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

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(51) **Int. Cl.**
A61M 31/00 (2006.01)
A61M 5/00 (2006.01)
A61F 13/00 (2006.01)
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A61K 9/00 (2006.01)
A61K 31/485 (2006.01)
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A61M 11/02 (2006.01)
A61M 15/08 (2006.01)

(52) **U.S. Cl.**
 CPC *A61K 9/0043* (2013.01); *A61K 9/08* (2013.01); *A61K 31/485* (2013.01); *A61K 47/02* (2013.01); *A61K 47/183* (2013.01); *A61K 47/186* (2013.01); *A61M 11/02* (2013.01); *A61M 15/08* (2013.01); *A61M 31/00* (2013.01)

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

(56) **References Cited**
U.S. PATENT DOCUMENTS

4,181,726 A	1/1980	Bernstein
4,464,378 A	8/1984	Hussain
5,866,154 A	2/1999	Bahal et al.
2003/0073300 A1	4/2003	Wermeling
2006/0120967 A1	6/2006	Namburi 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.

FOREIGN PATENT DOCUMENTS

CN	1575795	2/2005	
EP	1681057 B1	8/2008	
GB	WO 2009/040595 A1 *	4/2009 A61K 9/0043
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	2007083073 A1	7/2007	
WO	WO 2012026963 A2	3/2012	
WO	WO 2012156317 A2	11/2012	
WO	WO 2013128447 A1	9/2013	
WO	2015095644 A1	6/2015	
WO	2015136373 A1	9/2015	

OTHER PUBLICATIONS

U.S. Patent Documents—None.*
 SciFinder search results; downloaded Sep. 25, 2015.*
 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 who 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, 2011).
 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).
 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 Mar. 2006).

(Continued)

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(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

OTHER PUBLICATIONS

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 life 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. 1992).

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.

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 pages.

* cited by examiner

FIGURE 1

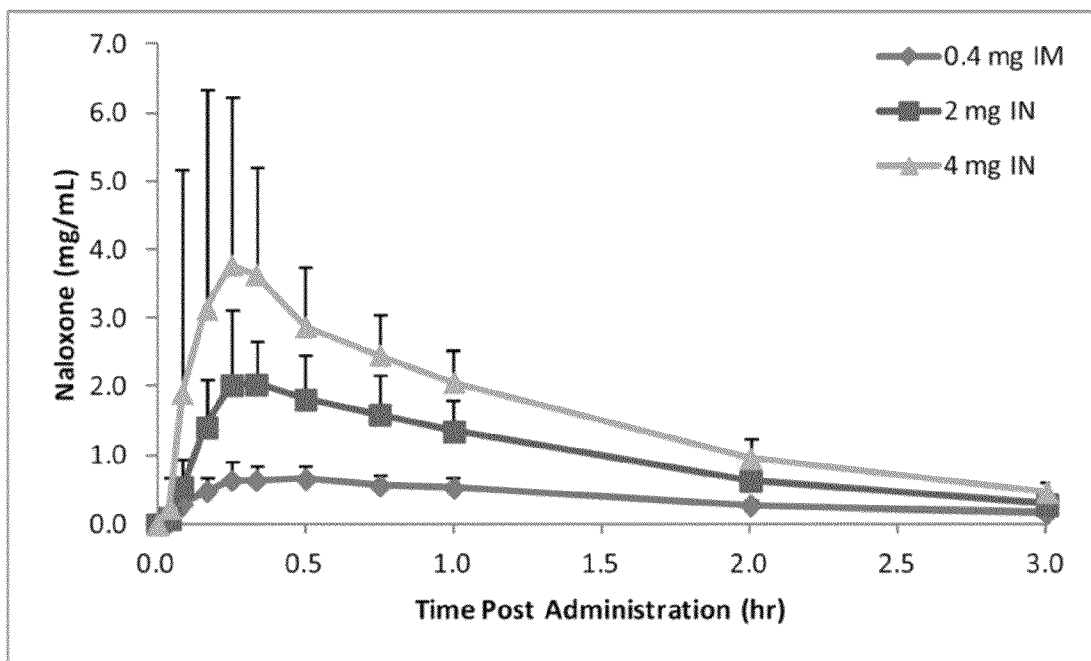


FIGURE 2

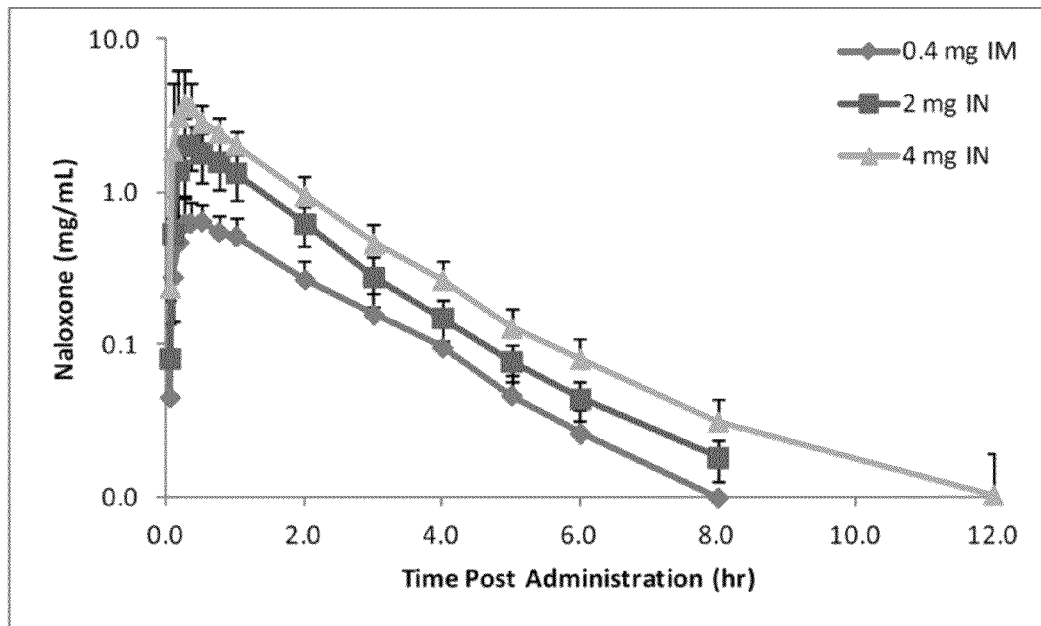


FIGURE 3

FIG. 3A

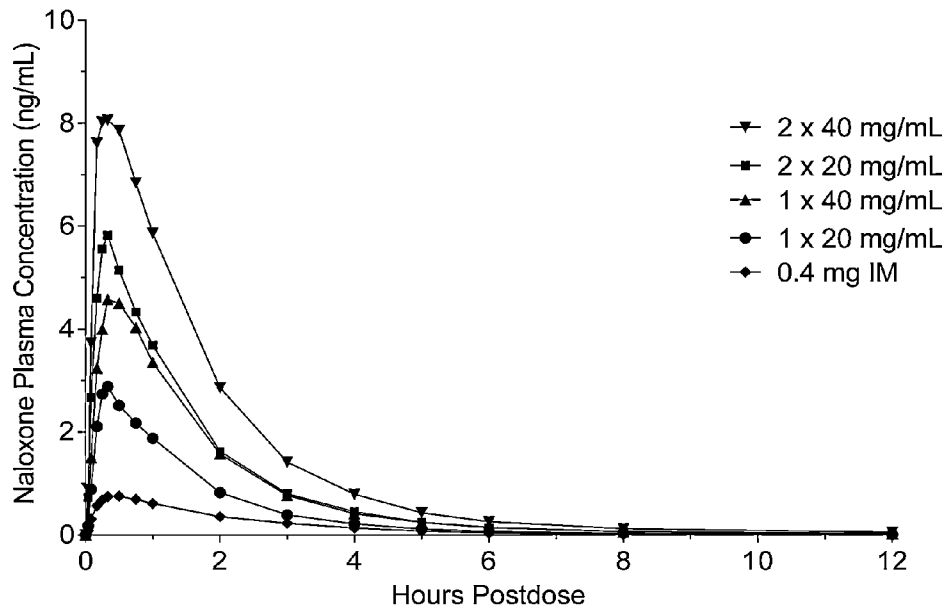
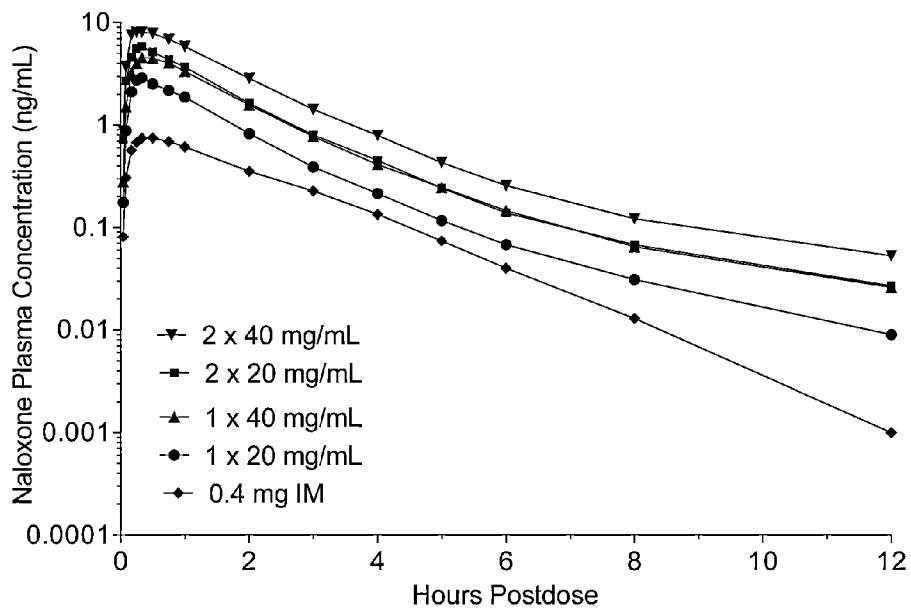


FIG. 3B



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