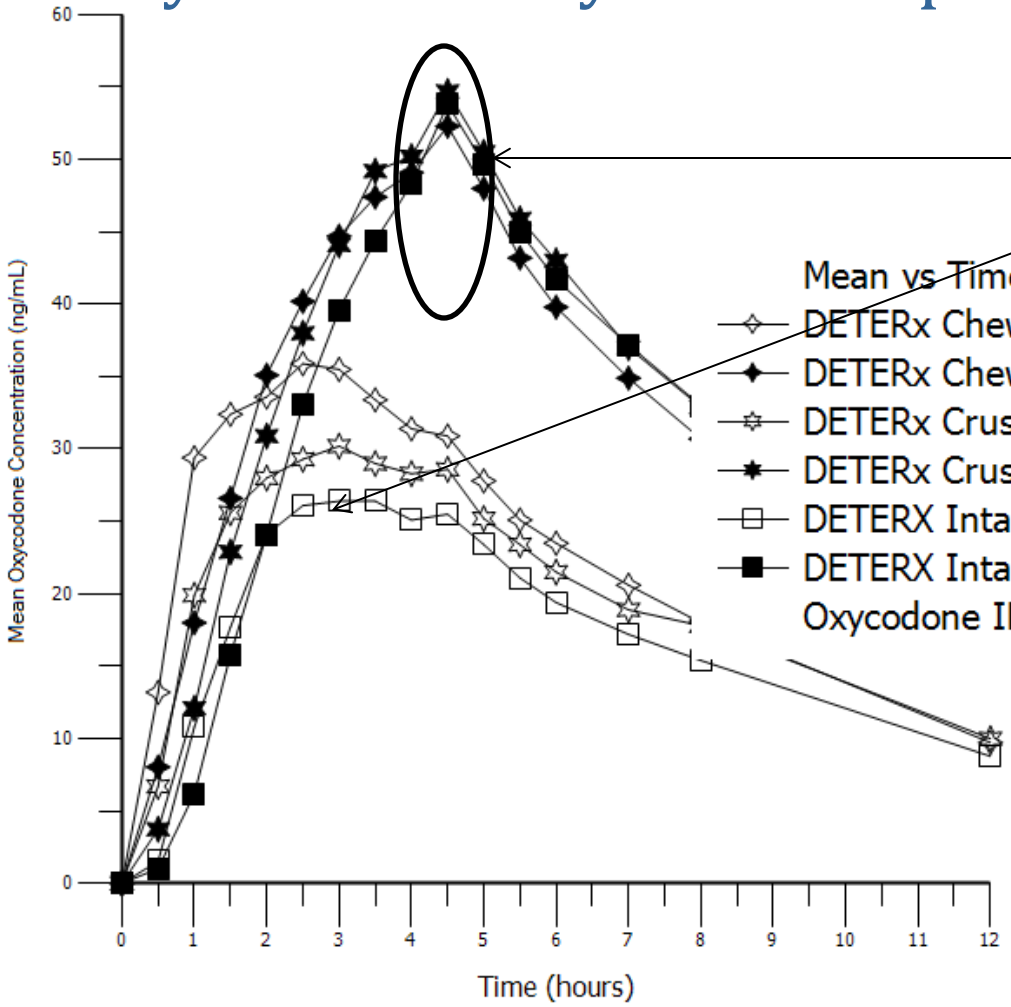
- Relative bioavailability study CP-OXYDET-17.
  - Category 2 PK only Abuse Liability Study
- PK of Xtampza (Oxycodone DETERx) 40 mg was determined
  - Intact capsule with a HFHC meal
  - Capsule contents crushed with a HFHC meal
  - Capsule contents chewed with a HFHC meal
  - **Intact capsule in the fasted state (Used as reference by Agency)**
  - Capsule contents crushed in the fasted state
  - Capsule contents chewed in the fasted state
  - Oxycodone Solution 40 mg (Used as reference by Collegium) in the fasted state
- Naltrexone-blocked subjects (n=38 to 42)
  - 7 x 7 Williams square randomization

Two-fold Increase in Xtampza Cmax Noted When Taken with HFHC Meal (Fed state vs. Fasted state)

	Xtampza Crushed Fasted	Xtampza Chewed Fasted	Xtampza Intact Fed	Xtampza Crushed Fed	Xtampza Chewed Fed	Oxycodone IR Fasted
			Cmax			
Ratio % [a]	110.4	**127.7**	**204.4**	**188.6**	**169.6**	376.7
90% CI Lower	100.3	116.1	185.8	171.4	154.0	342.4
90% CI Upper	121.5	140.5	225.0	207.5	186.8	414.3
			AUClast			
Ratio % [a]	106.4	**115.9**	**162.6**	**155.9**	**143.5**	140.9
90% CI Lower	92.9	101.3	142.0	136.1	125.1	123.1
90% CI Upper	122.0	132.7	186.2	178.5	164.5	161.2

Data from Xtampza Intact given in fasting state was used as reference.

Two-fold Increase in Cmax with Food Masks Any Effect of Physical Tampering



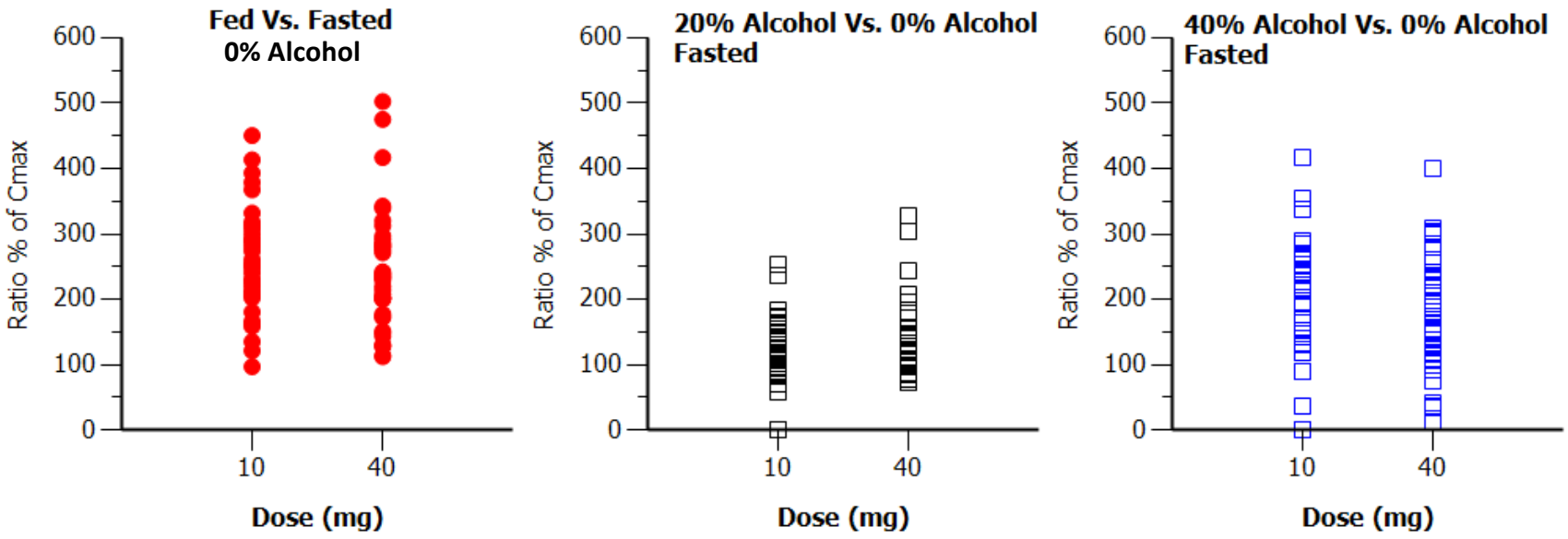
Full Symbols – Fed State
Open Symbols – Fasting

CP-OXYDET-17

Alcohol Interaction with Xtampza 10 mg and 40 mg

- Alcohol interaction study CP-OXYDET-26
- PK of Xtampza 10 mg or 40 mg
  - Treatment A: coingested with 40% alcohol, Fasted
  - Treatment B: coingested with 20% alcohol, Fasted
  - Treatment C: coingested with 0% alcohol, Fasted
  - Treatment D: coingested with 0% alcohol, Fed
- Naltrexone blocked subjects (n = 37 - 44)

Higher Bioavailability and Variable Food-effect Compared to Alcohol-effect in Fasting Subjects



Significant Food-effect Noted in Study -26

Treatment	Parameter	Fasted (Reference) LSGM	HFHC (Test) LSGM	Fed/Fasted Ratio %[a] (90% CI)
Xtampza 10 mg	Cmax (ng/mL)	6.1	14.83	244 (219- 273)
	AUClast (ng.h/mL)	84.28	128.57	152 (107 – 216)
	AUCinf (ng.h/mL)	107.59	139.93	132 (122 – 144)
Xtampza 40 mg	Cmax (ng/mL)	23.35	52.62	226 (197 – 258)
	AUClast (ng.h/mL)	337.78	498.37	148 (111 – 196)
	AUCinf (ng.h/mL)	352.59	516.39	142 (128 – 158)

Summary

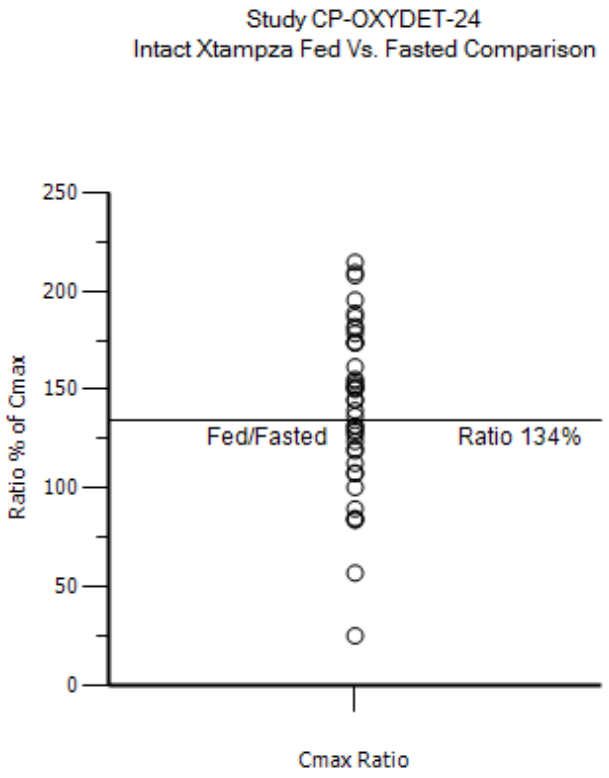
- Xtampza has lower bioavailability in fasted state compared to OxyContin in fasted state.
  - Higher variability in PK of Xtampza noted in fasting state
- Xtampza bioavailability increased with increased caloric/fat content.
- Food-effect is of sufficient magnitude and may mask any additional impact due to
  - Physical manipulation (crushing/chewing)
  - Alcohol-effect
- Significant difference in food-effect noted across studies.

CP-OXYDET-24: Drug Liking Study

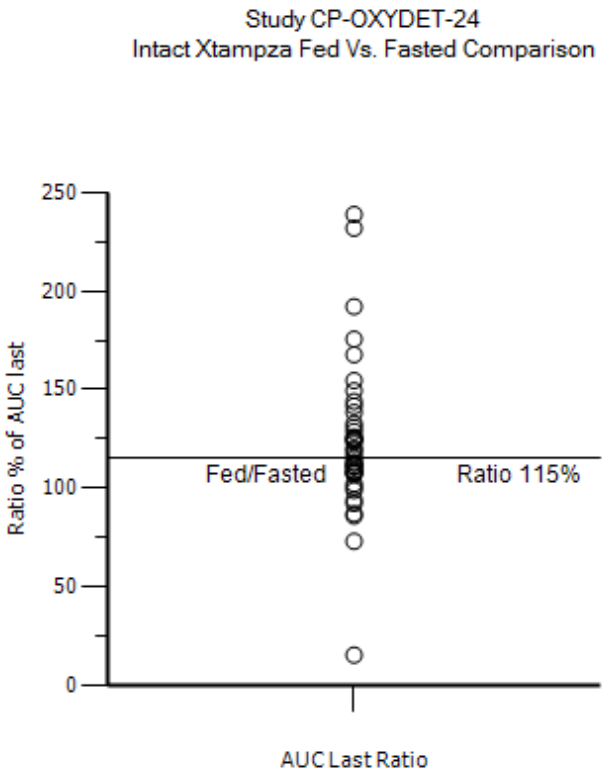
- Human abuse liability study
- Opioid-experienced non-dependent subjects (n=38 -47)
- randomized, double-blind, triple-dummy, active- and placebo-controlled, single-dose, 6-treatment, 6-period, cross-over comparison study.
- Oxycodone DETERx 40 mg administered under
  - Intact Fasted
  - Intact Fed
  - Chewed Fasted
  - Chewed Fed
  - IR oxycodone tablet chewed
- Naltrexone-block is not employed in drug liking study.

Food-effect
35% Increase in Cmax, 15% Increase in AUC Noted

Cmax



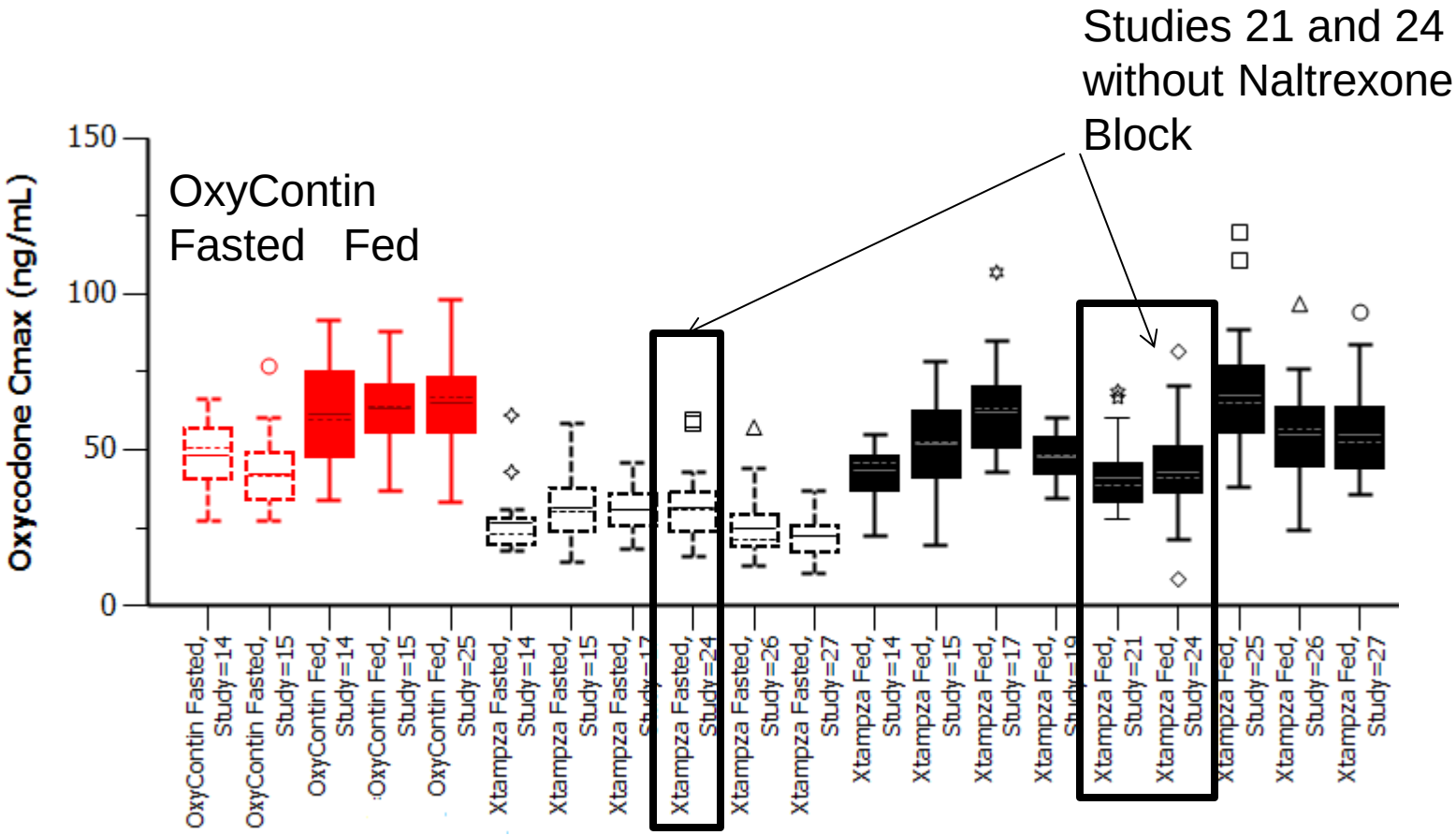
AUC



Sponsor's Rationale for Using Low Food-Effect Data from "Study 24"

- Morphine co-administered with NTX leads to increases in Cmax of 15% and AUC increases by 23% (Bashaw et al., 1995).
  - Study compares naltrexone effect in fasting state.
- Hydromorphone dosed with NTX increased Cmax by 39%, AUC was unchanged, and the apparent half-life decreased by approximately 4.5 hours (Sathyan et al., 2007).
  - Study compares naltrexone effect in fasting state.
- A crossover study examined the influence of NTX on oxymorphone exposure, and found that NTX increased Cmax by 38% (NDA Review 021610; NDA Review 021611).
- Regarding oxycodone, the prescribing information for OxyContin states "data obtained while subjects received naltrexone, which can enhance absorption" (Purdue Pharma L.P., 2014).
  - Data on naltrexone effect in fasting state.

Cmax Across Different Studies



Only Study # 24 employed naltrexone block in the above figure.

Comparison of Xtampza PK Parameters (mean (SD)) Across Different Single Dose Studies

	Fasted		HFHC Meal	
Study Number	Cmax (ng/mL)	AUCINF (hr•ng/mL)	Cmax (ng/mL)	AUCINF (hr•ng/mL)
Naltrexone-blocked studies				
-15	31.5 (9.52)	373 (134)	51.9 (14.3)	518 (156)
-17	30.7 (7.09)	369 (89.5)	62.3 (13.0)	561 (124)
-19	ND	ND	47.5 (7.89)	499 (110)
-25	ND	ND	67.5 (17.6)	581 (138)
-26	24.7 (9.41)	398 (114)	54.8 (14.6)	531 (105)
-27	22.3 (6.60)	339 (98.9)	55.3 (13.6)	540 (143)
Non-naltrexone blocked studies				
-21	ND	ND	41.0 (9.95)	477 (89.6)
-24	30.9 (9.91)	469 (107)	41.9 (12.4)	553 (131)

ND- not determined.
Source: Adapted from Table 36 section 2.7.2 Summary of Clinical Pharmacology studies.

Summary

- Bashaw et. al. 1995 conclude limited effect of naltrexone on morphine ER PK under fasting condition.
  - Conclude that the results support use of naltrexone-block in opioid BA studies.
- There is no evidence of naltrexone effect on opioid PK in fed state.
- Xtampza bioavailability is low under fasting condition across different studies.
- Xtampza PK has significant variability under fasting and fed condition across different studies.

Results of the Oral Human Abuse Liability Study

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Controlled Substance Staff (CSS)

September 11, 2015

FDA Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety & Risk Management Advisory Committee

Silver Spring, Maryland

Oral Study CP-OXYDET-24

Randomized, double-blind, triple-dummy, active- and placebo-controlled, single-dose, 6-treatment, 6-period, crossover study.

Primary Objective - Evaluate the abuse potential and pharmacokinetics (PK) of Xtampza ER 40 mg intact in the fed state, Xtampza ER 40 mg intact in the fasted state, Xtampza ER 40 mg chewed in the fed state, Xtampza ER 40 mg chewed in the fasted state, and IR oxycodone HCl 40 mg crushed in the fasted state.

Pharmacodynamic (PD) Population: 38 Non-dependent, recreational drug users subjects who completed all 6 Treatment Periods with at least one PD assessment in each Treatment Period.

Oral Treatments:

A: Intact Xtampza ER 40 mg Fed (HFHC)
B: Intact Xtampza ER 40 mg Fasted
C: Chewed Xtampza ER 40 mg Fed (HFHC)
D: Chewed Xtampza ER 40 mg Fasted
E: Crushed IR Oxycodone HCl 40 mg in Solution Fasted
F: Placebo

Pharmacodynamic Measures

Drug Liking Visual Analog Scale (VAS) – 0-100 mm Bipolar Scale (Primary Measure)
- Question: "Do you like the effect that you are feeling now?"
- 0 = "Strong disliking" ; 50 = "Neither like nor dislike"; 100 = "Strong liking"

High VAS – 0–100 mm Unipolar Scale (Secondary Measure)
- Question: "How high are you now?"
- 0 = "None"; 100 = "Extremely"

Take Drug Again VAS - 0–100 mm Bipolar Scale (Secondary Measure)
- Question: "Would you want to take the drug you just received again, if given the opportunity?"
- 0 = "Definitely would not"; 50 = "Do not care"; 100 = "Definitely would"

Addiction Research Center Inventory/Morphine Benzedrine Group Subscale (ARCI/MBG) (Secondary Measure)
- Used to assess euphoria and positive mood
- 16 questions scored on a 2-point scale (0-1), where 0 = false, 1 = true.
- Add the individual scores, with a possible total score of 16 for the MBG subscale.

Statistical Analysis

Conducted by the CDER Office of Biostatistics

Statistical analysis conducted using a mixed-effect model with fixed effects for sequence, period, and treatment with subject nested within sequence as a random effect. Least square means (LS means) and 95% confidence intervals (CIs) were calculated for each treatment. LS means differences and 95% CIs were generated for each pairwise treatment comparison.

Emax = Maximum response to each PD measure over the observation period

Primary differences examined:

- Crushed IR oxycodone 40 mg in solution fasted (Trt E) versus Chewed Xtampza ER 40 mg Fed (Trt C)
- Crushed IR oxycodone 40 mg in solution fasted (Trt E) versus Chewed Xtampza ER 40 mg Fasted (Trt D)

Statistical analysis validated all four measures (Drug Liking VAS, High VAS, Take Drug Again VAS, and ARCI/MBG Subscale).

Drug Liking VAS (Primary)

0.0007 **Point Bipolar Drug Liking VAS** (0 = "Strong disliking, 50 = "Neither like or dislike". 100 = "Strong liking")	LS Mean Emax	Standard Error	P-Value	95% CI
Treatments				
A: Intact Xtampza ER 40 mg Fed	68.94	1.92	<0.0001	(65.16, 72.72)
B: Intact Xtampza ER 40 mg Fasted	69.31	1.92	<0.0001	(65.53, 73.09)
C: Chewed Xtampza ER 40 mg Fed	70.73	1.92	<0.0001	(66.95, 74.51)
D: Chewed Xtampza ER 40 mg Fasted	73.83	1.92	<0.0001	(70.05, 77.61)
E: Crushed IR Oxycodone 40 mg Solution Fasted	81.56	1.92	<0.0001	(77.78, 85.34)
F: Placebo	54.70	1.92	<0.0001	(50.92, 58.48)
LS mean Differences				
Treatment E vs Treatment C	10.84	2.25	<0.0001	(6.40, 15.27)
Treatment E vs Treatment D	7.73	2.23	0.0007	(3.32, 12.14)

Crushed IR oxycodone 40 mg solution fasted produces a limited Emax of drug liking that is statistically significantly higher than the Emax produced by chewed Xtampza ER (fed or fasted). But are these differences (10.84 mm and 7.73 mm) clinically relevant?

High VAS

0–100 mm Unipolar High VAS (0 = "None", 100 = "Extremely")	LS Mean Emax	Standard Error	P-Value	95% CI
Treatments				
A: Intact Xtampza ER 40 mg Fed	37.32	4.08	<0.0001	(29.27, 45.37)
B: Intact Xtampza ER 40 mg Fasted	34.96	4.08	<0.0001	(26.9, 43.01)
C: Chewed Xtampza ER 40 mg Fed	37.70	4.08	<0.0001	(29.65, 45.75)
D: Chewed Xtampza ER 40 mg Fasted	45.56	4.08	<0.0001	(37.51, 53.61)
E: Crushed IR Oxycodone 40 mg Solution Fasted	68.32	4.08	<0.0001	(60.27, 76.38)
F: Placebo	9.87	4.08	<0.0001	(1.82, 17.92)
LS mean Differences				
Treatment E vs Treatment C	30.63	4.49	<0.0001	(27.76, 39.49)
Treatment E vs Treatment D	22.77	4.47	<0.0001	(13.95, 31.59)

Crushed IR oxycodone 40 mg solution fasted produces a maximum high that is statistically significantly higher than the maximum high produced by chewed Xtampza ER (fed or fasted). The reduction in maximum high of 30.63 mm associated with chewed Xtampza ER 40 mg fasted may be clinically relevant; however, the clinical relevancy of the 22.77 mm reduction associated with chewed Xtampza ER 40 mg fed is not known.

Take Drug Again VAS

0-100 mm Bipolar Take Drug Again VAS (0 = "Definitely would not", 50 = "Do not care", 100 = "Definitely would")	LS Mean Emax	Standard Error	P-Value	95% CI
Treatments				
A: Intact Xtampza ER 40 mg Fed	70.46	2.66	<0.0001	(65.20, 75.71)
B: Intact Xtampza ER 40 mg Fasted	70.40	2.66	<0.0001	(65.14, 75.65)
C: Chewed Xtampza ER 40 mg Fed	68.85	2.66	<0.0001	(63.59, 74.10)
D: Chewed Xtampza ER 40 mg Fasted	73.63	2.66	<0.0001	(68.38, 78.89)
E: Crushed IR Oxycodone 40 mg in Solution Fasted	74.73	2.66	<0.0001	(69.47, 79.98)
F: Placebo	51.79	2.66	<0.0001	(46.54, 57.05)
LS mean Differences				
Treatment E vs Treatment C	5.88	2.96	0.0484	(0.05, 11.71)
Treatment E vs Treatment D	1.09	2.94	0.7105	(-4.71, 6.90)

Crushed IR oxycodone 40 mg in solution fasted produced a limited maximum take drug again response that was higher than that produced by chewed Xtampza ER 40 mg fed but not different from chewed Xtampza ER 40 mg fasted. The difference of 5.88 mm associated with Xtampza ER, may not be clinically relevant.

ARCI/MBG Subscale

1-16 Point ARCI/MBG Scale	LS Mean	Standard Error	P-Value	95% CI
Treatments				
A: Intact Xtampza ER 40 mg Fed	4.34	0.74	<0.0001	(2.88, 5.80)
B: Intact Xtampza ER 40 mg Fasted	4.60	0.74	<0.0001	(3.14, 6.06)
C: Chewed Xtampza ER 40 mg Fed	4.35	0.74	<0.0001	(2.89, 5.82)
D: Chewed Xtampza ER 40 mg Fasted	5.22	0.74	<0.0001	(3.76, 6.68)
E: Crushed IR Oxycodone 40 mg in Solution Fasted	7.25	0.75	<0.0001	(5.77, 8.72)
F: Placebo	1.54	0.75	0.0413	(0.06, 3.01)
LS mean differences				
Treatment E vs Treatment C	2.89	0.76	0.0002	(1.39, 4.40)
Treatment E vs Treatment D	2.03	0.76	0.0081	(0.53, 3.53)

Crushed IR oxycodone 40 mg solution fasted produces a limited maximum score on the ARCI/MBG subscale that is statistically significantly higher than the maximum score produced by chewed Xtampza ER (fed or fasted). But is this difference (2.89 mm and 2.03 mm) clinically relevant?

Conclusions

1. The positive control, crushed IR oxycodone 40 mg solution fasted, produced limited maximum responses using the Drug Liking VAS, High VAS, Take Drug Again VAS, and the ARCI/MBG subscale.

2. Although crushed IR oxycodone 40 mg solution fasted produced maximum drug liking and euphoria (as measured by the ARCI/MBG scale) that was statistically significantly higher than that produced by chewed Xtampza ER fed or fasted, the differences were limited and of questionable clinical relevance.

3. The maximum take drug again response produced by crushed IR oxycodone 40 mg solution fasted was statistically significantly higher than the maximum response produced by chewed Xtampza ER 40 mg fed, but not chewed Xtampza ER 40 mg fasted. The 5.88 mm reduction in maximum take drug again response associated with Xtampza ER 40 mg fed may well not be of clinical significance. This data does not support a deterrent effect of Xtampza ER to abuse by chewing.

4. Crushed IR oxycodone 40 mg solution fasted produced a mean maximum high that was statistically significantly higher than the maximum high produced by Xtampza ER 40 mg under fed or fasted conditions. The 30.62 mm reduction in maximum high following Xtampza ER fed may be clinically relevant. The clinical relevancy of the 22.77 mm reduction in maximum high associated with chewed Xtampza ER fasted is not known.

Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee

Clinical Implications of Xtampza ER's Food Effect

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DAAAP

Outline

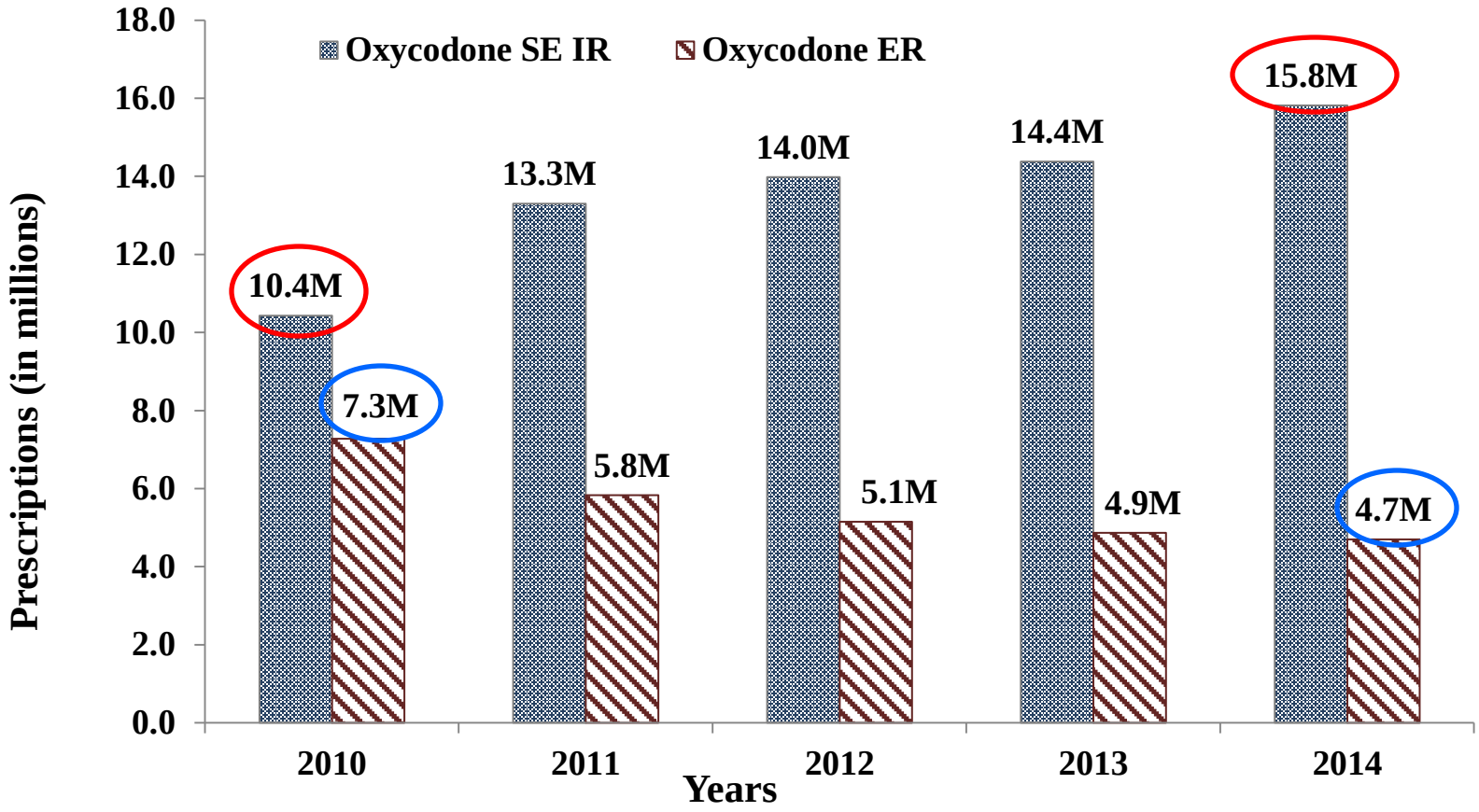
- Drug utilization patterns of oxycodone
- Label instructions for administration of opioids
- Clinical implications of Xtampza's food effect

Dispensed Prescription Data U.S. Outpatient Retail Pharmacies, 2010-2014

Dispensed Prescription Data: Outpatient Retail Pharmacy Settings

- IMS Health, National Prescription Audit (NPA™)
- Captures U.S. adjudicated prescription activity
  - Across all payment types
- Data are nationally projected to the outpatient pharmacy retail setting
  - Over 2.7 billion prescription claims/year
  - Approximately 57,000 pharmacies

Oxycodone SE IR and ER Prescription Data



Nationally estimated number of prescriptions dispensed for oxycodone single entity (SE) immediate release (IR) and oxycodone extended release (ER) products from U.S. outpatient retail pharmacies, 2010-2014

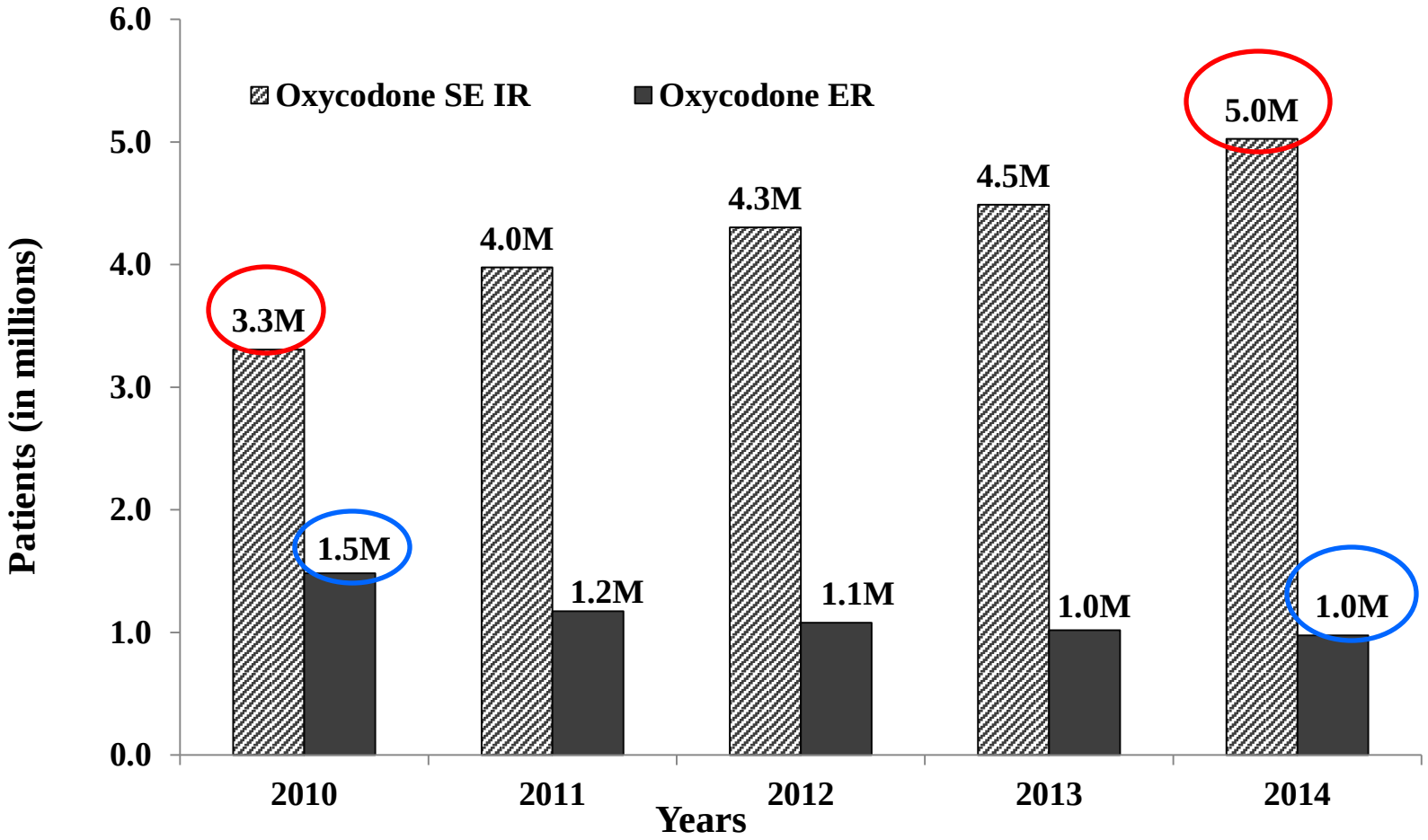
Source: IMS Health, National Prescription Audit ™ Extracted May 2015

Patient Level Data
U.S. Outpatient Retail Pharmacies, 2010-2014

Unique Patient Utilization:
Outpatient Retail Pharmacy Settings

- IMS Health, Total Patient Tracker(TPT)
- Captures U.S. adjudicated prescription activity
  - Across all payment types
- Data are nationally projected to the outpatient pharmacy retail setting
  - Receives >1.9 billion prescription claims per year
  - 158 million unique patients

Oxycodone SE IR and ER Unique Patient Data



Nationally estimated number of patients who received dispensed prescriptions for oxycodone single entity (SE) immediate-release (IR) or oxycodone extended-release (ER) products from U.S. outpatient retail pharmacies, 2010-2014

Source: IMS Health, National Prescription Audit ™ Extracted May 2015

Label Instructions for Administration Opioids

Extended- and Immediate-release Opioid Analgesics

- Generally labeled to take without regard to food, e.g., no significant food effect
- Opana ER (oxymorphone ER) and Opana (oxymorphone IR) are labeled to take on an empty stomach due to food effect (Cmax increased by 50% in fed state compared to fasted, slight increase in AUC)

Concern

Because most opioids are labeled to take without regard to food, prescribers and patients may not comply with labeling for this product based on long-standing behaviors

Clinical Implications of Xtampza's Food Effect

Pharmacokinetics (PK)

- Xtampza ER bioavailability is lower compared to OxyContin under fasting conditions
- Xtampza ER bioavailability increases with fat/calorie content in food
- Xtampza ER bioavailability varies depending on type of meal consumed
- Xtampza ER must be taken with meals due to its PK characteristics

Efficacy and Safety Implications

- Efficacy
  - Concern whether patients will take their medication consistently with the same type of meal twice daily
  - Variability in absorption of oxycodone due to administration with different types of meals (fat/calorie content) or without regard to meals may result in variable or decreased efficacy
- Safety
  - Patients may take extra doses if analgesia not adequate, possibly resulting in adverse events
  - Risk of accidental overdose with all opioids; food effect for this product adds another factor that contributes to this risk

Summary

- There is extensive use of ER and IR oxycodone products
- The majority of products are labeled to take without regard to food
- Xtampza ER has a significant food effect such that it must be administered with food
- The food effect is variable and depends on the fat/calorie content of the meal
- Inconsistent administration of Xtampza ER with regard to type of meal or fed/fasting state may result in increased risk of adverse events and accidental overdose
- Because most opioids are labeled to take without regard to food, prescribers and patients may not comply with labeling for this product based on long-standing behaviors

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BACKUP SLIDES SHOWN

Multiple Dose PK Study Xtampza PK Parameters

- **Study CP-OXYDET-18:** Open-label, randomized, active-controlled, NTX-blocked, cross-over comparison study
- To assess the safety and PK of multiple-dose (five day dosing) administration of 40 mg Oxycodone DETERx compared with OxyContin OP 40 mg under 2 different fed states.
- Subjects were randomized to receive each of the following 4 treatments in random order:
  - Treatment A: OxyContin OP 40 mg with a HFHC meal for all doses
  - Treatment B: OxyContin OP 40 mg in the fasted state for all morning doses and with a HFHC calorie meal for all evening doses
  - Treatment C: Oxycodone DETERX 40 mg with a HFHC meal for all doses
  - Treatment D: Oxycodone DETERx 40 mg in the fasted state for all morning doses and with a HFHC meal for all evening doses

Treatment		C_{max} (ng/mL)	T_{max} (hr)	C_{min} (ng/mL)	C_{ave} (ng/mL)	AUC_{tau} (hr•ng/mL)	AUC_{0-24} (hr•ng/mL)	%PTF
Oxycodone DETERx Fed/Fed (AM dosing)	N	35	35	35	35	35	NA	35
	Mean (SD)[a]	77.7 (23.6)	3.5 (1 - 5.5)	21.3 (7.09)	42.6 (9.66)	511 (116)	NA	134 (35.8)
OxyContin OP Fed/Fed (AM dosing)	N	37	37	37	37	37	NA	37
	Mean (SD)[a]	77.1 (17.8)	4.5 (1 - 6.5)	21.2 (6.39)	44.3 (9.81)	532 (118)	NA	127 (18.9)
Oxycodone DETERx Fasted/Fed (AM dosing)	N	36	36	36	36	36	NA	36
	Mean (SD)[a]	49.6 (15.1)	2.5 (1 - 5)	17.8 (7.32)	32.1 (10.3)	385 (124)	NA	101 (19.6)
Oxycodone DETERx Fasted/Fed (PM dosing)	N	36	36	36	36	36	NA	36
	Mean (SD)[a]	62.4 (12.9)	6 (2 - 8)	15.2 (6.57)	39.4 (8.99)	473 (108)	NA	122 (21.5)
Oxycodone DETERx Fasted/Fed (24-hr profile)	N	36	36	36	36	NA	36	36
	Mean (SD)[a]	63.7 (13.9)	17.3 (1 - 20)	15.1 (6.48)	35.7 (9.14)	NA	858 (219)	140 (27.5)
OxyContin OP Fasted/Fed (AM dosing)	N	36	36	36	36	36	NA	36
	Mean (SD)[a]	54.9 (10.5)	3 (1 - 5)	19.2 (7.35)	37 (8.39)	444 (101)	NA	99.3 (27.1)
OxyContin OP Fasted/Fed (PM dosing)	N	36	36	36	36	36	NA	36
	Mean (SD)[a]	71.3 (14.7)	5 (1.5 - 8)	18.7 (5.6)	42.7 (8.58)	512 (103)	NA	125 (27.7)
OxyContin OP Fasted/Fed (24-hr profile)	N	36	36	36	36	NA	36	36
	Mean (SD)[a]	72 (13.9)	16.5 (3 - 20)	17.7 (6.15)	39.9 (8.26)	NA	957 (198)	139 (34.4)

[a] Values shown for T_{max} are median (minimum - maximum).

AUC = area under the plasma concentration vs time curve; AUC_{tau} = AUC from time 0 to the end of the dosing interval; AUC_{0-24} = AUC summed for 2 dosing intervals; C_{ave} = average plasma concentration; C_{max} = maximum observed plasma concentration; NA = not applicable; PK = pharmacokinetic; %PTF = percentage of peak-trough fluctuation within a dosing interval; SD = standard deviation; T_{max} = time to reach maximum plasma concentration

Source: Study CP-OXYDET-18 Pharmacokinetic Report, Table 2 and Table 3.

Treatment		C_{max} (ng/mL)	T_{max} (hr)	C_{min} (ng/mL)	C_{ave} (ng/mL)	AUC_{tau} (hr•ng/mL)	AUC_{0-24} (hr•ng/mL)	%PTF
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	Mean (SD)[a]	77.7 (23.6)	3.5 (1 - 5.5)	21.3 (7.09)	42.6 (9.66)	511 (116)	NA	134 (35.8)
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Source: Study CP-OXYDET-18 Pharmacokinetic Report, Table 2 and Table 3.