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Medication Use in the Neonatal Intensive Care Unit and Changes from 2010–2018

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Abstract

Objective: To provide up-to-date medication prescribing patterns in United States NICUs and to examine trends in prescribing patterns over time.

Study design: We performed a cohort study of 799,016 infants treated in NICUs managed by the Pediatrix Medical Group from 2010–2018. We used three different methods to report counts of medication: exposure, courses, and days of use. We defined the change in frequency of medication administration by absolute and relative change. We examined the FDA package insert for each medication to determine if a medication was labeled for use in infants and used Pubmed to search for pharmacokinetics (PK) studies.

Results: The most prescribed medications included: ampicillin, gentamicin, caffeine citrate, poractant alpha, morphine, vancomycin, furosemide, fentanyl, midazolam, and acetaminophen. Of the top 50 medications used in infants with extremely low birth weights (ELBW), only 20 (40%) are FDA labeled for use in infants; of those that are not labeled for use in infants, 13/30 (43%) had at least 2 published pharmacokinetic (PK) studies. Medications with the greatest relative increase in use from 2010 to 2018 included: dexmedetomidine, clonidine, rocuronium, levetiracetam, atropine, and diazoxide. Medications with the greatest relative decrease in use

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included: tromethamine (THAM) acetate, pancuronium, chloral hydrate, imipenem+cilastatin, and amikacin.

Conclusion: Trends of medication use in the NICU change substantially over time. It is imperative to identify changes in medication usage in the NICU to better inform further prospective studies.

The most commonly used medications in the neonatal intensive care unit (NICU) frequently change over time. Of great concern is that the majority of these medications are not labeled for use in infants, nor are they supported by robust clinical trial data, leaving many clinicians to rely on anecdotal or outdated information (1–3). Pharmacokinetics (PK) studies conducted in infants are difficult to perform, primarily due to issues with recruitment and obtaining consent, and required time and financial expense (1). Additionally, infants hospitalized in a NICU are more likely to meet exclusionary criteria in clinical trials for safety, dosing, and efficacy, as they often are born preterm with a greater likelihood of renal and/or hepatic dysfunction (4). Recent PK trials have begun to inform proper dosing on some medications, yet many of these drugs still have not undergone United States Food and Drug Administration (FDA) label changes, and NICUs have been slow to adopt such recommendations in dosing changes based on PK data alone (5–8).

Previous publications detailing trends in medication use in the NICU were described through 2010 (4, 9). However, medication use in the NICU changes frequently, secondary to evolving clinical trial data, FDA label changes, changes in disease treatment, concerns regarding medication safety, and medication shortages. It is important to recognize that changes in medication usage are not always a reflection of updated safety and efficacy data or on FDA approval. Clinicians must stay abreast with the most current data regarding medication use. Thus, the objectives of this study were to provide the most up-to-date prescribing patterns amongst NICUs; to identify trends in prescribing patterns over time, and to compare to previously published data.

Methods

We performed a cohort study including a total of 363 NICUs from the Pediatrix Medical Group from 2010 to 2018. The Pediatrix Medical Group manages a prospective database that collects information from daily progress notes written by clinicians, which is then de-identified and compliant with the Health Insurance Portability and Accountability Act of 1996. To facilitate comparison with previous reports, vitamins (except vitamin A), nutritional supplements, vaccines, eye drops, and topical medications were excluded (4, 9). This study was approved by the Duke Institutional Review Board with a waiver of informed consent.

Definitions

We used three different methods to report counts of medication usage. Exposure was defined as the number of unique medication names reported for each infant. Total medication courses was defined as the number of times a unique medication name was reported in the database. Days of use was defined as the total number of days each medication

was administered throughout the entire database. Figure 1 (online only) shows example calculations for exposure, total medication courses, and days of use. Separate calculations were performed for extremely low birth weight (ELBW, <1000g birth weight) infants.

We examined the FDA package insert for each medication. A medication was deemed "labeled for use" if dosing recommendations that specifically mentioned infants were listed. If a medication was listed as labeled for use for infants of a specific month of age and older, it was not considered labeled for use within the context of our study. For example, if the package insert specifically stated "safety and effectiveness of medication X have been approved in pediatric patients age 2 months and older," it was not considered labeled for use for our population. PK studies were identified through PubMed search of keywords including the drug name and "pharmacokinetics".

Statistical Analysis

We described the change in frequency of medication administration between 2010 and 2018 by absolute and relative change. We calculated the relative increase in medication use for medications with greater than 1/1,000 exposures in 2018 and the relative decrease in medication use for medications with greater than 1/1000 exposures in 2010. Calculations were repeated separately for infants with ELBW. Analyses were conducted using Stata 16.1 (College Station, TX).

Results

Our study included 799,016 infants, of which 43,102 (5%) were born with ELBW (Table 1, online). The median gestational age (GA) was 36 weeks (25^{th}-75^{th} percentile: 34–39 weeks) and median birth weight was 2640 g (25^{th}-75^{th} percentile: 1950– 3301 g). The median length of hospitalization was 9 days (25^{th}-75^{th} percentile: 4–20 days) with a 1.8% mortality.

We identified 2,575,536 unique medication courses for 276 medications, of which 631,144 (25%) of those courses were unique to infants with ELBW. The median number of medication courses per infant was 2 (25^{th}-75^{th} percentile: 0–3), and the number of unique medications per infant was 2 (25^{th}-75^{th} percentile: 0–3). For infants with ELBW specifically, the median number of medication courses was 11 (25^{th}-75^{th} percentile: 6–19), and the number of unique medications per infant was 9 (25^{th}-75^{th} percentile: 5–14).

The 10 most common medications by exposure for the entire cohort included: ampicillin, gentamicin, caffeine citrate, poractant alfa, morphine, vancomycin, furosemide, fentanyl, midazolam, and acetaminophen (Table 2). The 10 most common medications by exposure for infants with ELBW included: gentamicin, ampicillin, caffeine citrate, vancomycin, poractant alfa, furosemide, dopamine, fluconazole, fentanyl, and indomethacin (Table 3). Of the top 50 medications used in infants with ELBW from 2010 to 2018, only 20 (40%) were FDA approved. Of those medications that did not have FDA approval, 13/30 (43%) had at least 2 published PK studies. Of the 14 medications to which >20% of infants with ELBW were exposed, only 50% were FDA approved. Ninety-four percent of infants with ELBW were exposed to a medication that did not have FDA approval.

Medication Increases between 2010 and 2018

The medications with the greatest absolute increase based on total exposures between 2010 and 2018 included: poractant alfa, morphine, erythromycin, glucose gel, simethicone, budesonide, clonidine, acetaminophen, and dexmedetomidine (Table 4). Notably, poractant alfa showed the greatest absolute increase in both the entirety of our cohort as well as the ELBW cohort (Table 5, online). The medications with the greatest relative increase based on total exposures between 2010 and 2018 included: dexmedetomidine, clonidine, rocuronium, levetiracetam, atropine, diazoxide, vasopressin/desmopressin, glycopyrrolate, simethicone, and glucagon (Table 6). Dexmedetomidine showed the greatest relative increase in both cohorts (Table 7, online). Four of the top 20 (20%) medications that showed the greatest absolute increase from 2010 to 2018 were FDA approved, whereas 4/20 (20%) of medications that showed the greatest relative increase during this same time were FDA approved.

Medication Decreases between 2010 and 2018

The medications with the greatest absolute decrease based on total exposures between 2010 and 2018 included: ampicillin, gentamicin, beractant, vancomycin, calfactant, furosemide, cefotaxime, ranitidine, fentanyl, and midazolam (Table 8, online). Medications also showing the greatest absolute decrease based on total exposures in infants with ELBW included: beractant, vancomycin, calfactant, cefotaxime, ranitidine, and ampicillin (Table 9, online). Notably, although ampicillin and gentamicin were ranked number 1 and 2, respectively, in medication exposure and ranked number 2 and 1 in medication exposure for infants with ELBW, they were also the top two medications that showed the greatest absolute decrease. The medications with the greatest relative decrease based on total exposures between 2010 and 2018 included: tromethamine (THAM) acetate, pancuronium, chloral hydrate, imipenem+cilastatin, amikacin, metoclopramide, pentobarbital, beractant, vitamin A and diazepam (Table 10, online). Medications with the greatest relative decrease in infants with ELBW between 2010 and 2018 included: ticarcillin/ticarcillin+clavulanate, cimetidine, antacids, ammonium chloride, and flucytosine (Table 11, online).

Discussion

The medications used in the NICU change frequently over time. Notably, half of these medications (ampicillin, gentamicin, caffeine citrate, furosemide, and vancomycin) have remained in the top 10 most common medications since the initial study starting in 1996, whereas 7 (gentamicin, ampicillin, caffeine citrate, furosemide, vancomycin, fentanyl, and midazolam) have remained since the follow-up study starting in 2005 (4, 9). Of the 10 most common medications by exposure for infants with ELBW (Table 3), 8 have remained in the top 10 since 2005 (4).

Of concern is the continued use of medications that are not labeled for use in infants (4, 8, 9). Our study identified that only 40% of medications used in infants with ELBW are FDA approved, slightly improved from 2005–2010 when 35% of medications were approved in this population. In the current study, 94% of infants with ELBW were exposed to a medication that was not labeled for use in infants (4). However, our definition of

labeled for use was necessarily broad and unable to account for differences in approval for specific indications or of specific gestational ages but not others; thus, the percentage of FDA-approved drugs in the ELBW population is likely lower than our estimate. Nearly all infants admitted to the NICU receive at least one medication that is unlicensed or used off label, and it is estimated that >70% of infants in the NICU are exposed to drug-drug interactions (1, 3, 10). Off-label usage exposes infants to many risks including over-dosing and thus increasing the risk of adverse reactions or under-dosing, thus leading to ineffective treatment (11). Clinicians may be unaware that they are prescribing a medication that does not have FDA labeling. Without such labeling, clinicians may rely on reference guidelines based largely on adult and adolescent data that often do not account for variations in medication absorption, metabolism, and excretion of infants, or references databases that may not use the most up to date PK trial data (5, 8, 12–15). The FDA Modernization Act of 1997, which was extended in 2002 as the Best Pharmaceuticals for Children Act, attempted to bridge this gap by creating incentives such as exclusive marketing and patent extension for pharmaceutical companies to test medications in children; the 2003 Pediatric Research Equity Act requires new drug applications to submit dosing data in pediatric populations (15, 16). However, the process can be costly and time-consuming, and often approval for a new indication does not offset the cost of obtaining said approval, thus leaving pharmaceutical companies with little financial incentive to pursue such an endeavor (16). Lack of FDA approval for the majority of the most common medications used in infants is a public health concern.

Previous research has demonstrated publishing of PK studies has the potential to increase adherence to PK-based dosing in the neonatal population (8). Dexmedetomidine, a medication previously not within the top 100 medications used from 2005 to 2010, ranked as the medication with the greatest relative increase (9^{th} greatest absolute increase) and the 90^{th} most common medication used in the NICU from 2010 to 2018 (4). Although not currently labeled for use in infants, recently published PK studies support a low adverse effect profile, particularly with infants undergoing cardiopulmonary bypass (17–19). It is likely, given its supporting PK studies and advantageous safety profile in term infants, that dexmedetomidine will continue to be a common medication used in the NICU. However, there remains a lack of robust safety and efficacy data for infants exposed to dexmedetomidine, particularly those with ELBW.

Despite the lack of supporting data for many medications used in the NICU, well-designed studies of the different brands of medications such as surfactant are likely responsible for the changes in usage (20–23). Poractant alfa showed the greatest absolute increase of medications used in the NICU and was ranked as the fourth most common medication from 2010 to 2018. It was ranked as the fifth most common medication and the greatest absolute increase in infants with ELBW. A recent prospective trial of surfactants showed repeated dosing, increased FiO_2 requirements, and decreased PaO_2 values in the calfactant group compared with the poractant alfa and beractant groups (22). However, no differences were seen in prevention of combined outcomes such as air leak syndromes, including pneumothorax and pulmonary interstitial emphysema, BPD and death, and death (23). It is possible that although poractant alfa has not been shown to have a long-term benefit over

calfactant and beractant, clinicians prefer its use due to its more immediate and tangible effects.

Medication usage trends often follow trends in diseases of the neonate. Neonatal opioid withdrawal syndrome has become a rapidly increasing issue within NICUs nationally, with its incidence increasing more than five-fold from 2004 to 2014 in Medicaid-covered births and from 3.4 to 5.8 per 1000 hospital births from 2009 to 2012 (24, 25). Clonidine, a medication not noted in the previous study, is now one of the most commonly used drugs in the NICU (rank 66th) (4). Morphine also demonstrated an increase (second greatest absolute increase in medication use). Notably, neither morphine nor clonidine is FDA approved for use in infants. Although there is no consensus as to the best medication for neonatal opioid withdrawal syndrome following a failed non-pharmacotherapeutic intervention, there is concern for potential developmental harm with additional opiate exposure during the period of rapid brain development (26). Clonidine, as adjunctive therapy, has been shown to decrease the number of morphine doses and decrease the duration of treatment in term infants exposed to methadone or heroin with neonatal opioid withdrawal syndrome (27). A recent trial of monotherapy with clonidine versus morphine showed a decrease in treatment duration (39 versus 28 days, p=0.02), a decreased height of arousal and excitability during treatment, and no differences in cognitive, motor or language outcomes at one year of age (26).

The introduction of new research regarding the treatment of common neonatal problems similarly dictates medication usage in the NICU. Although gentamicin and ampicillin continued to hold the ranking for the first and second most commonly used medications in the NICU both from 2005 to 2010 and from 2010 to 2018 (ranked first and second, respectively, for the top medications used in infants with ELBW), both were listed as the two top medications that experienced the greatest absolute decrease from 2010 to 2018 (4). This is likely related to the publication of a risk-stratifying algorithm for early-onset sepsis in infants of >35 weeks GA in which empiric antibiotic administration within the first 24 hours after birth with no statistically significant differences seen in culture-confirmed early-onset sepsis or readmission (28–31). Quality improvement initiatives at additional sites have already demonstrated a decrease in antibiotic exposure after implementation of the algorithm (32). Implementation of this risk-stratification to hospitals outside of the initial study group may be responsible for the overall decrease seen in the usage of ampicillin and gentamicin.

Although the introduction of new research can dictate medication trends in the NICU, some medications are more frequently used without any supporting data or data with mixed results. For example, simethicone, a medication that has very little data supporting its use, particularly in the neonatal population, was ranked as the 5th greatest absolute increase and 9th greatest relative increase from 2010 to 2018 and 28th overall for most used medications. However, multiple studies have shown that it is no more effective than a placebo and its use in premature infants is scarce (33, 34). Comparatively, early inhaled budesonide usage in extremely premature infants shows promise in decreasing the incidence of bronchopulmonary dysplasia, however these infants showed increased overall mortality

(35, 36). Nonetheless, budesonide usage increased amongst both the entirety of our cohort and infants with ELBW.

Strengths of this study include a large, representative cohort spanning many NICUs across the country as well as daily documentation of medication usage, but there were also limitations. The Pediatrix Medical Group is a prospectively collected database that is not subject to independent monitoring. Additionally, the database does not include the indications for medication usage, which may provide more in-depth information as to why certain medications experience an increase or decrease in usage. Lastly, our method of counting and threshold of >1/1000 exposures may have led us to rank more highly large relative increases or decreases in the usage of medications that are rarely used overall.

We identified the most commonly used medications in the NICU, particularly amongst infants with ELBW, how medication usage has changed over time, and how such changes may be related to ongoing medication research. Safe prescribing of medications, as directed by guidelines, PK, safety and efficacy studies, and FDA label changes, should remain a priority focus within neonatal research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 2:

Medications Most Commonly Used in the NICU Ranked by Exposure

Rank	Medication	Exposure[a]	Courses[a]	Days of Use[a]
1	Ampicillin	582	602	2266
2	Gentamicin	579	649	2452
3	Caffeine citrate	153	191	4221
4	Poractant alfa	89	100	100
5	Morphine	68	82	814
6	Vancomycin	61	93	502
7	Furosemide	58	118	389
8	Fentanyl	56	69	453
9	Midazolam	47	55	421
10	Acetaminophen	42	49	274
11	Dopamine	40	48	164
12	Calfactant	34	40	39
13	Beractant	30	34	34
14	Phenobarbital	27	34	218
15	Fluconazole	27	31	411
16	Erythromycin	26	27	78
17	Hydrocortisone	23	30	241
18	Indomethacin	22	28	66
19	Lorazepam	22	25	262
20	Cefotaxime	22	25	138
21	Albuterol	19	24	366
22	Ranitidine	18	21	144
23	Acyclovir	17	18	75
24	Dexamethasone	16	23	141
25	Epoietin alpha	14	18	296
26	Nitric oxide	14	15	86
27	Tobramycin	13	18	93
28	Simethicone	12	13	103
29	Piperacillin-tazobactam	12	16	96
30	Epinephrine	12	13	18
31	Nystatin oral	11	12	97
32	Alprostadil	11	11	20
33	Ursodeoxycholic acid	10	12	178
34	Cefazolin	10	12	36
35	Budesonide	10	12	222
36	Dobutamine	10	10	28

Rank	Medication	Exposure[a]	Courses[a]	Days of Use[a]
37	Chlorothiazide	10	12	157
38	Clindamycin	9	11	62
39	Insulin	9	11	33
40	Metronidazole	9	11	69
41	Lansoprazole	9	10	55
42	Vecuronium	9	10	29
43	Nafcillin	8	10	49
44	Spironolactone	8	10	136
45	Meropenem	8	10	80
46	Palivizumab	8	8	8
47	Amoxicillin	8	8	43
48	Methadone	8	9	122
49	Ceftazidime	8	9	56
50	Cefepime	7	9	56
51	Clotrimazole	7	7	39
52	Fluticasone	6	7	113
53	Phenylephrine	6	7	24
54	Oxacillin	6	7	34
55	Ibuprofen	6	8	23
56	Vitamin-A	6	6	135
57	Epinephrine - racemic	5	6	16
58	Famotidine	5	6	49
59	Penicillin G	5	5	39
60	Levothyroxine	4	5	68
61	Cholestyramine	4	4	27
62	Milrinone	4	4	21
63	Metoclopromide	4	5	40
64	Propranolol	4	4	13
65	Levetiracetam	4	4	15
66	Clonidine	4	4	79
67	Omeprazole	4	4	25
68	Prednisone	4	5	44
69	Aminophylline	4	4	40
70	Amikacin	3	4	21
71	Amphotericin B deoxycholate	3	3	26
72	Hyaluronidase	3	3	3
73	Hydrochlorothiazide	3	3	44
74	Naloxone	3	3	3
75	Beclomethasone	3	3	47

Rank	Medication	Exposure[a]	Courses[a]	Days of Use[a]
76	Sildenafil	3	3	30
77	Digoxin	3	3	11
78	Filgrastim	2	3	7
79	Aluminum/Magnesium Hydroxide	2	2	14
80	Cephalexin	2	2	11
81	Ceftriaxone	2	2	5
82	Dornase Alpha	2	3	18
83	Zidovudine	2	2	12
84	Adenosine	2	2	3
85	Sucralfate	2	2	13
86	Cefoxitin	2	2	5
87	Bumetanide	2	2	10
88	Azithromycin	2	2	10
89	Acetazolamide	2	3	14
90	Dexmedetomidine	2	2	16
91	Atropine	2	2	2
92	Heparin	2	2	14
93	Chloral hydrate	1	2	7
94	Pentobarbital	1	2	13
95	Linezolid	1	2	12
96	Rifampin	1	1	12
97	Hydralazine	1	1	14
98	Captopril	1	1	9
99	Diazoxide	1	1	7
100	Enalapril	1	1	8

[a]Units for exposure, courses, and days of use, per 1000 infants.

Table 3:

Medications Most Commonly Used in the NICU for ELBW Infants Ranked by Exposure

Rank	Medication	Exposure[a]	Courses[a]	Days of Use[a]	FDA Label for Use
1	Gentamicin	897	1613	7392	Yes
2	Ampicillin	872	1032	4466	Yes
3	Caffeine citrate	866	1135	38051	Yes
4	Vancomycin	480	905	4987	Yes
5	Poractant alfa	460	556	562	Yes
6	Furosemide	455	1238	4366	No
7	Dopamine	351	488	1748	No
8	Fluconazole	321	380	5654	No
9	Fentanyl	302	439	4329	No
10	Indomethacin	297	381	900	Yes
11	Hydrocortisone	237	342	3252	No
12	Morphine	222	324	3426	No
13	Midazolam	209	292	3656	Yes
14	Albuterol	203	282	5170	No
15	Calfactant	188	240	235	Yes
16	Dexamethasone	182	292	2051	No
17	Acetaminophen	166	214	1102	Yes
18	Beractant	159	189	192	Yes
19	Budesonide	131	159	3390	No
20	Insulin	127	162	505	No
21	Cefotaxime	126	167	1023	Yes
22	Chlorothiazide	113	152	2203	No
23	Lorazepam	108	141	2448	No
24	Epinephrine	105	117	161	No
25	Phenobarbital	100	133	1808	No
26	Spironolactone	99	130	1938	No
27	Epoietin alpha	98	134	2799	No
28	Piperacillin-tazobactam	96	135	848	No
29	Ursodeoxycholic acid	94	121	2421	No
30	Ranitidine	88	112	991	No
31	Tobramycin	85	149	912	Yes
32	Dobutamine	80	92	245	No
33	Meropenem	78	107	857	Yes
34	Nitric oxide	77	92	729	No
35	Nafcillin	75	102	522	No
36	Ceftazidime	74	97	610	Yes

Rank	Medication	Exposure[a]	Courses[a]	Days of Use[a]	FDA Label for Use
37	Fluticasone	73	93	1635	No
38	Metronidazole	70	88	538	No
39	Vitamin-A	69	71	1788	No
40	Ibuprofen	67	95	281	Yes
41	Clindamycin	64	74	443	Yes
42	Cefepime	63	81	545	No
43	Cefazolin	61	72	224	No
44	Erythromycin	57	65	531	Yes
45	Vecuronium	55	74	232	No
46	Oxacillin	51	68	335	Yes
47	Lansoprazole	47	53	446	No
48	Levothyroxine	46	50	1063	Yes
49	Nystatin oral	44	48	678	Yes
50	Prednisone	43	58	601	No

[a]Units for exposure, courses, and days of use, per 1000 infants.

NICU = neonatal intensive care unit; ELBW = extremely low birthweight FDA = Federal Drug Administration

Table 4:

Greatest Absolute Increase in Exposure Between 2010 and 2018

Rank	Medication	Exposure Increase[a]	Exposure in 2010[a]	Exposure in 2018[a]	FDA Label for Use
1	Poractant alfa	45.0	63.4	108.4	Yes
2	Morphine	19.7	53.7	73.4	No
3	Erythromycin	9.8	24.1	33.9	Yes
4	Glucose gel	8.8	0.0	8.8	No
5	Simethicone	8.4	7.5	15.9	No
6	Budesonide	6.8	7.5	14.3	No
7	Clonidine	6.3	0.4	6.7	No
8	Acetaminophen	5.3	40.9	46.2	Yes
9	Dexmedetomidine	5.0	0.1	5.1	No
10	Fluconazole	4.7	20.8	25.5	No
11	Levetiracetam	4.7	1.7	6.4	No
12	Hydrocortisone	4.5	21.6	26.1	No
13	Cefepime	4.1	7.9	12.0	No
14	Cefazolin	2.9	8.4	11.3	No
15	Cholestyramine	1.9	3.4	5.3	No
16	Atropine	1.7	0.9	2.6	No
17	Rocuronium	1.4	0.2	1.6	No
18	Penicillin G	1.3	4.7	6.0	No
19	Ceftriaxone	1.2	1.3	2.5	Yes
20	Dexamethasone	1.1	15.7	16.8	No

[a]Per 1000 infants

FDA = Federal Drug Administration

Table 6:

Greatest Relative Increase in Exposure Between 2010 and 2018

Rank	Medication	% Change	Exposure (2010)[a]	Exposure (2018)[a]	FDA Label for Use
1	Dexmedetomidine	5000	0.1	5.1	No
2	Clonidine	1575	0.4	6.7	No
3	Rocuronium	700	0.2	1.6	No
4	Levetiracetam	276	1.7	6.4	No
5	Atropine	189	0.9	2.6	No
6	Diazoxide	150	0.6	1.5	Yes
7	Vasopressin/Desmopressin	140	0.5	1.2	No
8	Glycopyrrolate	120	0.5	1.1	No
9	Simethicone	112	7.5	15.9	No
10	Glucagon	100	0.5	1.0	No
11	Ceftriaxone	92	1.3	2.5	Yes
12	Budesonide	91	7.5	14.3	No
13	Sucralfate	71	1.4	2.4	No
14	Poractant alfa	71	63.4	108.4	Yes
15	Ampicillin-sulbactam	57	0.7	1.1	No
16	Cholestyramine	56	3.4	5.3	No
17	Cefepime	52	7.9	12.0	No
18	Ganciclovir	43	0.7	1.0	No
19	Erythromycin	41	24.1	33.9	Yes
20	Magnesium sulfate	38	0.8	1.1	No

[a]Per 1,000 infants

FDA = Federal Drug Administration