



US009561177B2

(12) **United States Patent**
Keegan et al.

(10) **Patent No.:** **US 9,561,177 B2**
(45) **Date of Patent:** ***Feb. 7, 2017**

(54) **NASAL DRUG PRODUCTS AND METHODS OF THEIR USE**

(2014.02); *A61M 11/006* (2014.02); *A61M 11/007* (2014.02); *A61M 15/08* (2013.01); *A61M 31/00* (2013.01)

(71) Applicants: **Adapt Pharma Limited**, Dublin (IE); **Opiant Pharmaceuticals**, Santa Monica, CA (US)

(58) **Field of Classification Search**
None
See application file for complete search history.

(72) Inventors: **Fintan Keegan**, Dublin (IE); **Robert Gerard Bell**, Clearwater, FL (US); **Roger Crystal**, Santa Monica, CA (US); **Michael Brenner Weiss**, New York, NY (US)

(56) **References Cited**

U.S. PATENT DOCUMENTS

(73) Assignees: **ADAPT PHARMA LIMITED**, Dublin (IE); **OPIANT PHARMACEUTICALS**, Santa Monica, CA (US)

4,181,726	A	1/1980	Bernstein	424/260
4,464,378	A	8/1984	Hussain	424/260
5,866,154	A	2/1999	Bahal et al.	424/423
9,192,570	B2	11/2015	Wyse et al.	
9,211,253	B2	12/2015	Crystal et al.	
2003/0077300	A1	4/2003	Wermeling	424/400
2006/0120967	A1	6/2006	Namburi et al.	424/45
2009/0017102	A1	1/2009	Stinchcomb et al.	424/449
2010/0113495	A1	5/2010	Wermeling et al.	514/282
2010/0168147	A1	7/2010	Chapleo et al.	514/282
2010/0331354	A1	12/2010	Wermeling	514/282
2011/0046172	A1	2/2011	Chapleo et al.	514/282
2012/0270895	A1	10/2012	Wermeling	514/282
2013/0023825	A1	1/2013	Edwards et al.	604/143
2015/0174061	A1	6/2015	Wyse et al.	A61K 9/0043
2015/0258019	A1	9/2015	Crystal et al.	A61K 9/0043
2016/0008277	A1	1/2016	Crystal et al.	

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/183,441**

(22) Filed: **Jun. 15, 2016**

(65) **Prior Publication Data**

US 2016/0303041 A1 Oct. 20, 2016

Related U.S. Application Data

(63) Continuation-in-part of application No. 14/950,707, filed on Nov. 24, 2015, now Pat. No. 9,468,747, which is a continuation of application No. 14/942,344, filed on Nov. 16, 2015, now Pat. No. 9,480,644, which is a continuation-in-part of application No. 14/659,472, filed on Mar. 16, 2015, now Pat. No. 9,211,253.

FOREIGN PATENT DOCUMENTS

CN	1575795	2/2005	A61K 31/485
EP	1681057	7/2006	A61K 31/485
WO	WO 82/03768	11/1982	A61K 31/40
WO	WO 98/30211	7/1998	A61K 9/72
WO	WO 00/62757	10/2000	A61K 9/00
WO	WO 00/74652	12/2000	A61K 9/12
WO	WO 01/58447	8/2001	A61K 31/44
WO	WO 01/82931	11/2001	A61M 31/52
WO	WO 02/11778	2/2002	A61L 9/04
WO	WO 03/084520	10/2003	A61M 31/00
WO	WO 2004/054511	7/2004	
WO	WO 2005/020906	3/2005	

(Continued)

(60) Provisional application No. 61/953,379, filed on Mar. 14, 2014, provisional application No. 62/274,536, filed on Jan. 4, 2016, provisional application No. 62/219,955, filed on Sep. 17, 2015.

OTHER PUBLICATIONS

Djupeusland; Drug Deliv. and Transl. Res. (2013) 3:42-62.*

(Continued)

(51) **Int. Cl.**

<i>A61M 31/00</i>	(2006.01)
<i>A61M 5/00</i>	(2006.01)
<i>A61F 13/00</i>	(2006.01)
<i>A61K 31/56</i>	(2006.01)
<i>A61K 9/00</i>	(2006.01)
<i>A61K 9/08</i>	(2006.01)
<i>A61K 31/485</i>	(2006.01)
<i>A61K 47/02</i>	(2006.01)
<i>A61K 47/18</i>	(2006.01)
<i>A61M 15/08</i>	(2006.01)
<i>A61M 11/00</i>	(2006.01)

Primary Examiner — Jeffrey T Palenik

(74) *Attorney, Agent, or Firm* — Harness, Dickey & Pierce, P.L.C.

(52) **U.S. Cl.**

CPC *A61K 9/0043* (2013.01); *A61K 9/08* (2013.01); *A61K 31/485* (2013.01); *A61K*

(57) **ABSTRACT**

Drug products adapted for nasal delivery, comprising a pre-primed device filled with a pharmaceutical composition comprising an opioid receptor antagonist, are provided. Methods of treating opioid overdose or its symptoms with the inventive drug products are also provided.

(56)

References Cited

FOREIGN PATENT DOCUMENTS

WO	WO 2006/089973	8/2006	A61K 9/28
WO	WO 2007/083073	7/2007	A61M 15/08
WO	2009/040595	4/2009	A61K 9/00
WO	WO 2012/026963	3/2012	A61M 15/00
WO	WO 2012/156317	11/2012	A61K 9/00
WO	WO 2013/128447	9/2013	A61M 15/08
WO	2014/016653	1/2014	A61K 31/485
WO	WO 2015/095644	6/2015	A61K 47/12
WO	WO 2015/136373	9/2015	A61K 31/485
WO	2016/007729	1/2016	A61K 9/00

OTHER PUBLICATIONS

Kundoor et al.; Pharm. Res. (2011) 28:189501904.*
 Makidon et al.; Journal of Aerosol Medicine and Pulmonary Drug Delivery; vol. 23, No. 2 (2010); pp. 77-89.*
 U.S. Patent Documents—None.*
 International Search Report (ISR), dated Sep. 2, 2015 in International Application No. PCT/IB2015/000941, 4 pgs.
 Krieter, P., et al. (2016) "Pharmacokinetic Properties and Human Use Characteristics of an FDA-Approved Intranasal Naloxone Product for the Treatment of Opioid Overdose." The Journal of Clinical Pharmacology, pp. 1-11.
 Aptar UnitDose and BiDose product information sheet, available at www.aptar.com/docs/pharmaprescription/uds-bds-datasheet.pdf, publication date unknown, last accessed Mar. 26, 2015.
 Ashton, H., et al., "Best evidence topic report. Intranasal naloxone in suspected opioid overdose.", Emerg. Med. J., 23(3):221-23 (published Mar. 2006).
 Bailey, A.M., et al., "Naloxone for opioid overdose prevention: pharmacists' role in community-based practice settings." Ann. Pharmacother, 48(5):601-06 (published May 2014).
 Barton, E.D. et al., "Intranasal administration of naloxone by paramedics." Prehosp. Emerg. Care, 6(1):54-58 (published Jan. 2002).
 Barton, E.D. et al., "Efficacy of intranasal naloxone as a needleless alternative for treatment of opioid overdose in the prehospital setting." J. Emerg. Med., 29(3):265-271 (published Oct. 2005).
 Beletsky, L. et al., "Physicians' Knowledge of and Willingness to Prescribe Naloxone to Reverse Accidental Opiate Overdose: Challenges and Opportunities." Journal of Urban Health: Bulletin of the New York Academy of Medicine, 84(1):126-136 (published 2006).
 Doe-Simkins, M. et al., "Saved by the nose: bystander-administered intranasal naloxone hydrochloride for opioid overdose." Am. J. Public Health, 99(5):788-791 (published May 2009).
 Dowling, J. et al., "Population pharmacokinetics of intravenous, intramuscular, and intranasal naloxone in human volunteers." Ther Drug Monit, 30(4):490-496 (published Aug. 2008).

Heard, C. et al., "Intranasal flumazenil and naloxone to reverse over-sedation in a child undergoing dental restorations." Paediatr. Anaesth., 19(8):795-99 (published Aug. 2009).
 Kelly, A.M. et al., "Intranasal naloxone for life threatening opioid toxicity." Emerg. Med. J., 19(4):375 (published Jul. 2002).
 Kelly, A.M. et al., "Randomised trial of intranasal versus intramuscular naloxone in prehospital treatment for suspected opioid overdose." Med. J. Aust. 182(1):24-27 (published Jan. 3, 2005).
 Kerr, D. et al., "Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose." Addiction 104(12):2067-2074 (Epub Nov. 9, 2009).
 Loimer, N. et al., "Nasal administration of naloxone for detection of opiate dependence." J. Psychiatr. Res., 26(1):39-43 (published Jan. 1992).
 Loimer, N. et al., "Nasal administration of naloxone is as effective as the intravenous route in opiate addicts." Int. J. Addict., 29(6):819-27 (published Apr. 1994).
 Merlin, M. A. et al., "Intranasal naloxone delivery is an alternative to intravenous naloxone for opioid overdoses." Am. J. Emerg. Med., 28(3):296-303 (Epub Jan. 28, 2010).
 Robertson, T. M., "Intranasal naloxone is a viable alternative to intravenous naloxone for prehospital narcotic overdose." Prehosp. Emerg. Care, 13(4):512-15 (Published Oct. 2009).
 Walley, A.Y., et al., "Opioid overdose prevention with intranasal naloxone among people who take methadone." J. Subst. Abuse Treat., 44(2):241-47 (Epub Sep. 12, 2012).
 Walley, A.Y., et al., "Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis." BMJ 346:f174, (Published Jan. 31, 2013).
 Weber, J. M. et al., "Can nebulized naloxone be used safely and effectively by emergency medical services for suspected opioid overdose?" Prehosp. Emerg. Care, 16(2):289-92 (Epub Dec. 22, 2011).
 Wermeling, D.P. et al., "Opioid harm reduction strategies: focus on expanded access to intranasal naloxone." Pharmacotherapy 30(7):627-31 (published 2010).
 Wermeling, D.P. et al., "A response to the opioid overdose epidemic: naloxone nasal spray." Drug Delivery Transl. Res., 3(1):63-74 (published Feb. 1, 2013).
 International Search Report (ISR) and Written Opinion (WO), dated Aug. 25, 2014 in International Application No. PCT/EP2014/064032 (WO 2015/000941) 11 pgs.
 Notice of Allowance and Fees Due, dated Oct. 9, 2015 in U.S. Appl. No. 14/659,472, 9 pgs.
 Corrected Notice of Allowance and Fees Due, dated Nov. 9, 2015 in U.S. Appl. No. 14/659,472, 9 pgs.
 TEVA Pharmaceuticals USA, Inc., "Notice of ANDA No. 209522 naloxone hydrochloride nasal spray, 4 mg/spray, with paragraph IV certification concerning U.S. Pat. No. 9,211,253", dated Sep. 13, 2016.

* cited by examiner

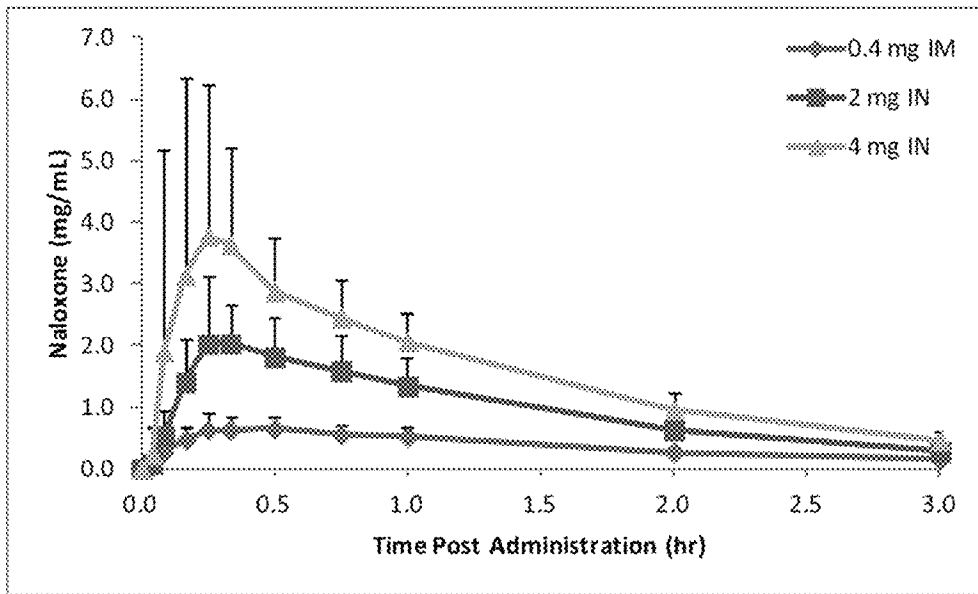


FIG. 1

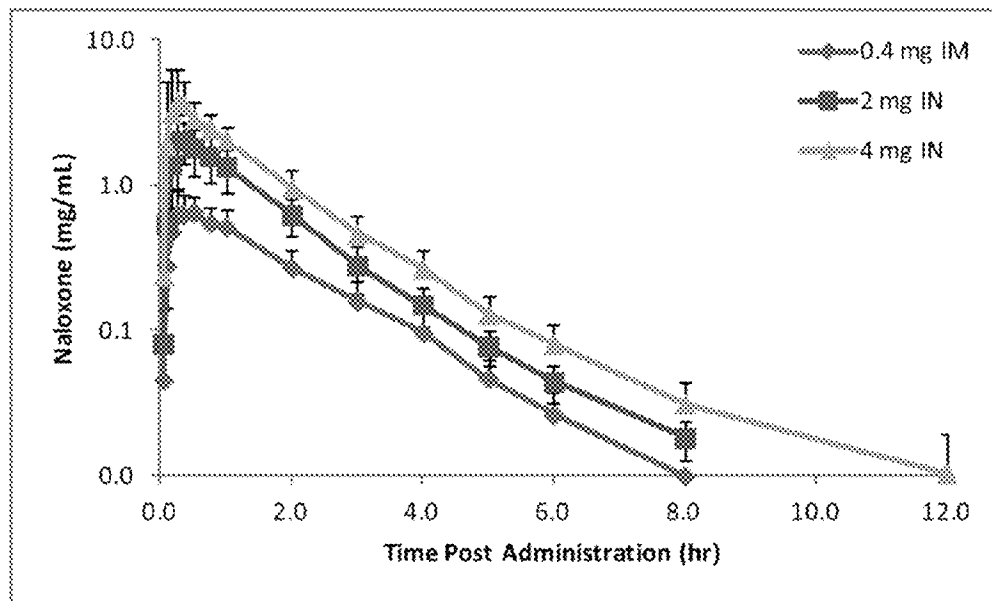


FIG. 2

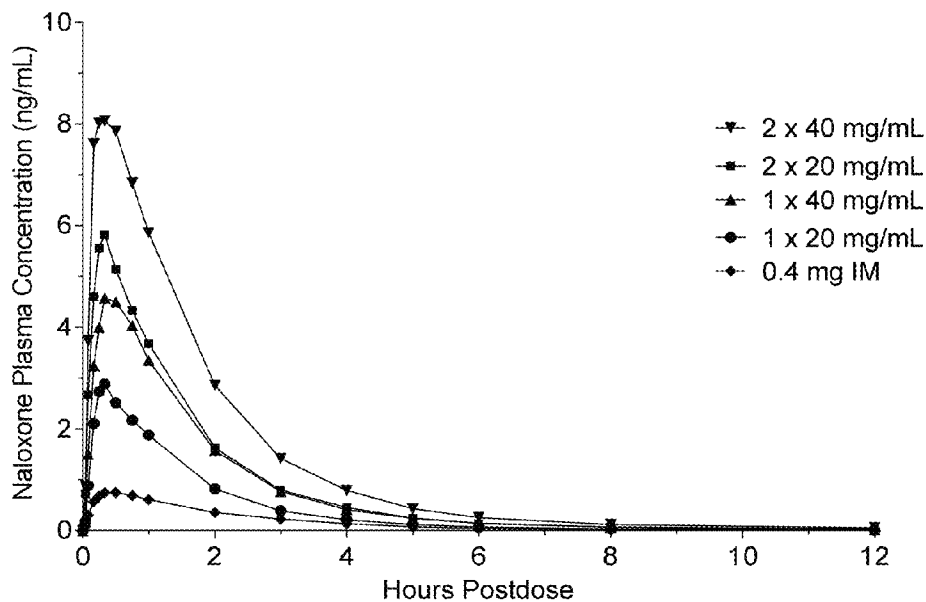


FIG. 3A

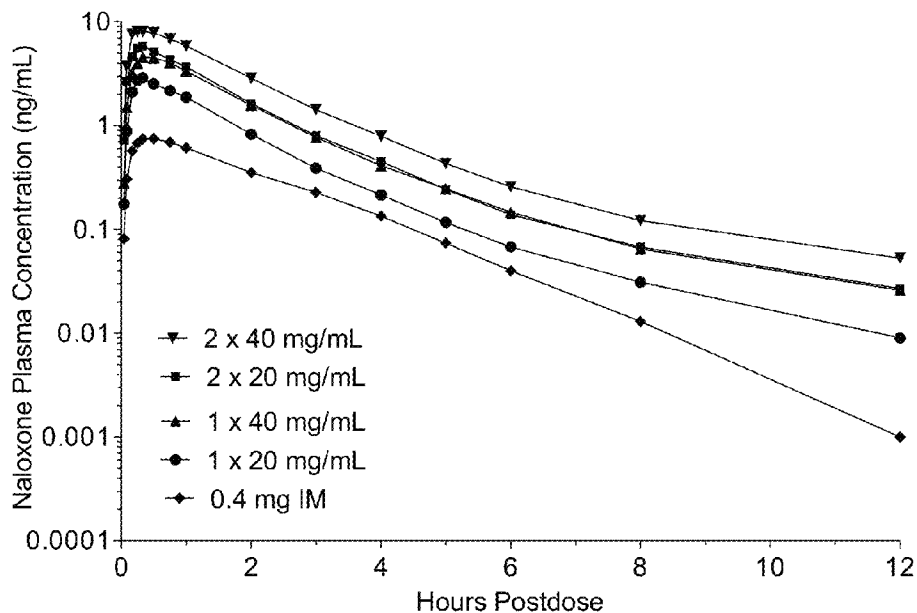


FIG. 3B

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.