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Crystal et al.

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(54) NASAL DRUG PRODUCTS AND METHODS OF THEIR USE

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> This patent is subject to a terminal disclaimer.

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- (60) Provisional application No. 61/953,379, filed on Mar. 14, 2014.

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(58) Field of Classification Search

See application file for complete search history.

(56)References Cited

U.S. PATENT DOCUMENTS

4,181,726	\mathbf{A}	1/1980	Bernstein
4,464,378	A	8/1984	Hussain
5,866,154	A	2/1999	Bahal et al.
9,192,570	B2 *	11/2015	Wyse A61K 9/0043
2003/0077300	A1	4/2003	Wermeling
2006/0120967	A1	6/2006	Namburi et al.
2009/0017102	A1	1/2009	Stinchcomb et al.
2010/0113495	A1	5/2010	Wermeling et al.
2010/0168147	A1	7/2010	Chapleo et al.
2010/0331354	A1	12/2010	Wermeling
2011/0046172	A1	2/2011	Chapleo et al.
2012/0270895	A1	10/2012	Wermeling
2013/0023825	A1	1/2013	Edwards et al.

6/2015 Wyse et al. 2015/0258019 A1 9/2015 Crystal et al. 2016/0008277 A1 1/2016 Crystal et al.

FOREIGN PATENT DOCUMENTS

CN	1575795	2/2005
EP	1681057 B1	8/2008
WO	WO 8203768 A1	11/1982
WO	WO 9830211 A1	7/1998
WO	WO 0062757 A1	10/2000
WO	WO 0074652 A1	12/2000
WO	WO 0158447 A1	8/2001
WO	WO 0182931 A1	11/2001
WO	WO 0211778 A1	2/2002
WO	WO 03084520 A2	10/2003
WO	WO 2004054511 A2	7/2004
WO	WO 2005020906 A2	3/2005
WO	WO 2006089973 A2	8/2006
WO	WO 2007083073 A1	7/2007
WO	WO 2009040595 A1	2/2009
WO	WO 2012026963 A2	3/2012
WO	WO 2012156317 A2	11/2012
WO	WO 2013128447 A1	9/2013
WO	WO 2014016653 A1	1/2014
WO	WO 2015095644 A1	6/2015
WO	WO 2015136373 A1	9/2015
WO	WO 2016007729 A1	1/2016

OTHER PUBLICATIONS

U.S. Appl. No. 14/942,344, filed Nov. 16, 2015, Crystal et al. 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).

Walley A Y et al., "Opioid overdose prevention with intranasal naloxone among people wno take methadone," J Subst Abuse Treat 44:2, 241-47 (Epub Sep. 12, 2012). 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,

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).

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, 2067-74 (Epub Nov. 9, 2009).

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).

(Continued)

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ABSTRACT (57)

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.

45 Claims, 7 Drawing Sheets



(56)References Cited

OTHER PUBLICATIONS

Doe-Simkins M et al., "Saved by the nose: bystander-administered intranasal naloxone hydrochloride for opioid overdose," Am J Public Health 99:5, 788-91 (published May 2009).

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).

Dowling J et al., "Population pharmacokinetics of intravenous, intramuscular, and intranasal naloxone in human volunteers," Ther Drug Monit 30:4 490-96 (published Aug. 2008).

Ashton H et al., "Best evidence topic report. Intranasal naloxone in suspected opioid overdose," Emerg Med J 23:3, 221-23 (published

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, 265-71 (published Oct. 2005).

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).

Kelly A M et al., "Intranasal naloxone for lite threatening opioid toxicity," Emerg Med J 19:4, 375 (published Jul. 2002).

Barton E D et al., "Intranasal administration of naloxone by paramedics," Prehosp Emerg Care 6:1, 54-58 (published Jan. 2002). 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).

Loimer N et al., "Nasal administration of naloxone for detection of opiate dependence," J Psychiatr Res 26:1, 39-43 (published Jan.

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).

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).

Wermeling D P et al., "Opioid harm reduction strategies: focus on expanded access to intranasal naloxone," Pharmacotherapy 30:7, 627-31, 2010.

Aptar UnitDose and BiDose product information sheet, available at www.aptar.com/docs/pharma-prescription/uds-bds-datasheet.pdf, publication date unknown, last accessed Mar. 26, 2015.

International Search Report and Written Opinion for Application

No. IB/2015/000941; Sep. 2, 2015, 11 pgs. Notice of Allowance, U.S. Appl. No. 14/659,472, Oct. 9, 2015, 9

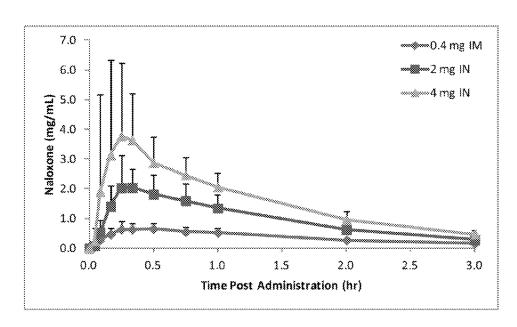
Corrected Notice Allowance, U.S. Appl. No. 14/659,472, Nov. 2015, 9 pgs

U.S. Appl. No. 15/183,441, filed Jun. 14, 2016, Keegan F. et al. Krieter P. et al., Pharmacokinetic Properties and Human Use Characteristics of an FDA Approved Intranasal Naloxone Product for the Treatment of Opioid Overdose, J Clin Pharmacol, 2016, pp. 1-11. International Search Report and Written Opinion for WO2016/ 007729, Dec. 4, 2015, 16 pages.

* cited by examiner

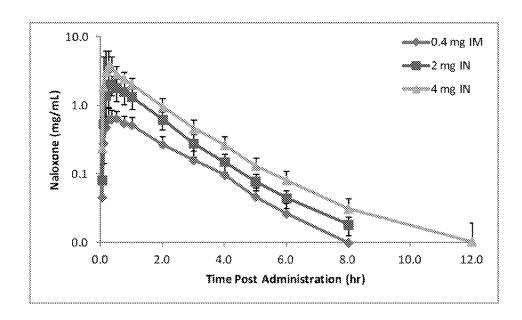


FIG. 1

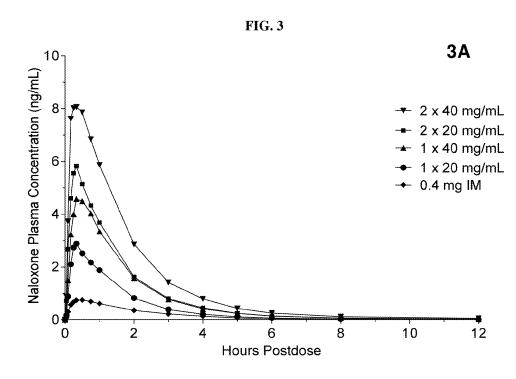


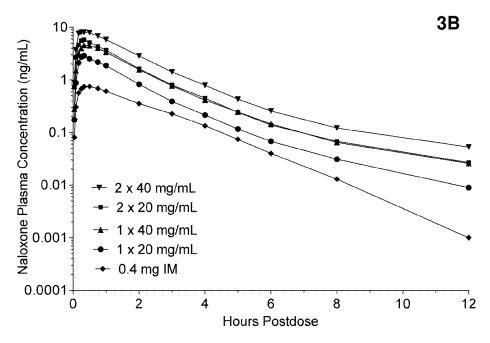
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FIG. 2



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