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**Crystal et al.**

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

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*A61K 9/00* (2006.01)  
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*A61K 47/18* (2006.01)  
*A61K 9/08* (2006.01)  
*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](http://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

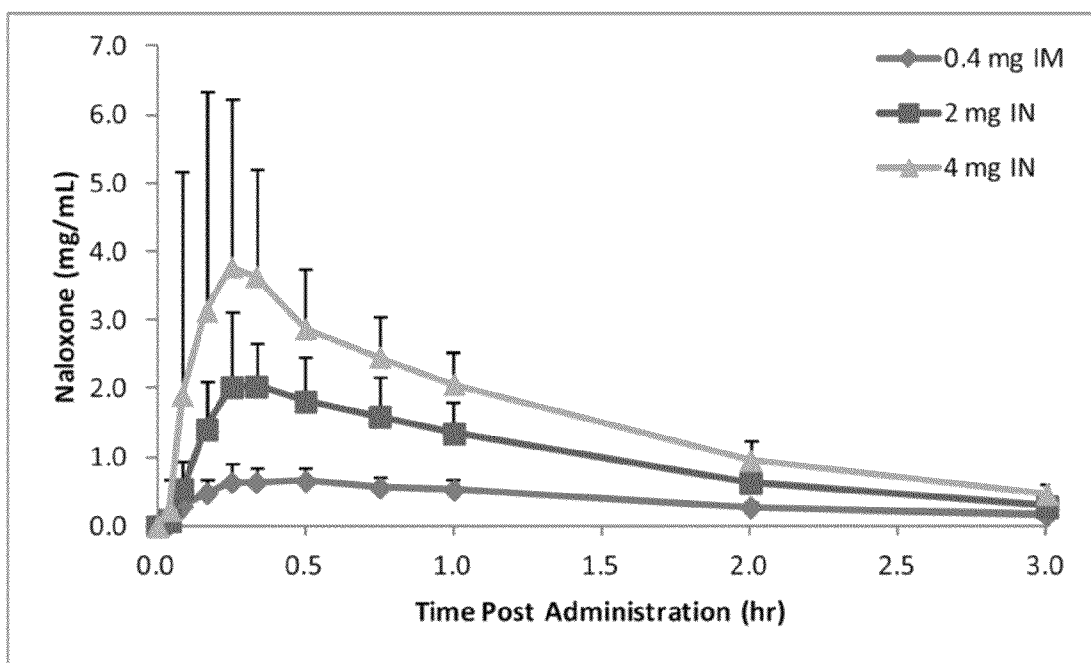


FIGURE 2

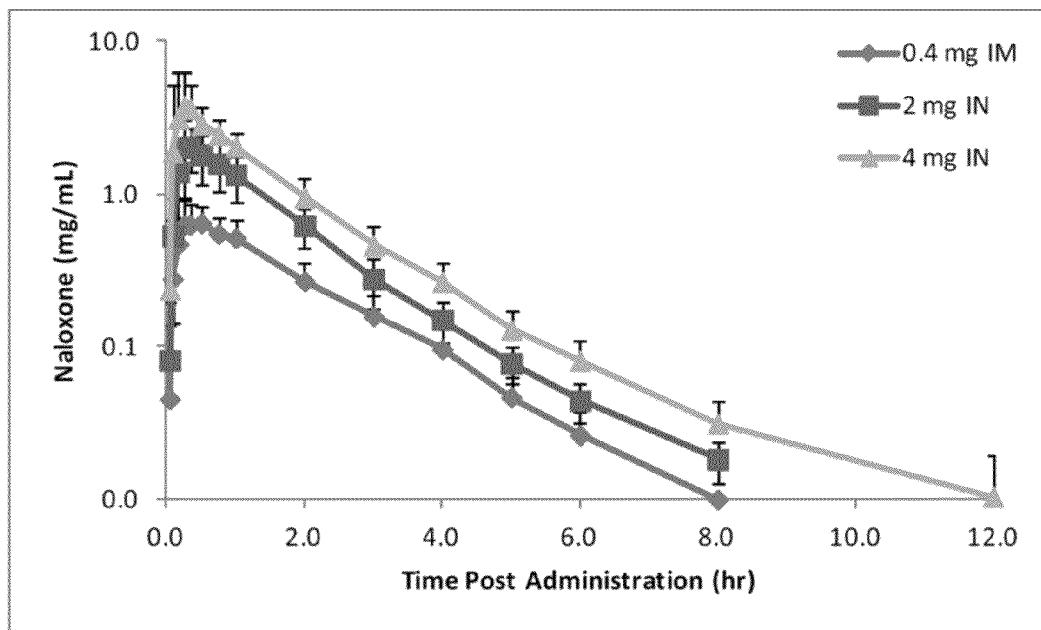


FIGURE 3

FIG. 3A

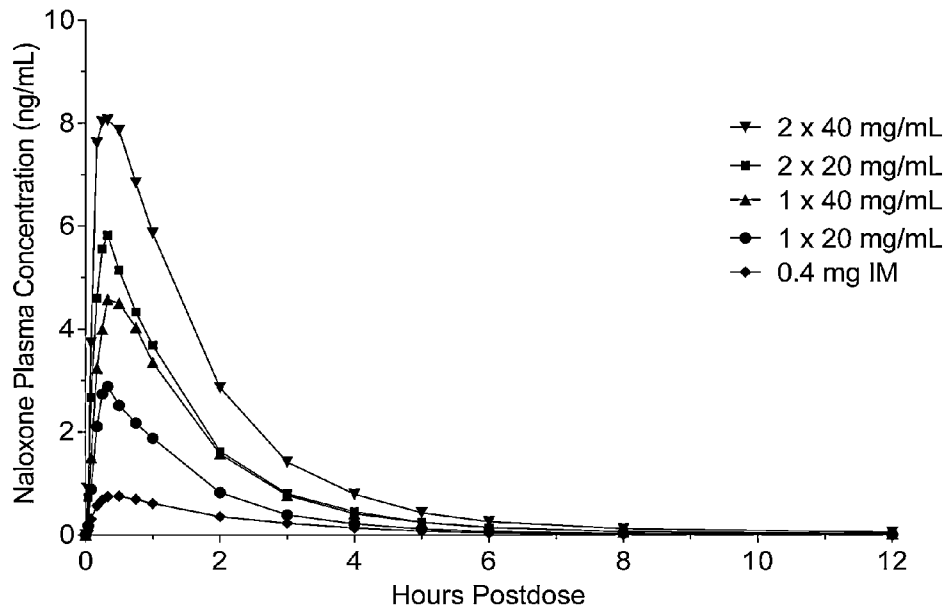
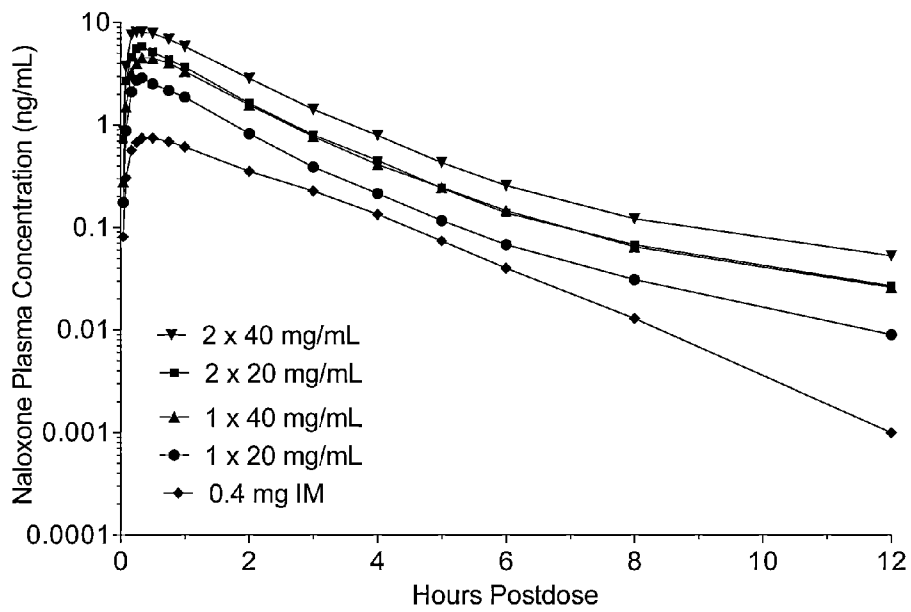


FIG. 3B



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