

US Post Marketing Commitments

Product/ Compound	Description of Commitment	NDA Number	Agreement Date	Projected Completion Date	Status
Benicar (olmesartan medoxomil) 5/20/40 MG	Pediatric assessment.	21-286	4/25/2002	Complete	Fulfilled
Benicar (olmesartan medoxomil) 5/20/40 MG	A study to evaluate olmesartan for effects on hERG and hNav1.5 currents in whole cell voltage clamp studies using ion channels expressed in a mammalian cell line.	21-286	5/26/2011	Complete	Fulfilled
Benicar (olmesartan medoxomil) 5/20/40 MG	Perform a thorough QT/QTc study for olmesartan in accordance with the FDA Guidance, "Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Anti-arrhythmic Drugs.	21-286	5/26/2011	Complete	Fulfilled

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Benicar (olmesartan medoxomil) 5/20/40 MG	Conduct an epidemiologic study using claims or electronic health records data to evaluate the comparative incidence of sudden cardiac death, in hospital fatal myocardial infarction and total mortality in olmesartan users vs. users of other angiotensin receptor blockers and in olmesartan users vs. ACE inhibitor users.	21-286	5/26/2011	Complete	Fulfilled
Benicar (olmesartan medoxomil) 5/20/40 MG	Conduct a patient-level meta-analysis evaluating the incidence of major cardiovascular events and total mortality in olmesartan treated patients compared to control patients in randomized clinical trials.	21-286	5/26/2011	Complete	Fulfilled

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Product/Compound	Description of Commitment	NDA Number	Agreement Date	Projected Completion Date	Status
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2065-1: Conduct one or more studies to provide quantitative estimates of the serious risks of misuse, abuse, addiction, overdose, and death associated with long-term use of opioid analgesics for management of chronic pain, among patients prescribed ER/LA opioid products. Include an assessment of risk relative to efficacy.	206544	10/2/2015	01/2018	Released & replaced with 3033 PMR
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2065-2: Develop and validate measures of the following opioid-related adverse events: misuse, abuse, addiction, overdose and death (based on DHHS definition, or any agreed-upon definition), which will be used to inform the design and analysis for PMR # 2065-1 and any future post-marketing safety studies and clinical trials to assess these risks. This can be achieved by conducting an instrument development study or a validation study of an algorithm based on secondary data sources.	206544	10/2/2015	08/2015	Released & replaced with 3033 PMR

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Morphabond ER (morphine sulfate) 15/30/60/100 MG	2065-3: Conduct a study to validate coded medical terminologies (e.g., ICD9, ICD10, SNOMED) used to identify the following opioid-related adverse events: misuse, abuse, addiction, overdose, and death in any existing post-marketing databases to be employed in the studies. Stratify misuse and overdose by intentionality wherever possible. These validated codes will be used to inform the design and analysis for PMR # 2065-1.	206544	10/2/2015	08/2015	Released & replaced with 3033 PMR
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2065-4: Conduct a study to define and validate “doctor/pharmacy shopping” as outcomes suggestive of misuse, abuse and/or addiction. These validated codes will be used to inform the design and analysis for PMR # 2065-1.	206544	10/2/2015	08/2015	Released & replaced with 3033 PMR
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2065-5: Conduct a clinical trial to estimate the serious risk for the development of hyperalgesia following use of ER/LA opioid analgesics for at least one year to treat chronic pain. We strongly encourage you to use the same trial to assess the development of tolerance following use of ER/LA opioid analgesics. Include an assessment of risk relative to efficacy.	206544	10/2/2015	08/2016	Released & replaced with 3033 PMR

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Product/ Compound	Description of Commitment	NDA Number	Agreement Date	Projected Completion Date	Status
Morphabond ER (morphine sulfate) 15/30/60/100 MG	<p>2961-1: Conduct epidemiologic to address whether the properties intended to deter misuse and abuse of MORPHABOND (morphine sulfate extended release tablets) actually result in a significant and meaningful decrease in misuse and abuse, and their consequences, addiction, overdose, and death, in the community. The post-marketing study program must allow FDA to assess the impact, if any, that is attributable to the abuse-deterrent properties of MORPHABOND. To meet this objective, investigations should incorporate recommendations contained in the FDA draft guidance, Abuse Deterrent Opioids—Evaluation and Labeling (January 2013) and proposed comparators need to be mutually agreed upon prior to initiating epidemiologic investigations. There must be sufficient drug utilization to allow a meaningful epidemiological assessment of overall and route-specific abuse deterrence.</p>	206544	10/2/2015	08/2020	Released & replaced with 2961-9 PMR on 5/12/17

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Morphabond ER (morphine sulfate) 15/30/60/100 MG	2961-2: Conduct a 9-month repeat-dose oral toxicology study in the nonrodent model characterizing the toxicological potential of [REDACTED]	206544	10/2/2015	07/2018	Pending
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2961-3: Conduct a 6-month repeat-dose oral toxicology study in the rodent model characterizing the toxicological potential of [REDACTED]	206544	10/2/2015	05/2017	Pending
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2961-4: Conduct a fertility and early embryonic development study in both male and female rats with [REDACTED]	206544	10/2/2015	05/2018	Released from PMR on 01/15/2016
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2961-5: Conduct an embryofetal development study for [REDACTED] in the rat model.	206544	10/2/2015	10/2017	Released from PMR on 01/15/2016
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2961-6: Conduct an embryofetal development study for [REDACTED] in the rabbit model.	206544	10/2/2015	10/2017	Released from PMR on 01/15/2016

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Morphabond ER (morphine sulfate) 15/30/60/100 MG	2961-7: Conduct an embryofetal development study for [REDACTED] in the rat model.	206544	10/2/2015	07/2018	Released from PMR on 01/15/2016
Morphabond ER (morphine sulfate) 15/30/60/100 MG	2961-8: Conduct a 2-year rodent oral carcinogenicity assessment of [REDACTED]	206544	10/2/2015	04/2020	Pending

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Morphabond ER (morphine sulfate) 15/30/60/100 MG	<p>2961-9: Conduct epidemiologic to address whether the properties intended to deter misuse and abuse of MORPHABOND (morphine sulfate extended release tablets) actually result in a significant and meaningful decrease in misuse and abuse, and their consequences, addiction, overdose, and death, in the community. The post-marketing study program must allow FDA to assess the impact, if any, that is attributable to the abuse-deterrent properties of MORPHABOND. To meet this objective, investigations should incorporate recommendations contained in the FDA draft guidance, Abuse Deterrent Opioids—Evaluation and Labeling (January 2013) and proposed comparators need to be mutually agreed upon prior to initiating epidemiologic investigations. There must be sufficient drug utilization to allow a meaningful epidemiological assessment of overall and route-specific abuse deterrence.</p>	206544	10/2/2015	09/2020	Ongoing

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Product/Compound	Description of Commitment	NDA Number	Agreement Date	Projected Completion Date	Status
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-1: Conduct a prospective, observational study designed to quantify the serious risks of misuse, abuse, and addiction associated with long-term use of opioid analgesics for management of chronic pain among patients prescribed ER/LA opioid analgesics.	206544	2/4/2016	10/2019	Ongoing
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-2: Conduct an observational study designed to measure the incidence and predictors of opioid overdose and death (OOD), as well as opioid abuse/addiction, using patient health records, insurance claims, and death records.	206544	2/4/2016	04/2019	Delayed
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-3: Conduct a prospective observational study designed to assess the content validity and patient interpretation of the Prescription Opioid Misuse and Abuse Questionnaire (POMAQ). Patient understanding of the concepts of misuse and abuse will also be obtained.	206544	2/4/2016	10/2015	Submitted* *Pending FDA confirmation as fulfilled

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Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-4: Conduct an observational study to evaluate the validity and reproducibility of the Prescription Opioid Misuse and Abuse Questionnaire (POMAQ), which will be used to identify opioid abuse and misuse behaviors among participants who have chronic pain which requires long-term opioid analgesic use.	206544	2/4/2016	10/2016	Submitted* *Pending FDA confirmation as fulfilled
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-5: Conduct an observational study to validate measures of prescription opioid Substance Use Disorder and addiction in patients who have received or are receiving opioid analgesics for chronic pain.	206544	2/4/2016	12/2016	Submitted* *Pending FDA confirmation as fulfilled
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-6: Conduct an observational study to develop and validate an algorithm using coded medical terminologies and other electronic healthcare data to identify opioid-related overdose and death.	206544	2/4/2016	09/2016	Submitted* *Pending FDA confirmation as fulfilled

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Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-7: Conduct an observational study to develop and validate an algorithm using coded medical terminologies to identify patients experiencing prescription opioid abuse or addiction, among patients receiving an ER/LA opioid analgesic.	206544	2/4/2016	10/2016	Submitted* *Pending FDA confirmation as fulfilled
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-8: Conduct an observational study using coded medical terminologies and other electronic healthcare data to define and validate doctor and/or pharmacy shopping outcomes by examining their association with abuse and/or addiction.	206544	2/4/2016	10/2017	Submitted* *Pending FDA confirmation as fulfilled
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-9: Conduct an observational study using a validated patient survey to evaluate the association between doctor/pharmacy shopping outcomes and self-reported misuse and abuse.	206544	2/4/2016	09/2018	Fulfilled

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Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-10: Conduct an observational study using medical record review to evaluate the association between doctor/pharmacy shopping outcomes and patient behaviors suggestive of misuse, abuse and/or addiction.	206544	2/4/2016	03/2017	Submitted* *Pending FDA confirmation as fulfilled
Morphabond ER (morphine sulfate) 15/30/60/100 MG	3033-11: Conduct a clinical trial to estimate the serious risk for the development of hyperalgesia following the long-term use of high-dose ER/LA opioid analgesics for at least one year to treat chronic pain. Include an assessment of risk relative to efficacy.	206544	2/4/2016	02/2019	Fulfilled

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Savaysa (edoxaban)	2852-1: Pediatric Development in VTE (AF waived) Single-dose PK/PD study	206316	01/08/2015	6/30/2020	Ongoing
Savaysa (edoxaban)	2852-2: Phase 3 multicenter, randomized, active control study of Edoxaban in pediatric patients with documented venous thromboembolism	206316	01/08/2015	6/30/2022	Ongoing
Welchol for Oral Suspension PMC	1-year, pediatric efficacy and safety study under PREA for the treatment of type 2 Diabetes in pediatric patients ages 10 to 17 years.	22362 & 21176/S-022	10/02/2009	11/30/2019	Ongoing
Welchol Chewable Bar	3593-1: 1-year, pediatric efficacy and safety study under PREA for the treatment of type 2 Diabetes in pediatric patients ages 10 to 17 years.	210895	04/26/2019	09/2027	Pending

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Welchol (colesevelam HCl) tablets	To study Welchol as monotherapy treatment for type 2 diabetes mellitus.	21176	05/26/2000	Complete	Fulfilled
Welchol (colesevelam HCl) tablets	To study Welchol in combination with thiazolidinediones as treatment for type 2 diabetes mellitus.	21176	05/26/2000	Complete	Fulfilled
ROXYBOND (oxycodone hydrochloride) 5, 15, 30 mg	3204-1: Conduct a 9-month repeat-dose oral toxicology study in the nonrodent model characterizing the toxicological potential of [REDACTED]	209777	04/20/2017	07/01/2019	Pending
ROXYBOND (oxycodone hydrochloride) 5, 15, 30 mg	3204-2: Conduct a 6-month repeat-dose oral toxicology study in the rodent model characterizing the toxicological potential of [REDACTED]	209777	04/20/2017	05/30/2018	Pending
ROXYBOND (oxycodone hydrochloride) 5, 15, 30 mg	3204-3: Conduct a 2-year rodent oral carcinogenicity assessment of [REDACTED]	209777	04/20/2017	04/30/2021	Pending

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ROXYBOND (oxycodone hydrochloride) 5, 15, 30 mg	<p>3204-4: Conduct a descriptive study to collect meaningful baseline data to support subsequent studies for formal epidemiologic assessment of abuse-deterrence of ROXYBOND. The descriptive study should include data on the following:</p> <p>1) Utilization of ROXYBOND and selected comparators. Reports should include nationally-projected quarterly dispensing data, overall and by age group and census region; AND</p> <p>2) Abuse of ROXYBOND and related clinical outcomes. These assessments should utilize multiple data sources in different populations to establish the scope and patterns of abuse for ROXYBOND as well as mutually agreed-upon, selected comparators to provide context. Data should include route-specific abuse outcomes, be nationally representative or from multiple large geographic areas, and use meaningful measures of abuse.</p>	209777	04/20/2017	03/30/2021	Pending

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ROXYBOND (oxycodone hydrochloride) 5, 15, 30 mg	3204-5: As part of the ongoing stability studies, commit to repeating the small volume extraction studies, using water and solvents at pH 2 and 3.5, using tablets that are pre-treated with heat and no heat, crushed and intact. Further use the same study conditions in the completed in vitro studies submitted to the NDA, to demonstrate that there is no change in syringeability of the product and in the extraction recovery of the drug product stored over time. Commit to repeating these studies yearly.	209777	04/20/2017	04/01/2022	Ongoing
ROXYBOND (oxycodone hydrochloride) 5, 15, 30 mg	3204-6: Commit to the submission of an updated in-process sampling plan and associated acceptance criteria for the stratified content uniformity for the cured diffusion coated tablets to ensure that batches of drug products meet appropriate statistical quality criteria. The proposed statistical plan and acceptance criteria shall be adequate to ensure that appropriate quality conclusions can be made about this in process material based on final critical quality attributes and shall be justified with supporting statistical analyses or rationale.	209777	04/20/2017	N/A	Fulfilled