

ABUSE DETERRENT FORMULATIONS CURRENT AND PIPELINE

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Table 1: Opioids with Abuse Deterrent Properties

Brand Name	Generic Name	Formulation	Approval Year	Manufacturer	Abuse Deterrent Technology	FDA Approved Abuse Deterrent Labeling
Buprenorphine Products						
Suboxone ¹	Buprenorphine co-formulated with naloxone	Sublingual film	2002	Indivior Inc.	<ul style="list-style-type: none"> Co-formulation with naloxone causes blockade of opioid receptors, preventing mu agonism when taken intranasal or intravenously^a 	No
Zubsolv ²	Buprenorphine co-formulated with naloxone	Sublingual tablets	2002	Orexo US, Inc.	<ul style="list-style-type: none"> Co-formulation with naloxone causes blockade of opioid receptors, preventing mu agonism when taken intranasal or intravenously^a 	No
Bunavail ³	Buprenorphine co-formulated with naloxone	Buccal films	2017	BioDelivery Sciences	<ul style="list-style-type: none"> Co-formulation with naloxone causes blockade of opioid receptors, preventing mu agonism when taken intranasal or intravenously^a 	No
Hydrocodone Products						
Zohydro ER ^{4,5}	Hydrocodone bitartrate	Extended-release capsules	2013 ^b	Zogenix, Inc.	<ul style="list-style-type: none"> BeadTek <i>technology</i> Excipients immediately form a viscous gel when crushed and dissolved in solvents or liquids 	No
Hysingla ER ^{6,7}	Hydrocodone bitartrate	Extended-release tablets	2014	Purdue Pharma L.P.	<ul style="list-style-type: none"> <i>RESISTEC Technology</i> Physiochemical properties allow increased resistance to 	Yes

					<ul style="list-style-type: none"> crushing, breaking, and dissolution When subjected to an aqueous environment, forms into a viscous hydrogel 	
Vantrela ER ^{8,9}	Hydrocodone bitartrate	Extended-release tablets	2017	Teva Pharmaceuticals USA, Inc.	<ul style="list-style-type: none"> CIMA Lab technology <i>Maintains ER profile even when reduced to a fine powder</i> 	Yes
Hydromorphone products						
Exalgo ER ¹⁰	Hydromorphone hydrochloride	Extended-release tablets	2010	Mallinckrodt, Inc.	<ul style="list-style-type: none"> Osmotic [Controlled] Release Oral [Delivery] System (OROS) technology Crush and extraction resistant 	No
Morphine Products						
Kadian ER ¹¹	Morphine sulfate	Extended-release capsules	1996	Actavis Kadian LLC	<ul style="list-style-type: none"> Polymer coated extended-release pellets of morphine sulfate 	No
Embeda ER ¹²	Morphine sulfate co-formulated with naltrexone hydrochloride	Extended-release capsules	2009 ^c	Pfizer Inc. ^d	<ul style="list-style-type: none"> Co-formulation with opioid antagonist naltrexone Naltrexone is released from sequestered bead core when capsule contents are manipulated by crushing 	Yes
MorphaBond ER ^{13,14}	Morphine sulfate	Extended-release tablets	2015	Daiichi Sankyo, Inc.	<ul style="list-style-type: none"> SentryBond™ technology Formulated with inactive ingredients that make it difficult to adulterate tablet Resistant to cutting, crushing, or breaking 	Yes

					<ul style="list-style-type: none"> On contact with liquid, forms a viscous material 	
Arymo ER ^{15,16}	Morphine sulfate	Extended-release tablets	2017	Egalet US Inc.	<ul style="list-style-type: none"> Guardian technology Polymer matrix tablet that resists manipulation On contact with liquid, forms viscous hydrogel 	Yes
Oxycodone Products						
Oxecta ^{17,18}	Oxycodone	Immediate-release tablets	2011	King Pharmaceuticals, Inc.	<ul style="list-style-type: none"> Aversion technology that uses inactive ingredients causing medication to form a viscous gel when tablets are dissolved in water or alcohol Also cause nasal discomfort when crushed and snorted 	No
OxyContin CR ¹⁹	Oxycodone	Controlled-release tablets	2013 ^e	Purdue Pharma L.P.	<ul style="list-style-type: none"> RESISTEC™ allows increased resistance to crushing, breaking, and dissolution When subjected to an aqueous environment, forms into viscous hydrogel 	Yes
Targiniq ER ²⁰	Oxycodone co-formulated with naloxone	Extended-release tablets	2014	Purdue Pharma L.P.	<ul style="list-style-type: none"> Co-formulation with naloxone causes blockade of opioid receptors, preventing mu agonism when taken intranasal or intravenously^a 	Yes
Xartemis XR ^{21,22}	Oxycodone with acetaminophen	Bilayer formulation provides both immediate and	2014	Mallinckrodt Pharmaceuticals	<ul style="list-style-type: none"> Incorporation of PolyOx increases difficulty of extraction of oxycodone 	No

		extended-release tablet				
Oxaydo ²³	Oxycodone	Immediate-release tablets	2015	Egalet US Inc.	<ul style="list-style-type: none"> • Aversion® technology: • Formulated with sodium lauryl sulfate (inactive ingredient) that causes nasal burning and throat irritation when snorted 	No
Xtampza ER ²⁴	Oxycodone	Extended-release capsules	2016	Collegium Pharmaceutical, Inc.	<ul style="list-style-type: none"> • DETERx microsphere technology: inactive ingredients form lipophilic salt permitting homogenous distribution of the active drug in each waxy microsphere • Microspheres solidify within a needle • Capsules can be emptied into G-tube or sprinkled on food 	Yes
Troxyca ER ²⁵	Oxycodone co-formulated with naltrexone	Extended-release capsules	2016	Pfizer	<ul style="list-style-type: none"> • If capsules are crushed or chewed, up to 100% of sequestered naltrexone is released, blocking opioid receptors and preventing mu receptor agonism • Capsule contents can be sprinkled on applesauce and then swallowed immediately without chewing 	Yes
RoxyBond ²⁶	Oxycodone	Immediate-release tablets	2017	Daiichi Sankyo, Inc.	<ul style="list-style-type: none"> • SentryBond™ technology that incorporates inactive ingredients making the tablet more difficult to manipulate, even if subjected to physical manipulation and/or chemical extraction 	Yes

Tapentadol Products						
Nucynta ER ²⁷	Tapentadol	Extended-release tablets	2011	Depomed, Inc.	<ul style="list-style-type: none"> • INTAC™ allows properties that make it difficult to crush, cut, or break tablets 	No
Pentazocine Products						
Talwin NX ²⁸	Pentazocine co-formulated with naloxone	Immediate-release tablets	2000	Sanofi-Aventis	<ul style="list-style-type: none"> • Co-formulation with naloxone causes blockade of opioid receptors, preventing mu agonism when taken by intranasal or intravenous routes^a • Also available by generic 	No

^a Products co-formulated with naloxone only have the mu-receptor antagonism effects when used intranasally or intravenously. Naloxone is not systemically absorbed when taken orally, thus these products may still be abused orally.

^b Zohydro ER was originally FDA approved in 2013, however it was reformulated in 2015 with the BeadTek abuse deterrent technology

^c Embeda was originally FDA approved in 2009; Labeling for Abuse Deterrent features was FDA approved in 2014

^d Pfizer discontinued Avinza following approval for updated labeling on Embeda

^e OxyContin was originally approved in 1996, however was reformulated in 2010 with abuse deterrent technology, and became the first opioid with FDA approved labeling describing abuse-deterrent characteristics in 2013.

Table 2: Abuse Deterrent Formulation Opioids in the Pipeline

<i>Abuse Deterrent Formulation Opioids in the Pipeline</i>					
Brand Name	Generic Name	Formulation	Current Clinical Trial Status	Manufacturer	Abuse Deterrent Technology
NKTR-181 ²⁹	New chemical entity mu-opioid agonist	Long acting	SUMMIT phase 3 program: includes SUMMIT-07 efficacy study, SUMMIT-LTS long-term safety study, and human abuse potential study	NEKTAR	<ul style="list-style-type: none"> • Structure designed to have reduced permeability across blood-brain barrier due to pegylation in order to slow rate of entry into the brain, and attenuate dopamine release to minimize euphoria and possibly neuroplasticity • 12-hour elimination half-life • Preclinical data has shown that these properties reduce rate of entry into the brain compared to standard mu-opioid, regardless of route of administration
REL-1015 (Levocap ER) ^{30,31}	Levorphanol	Extended-release capsules	Phase 3	Relmada	<ul style="list-style-type: none"> • SECUREL™ technology: prevent from being easily crushed for inhalation or to obtain rapid euphoria from high blood levels when swallowed • Also increases difficulty for IV abusers to extract active drug from the dosage form
FT227 ^{30,32}	Hydromorphone	Extended-release	Phase 2	Avadel Pharmaceuticals	<ul style="list-style-type: none"> • Trigger Lock™: contains sustained release Micropump®-based particles resistant to crushing • Resistance of drug extraction through alcohol, water, and other mediums

					<ul style="list-style-type: none"> • Prevention of injection through viscosifying ingredients
Remoxy ER ^{30,33}	Oxycodone	Extend-release capsules	N/a	Pain Therapeutics, Inc.	<ul style="list-style-type: none"> • ORADUR™ technology: gel matrices that accommodate high concentrations of active compounds, while providing resistance to improper release or extraction of active agents
Rexista ER ³⁴	Oxycodone	Extended-release tablets	N/a	Intellipharma	<ul style="list-style-type: none"> • When crushed and hydrolyzed, it is designed to coagulate instantaneously and form a viscous hydrogel • Contains blue dye emitted once tablet is tampered with/crushed

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Table created by

Jeffrey J, Bettinger, PharmD and Kerry A. Archer, PharmD

PGY1 Pharmacy Residents, Stratton VA Medical Center, Albany NY

Edited and revised by

Jeffrey Fudin, BS, PharmD, DAIPM, FCCP, FCCP

President and Director, Scientific and Clinical Affairs, Remitigate, LLC, Delmar NY

Owner & Managing Editor, PainDr.com & Pain Blog, Delmar NY

Adjunct Associate Professor of Pharmacy Practice & Pain Management, Albany College of Pharmacy & Health Sciences, Albany NY

Adjunct Associate Professor, Western New England University College of Pharmacy, Springfield MA

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