

Rocuronium Bromide Injection

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use rocuronium bromide safely and effectively. See full prescribing information for rocuronium bromide.
Rocuronium bromide injection solution for intravenous use.
Initial U.S. Approval: 1994

| RECENT MAJOR CHANGES | |
|---|--------|
| Dosage and Administration, Dosage in Specific Populations (2.5) | 8/2008 |
| Warnings and Precautions, Residual Paralysis (5.4) | 8/2008 |
| Long-term Use in an Intensive Care Unit (5.5) | 8/2008 |
| QT Interval Prolongation (5.8) | 8/2008 |

INDICATIONS AND USAGE
Rocuronium bromide is a nondepolarizing neuromuscular blocking agent indicated as an adjunct to general anesthesia to facilitate both rapid sequence and routine tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation. (1)

DOSE AND ADMINISTRATION
To be administered only by experienced clinicians and adequately trained individuals supervised by an experienced clinician familiar with the use, actions, characteristics, and complications of neuromuscular blocking agents. (2)

- Individualize the dose for each patient. (2)
- Peripheral nerve stimulator recommended for determination of drug response and need for additional doses, and to evaluate recovery. (2)
- **Tracheal intubation:** Recommended initial dose is 0.6 mg/kg (2.1)
- **Rapid sequence intubation:** 0.6 to 1.2 mg/kg (2.2)
- **Maintenance doses:** Guided by response to prior dose, not administered until recovery is evident. (2.3)
- **Continuous infusion:** Initial rate of 10 to 12 mcg/kg/min. Start only after early evidence of spontaneous recovery from an intubating dose. (2.4)

DOSE FORMS AND STRENGTHS

- 5 mL multiple dose vials containing 50 mg rocuronium bromide injection (10 mg/mL) (3)
- 10 mL multiple dose vials containing 100 mg rocuronium bromide injection (10 mg/mL) (3)

CONTRAINDICATIONS

- Hypersensitivity (e.g., anaphylaxis) to rocuronium bromide or other neuromuscular blocking agents (4)

WARNINGS AND PRECAUTIONS

- Appropriate Administration and Monitoring: Use only if facilities for intubation, mechanical ventilation, oxygen therapy, and an antagonist are immediately available. (5.1)
- Anaphylaxis: Severe anaphylaxis has been reported. Consider cross-reactivity among neuromuscular blocking agents. (5.2)
- Need for Adequate Anesthesia: Must be accompanied by adequate anesthesia or sedation. (5.3)
- Residual Paralysis: Consider using a reversal agent in cases where residual paralysis is more likely to occur. (5.4)

ADVERSE REACTIONS

- Most common adverse reactions (2%) are transient hypotension and hypertension. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact TEVA USA, PHARMACOVIGILANCE at 1-888-838-2872 x 6351 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Succinylcholine: Use before succinylcholine has not been studied. (7.11)
- Nondepolarizing muscle relaxants: Interactions have been observed. (7.7)
- Enhanced rocuronium bromide activity possible: Inhalation anesthetics (7.3), certain antibiotics (7.1), quinidine (7.10), magnesium (7.6), lithium (7.4), local anesthetics (7.5), procainamide (7.8)
- Reduced rocuronium bromide activity possible: Anticonvulsants (7.2)

USE IN SPECIFIC POPULATIONS

- Labor and Delivery: Not recommended for rapid sequence induction in patients undergoing Cesarean section. (8.2)
- Not recommended for rapid sequence intubation in pediatric patients. (8.4)
- Due to Organon USA Inc.'s marketing exclusivity rights, this drug product is not approved with certain pediatric use information. Labeling with additional information on pediatric use is approved for Organon USA Inc.'s rocuronium bromide injection. (8.4)

See 17 for PATIENT COUNSELING INFORMATION. Revised: 11/2008

FULL PRESCRIBING INFORMATION: CONTENTS*

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*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Rocuronium bromide injection is indicated for inpatients and outpatients as an adjunct to general anesthesia to facilitate both rapid sequence and routine tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation.

2 DOSE AND ADMINISTRATION

Rocuronium bromide is for intravenous use only. **This drug should only be administered by experienced clinicians or trained individuals supervised by an experienced clinician familiar with the use, actions, characteristics and complications of neuromuscular blocking agents. Doses of rocuronium bromide injection should be individualized and a peripheral nerve stimulator should be used to monitor drug effect, need for additional doses, adequacy of spontaneous recovery or antagonism, and to decrease the complications of overdose if additional doses are administered.**

The dosage information which follows is derived from studies based upon units of drug per unit of body weight. It is intended to serve as an initial guide to clinicians familiar with other neuromuscular blocking agents to acquire experience with rocuronium bromide.

In patients in whom potentiation of, or resistance to, neuromuscular block is anticipated, a dose adjustment should be considered [see *Dosage and Administration (2.5)*, *Warnings and Precautions (5.9, 5.12)*, *Drug Interactions (7.2, 7.3, 7.4, 7.5, 7.6, 7.8, 7.10)*, and *Use in Specific Populations (8.6)*].

2.1 Dose for Tracheal Intubation

The recommended initial dose of rocuronium bromide, regardless of anesthetic technique, is 0.6 mg/kg. Neuromuscular block sufficient for intubation (80% block or greater) is attained in a median (range) time of 1 (0.4 to 6) minute(s) and most patients have intubation completed within 2 minutes. Maximum blockade is achieved in most patients in less than 3 minutes. This dose may be expected to provide 31 (15 to 85) minutes of clinical relaxation under opioid/nitrous oxide/oxygen anesthesia. Under halothane, isoflurane, and enflurane anesthesia, some extension of the period of clinical relaxation should be expected [see *Drug Interactions (7.3)*].

A lower dose of rocuronium bromide (0.45 mg/kg) may be used. Neuromuscular block sufficient for intubation (80% block or greater) is attained in a median (range) time of 1.3 (0.8 to 6.2) minute(s) and most patients have intubation completed within 2 minutes. Maximum blockade is achieved in most patients in less than 4 minutes. This dose may be expected to provide 22 (12 to 31) minutes of clinical relaxation under opioid/nitrous oxide/oxygen anesthesia. Patients receiving this low dose of 0.45 mg/kg achieve less than 90% block (about 16% of these patients) may have a more rapid time to 25% recovery, 12 to 15 minutes.

A large bolus dose of 0.9 or 1.2 mg/kg can be administered under opioid/nitrous oxide/oxygen anesthesia without adverse effects to the cardiovascular system [see *Clinical Pharmacology (12.2)*].

2.2 Rapid Sequence Intubation

In appropriately premedicated and adequately anesthetized patients, rocuronium bromide 0.6 to 1.2 mg/kg will provide excellent or good intubating conditions in most patients in less than 2 minutes [see *Clinical Studies (14.1)*].

2.3 Maintenance Dosing

Maintenance dosages of 0.1, 0.15, and 0.2 mg/kg rocuronium bromide, administered at 25% recovery of control T₁ (defined as 3 twitches of train-of-four), provide a median (range) of 12 (2 to 31), 17 (6 to 50) and 24 (7 to 69) minutes of clinical duration under opioid/nitrous oxide/oxygen anesthesia [see *Clinical Pharmacology (12.2)*]. In all cases, dosing should be guided based on the clinical duration following initial dose or prior maintenance dose and not administered until recovery of neuromuscular function is evident. A clinically insignificant cumulation of effect with repetitive maintenance dosing has been observed [see *Clinical Pharmacology (12.2)*].

2.4 Use by Continuous Infusion

Infusion at an initial rate of 10 to 12 mcg/kg/min of rocuronium bromide should be initiated only after early evidence of spontaneous recovery from an intubating dose. Due to rapid redistribution [see *Clinical Pharmacology (12.3)*] and the associated rapid spontaneous recovery, initiation of the infusion after substantial return of neuromuscular function (more than 10% of control T₁), may necessitate additional bolus doses to maintain adequate block for surgery.

Upon reaching the desired level of neuromuscular block, the infusion of rocuronium bromide must be individualized for each patient. The rate of administration should be adjusted according to the patient's twitch response as monitored with the use of a peripheral nerve stimulator. In clinical trials, infusion rates have ranged from 4 to 16 mcg/kg/min.

Inhalation anesthetics, particularly enflurane and isoflurane, may enhance the neuromuscular blocking action of nondepolarizing muscle relaxants. In the presence of steady-state concentrations of enflurane or isoflurane, it may be necessary to reduce the rate of infusion by 30 to 50%, at 45 to 60 minutes after the intubating dose.

Spontaneous recovery and reversal of neuromuscular blockade following discontinuation of rocuronium bromide infusion may be expected to proceed at rates comparable to that following comparable total doses administered by repetitive bolus injections [see *Clinical Pharmacology (12.2)*].

Infusion solutions of rocuronium bromide can be prepared by mixing rocuronium bromide with an appropriate infusion solution such as 5% glucose in water or lactated Ringers [see *Dosage and Administration (2.6)*]. These infusion solutions should be used within 24 hours of mixing. Unused portions of infusion solutions should be discarded.

Infusion rates of rocuronium bromide can be individualized for each patient using the following tables for three different concentrations of rocuronium bromide solution as guidelines:

TABLE 1: Infusion Rates Using Rocuronium Bromide Injection (0.5 mg/mL)*

| Patient Weight | Drug Delivery Rate (mcg/kg/min) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 12 | 14 | 16 | Infusion Delivery Rate (mL/hr) | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| (kg) (lbs) | 2.2 | 4.8 | 6 | 7.2 | 8.4 | 9.6 | 10.8 | 12 | 14.4 | 16.8 | 19.2 | 22 | 24 | 28 | 32 | 36 | 40 | 44 | 48 | 52 | 56 | 60 | 64 | 68 | 72 | 76 | 80 | 84 | 88 | 92 | 96 | 100 | 104 | 108 | 112 | 116 | 120 | 124 | 128 | 132 | 136 | 140 | 144 | 148 | 152 | 156 | 160 | 164 | 168 | 172 | 176 | 180 | 184 | 188 | 192 | 196 | 200 | 204 | 208 | 212 | 216 | 220 | 224 | 228 | 232 | 236 | 240 | 244 | 248 | 252 | 256 | 260 | 264 | 268 | 272 | 276 | 280 | 284 | 288 | 292 | 296 | 300 | 304 | 308 | 312 | 316 | 320 | 324 | 328 | 332 | 336 | 340 | 344 | 348 | 352 | 356 | 360 | 364 | 368 | 372 | 376 | 380 | 384 | 388 | 392 | 396 | 400 | 404 | 408 | 412 | 416 | 420 | 424 | 428 | 432 | 436 | 440 | 444 | 448 | 452 | 456 | 460 | 464 | 468 | 472 | 476 | 480 | 484 | 488 | 492 | 496 | 500 | 504 | 508 | 512 | 516 | 520 | 524 | 528 | 532 | 536 | 540 | 544 | 548 | 552 | 556 | 560 | 564 | 568 | 572 | 576 | 580 | 584 | 588 | 592 | 596 | 600 | 604 | 608 | 612 | 616 | 620 | 624 | 628 | 632 | 636 | 640 | 644 | 648 | 652 | 656 | 660 | 664 | 668 | 672 | 676 | 680 | 684 | 688 | 692 | 696 | 700 | 704 | 708 | 712 | 716 | 720 | 724 | 728 | 732 | 736 | 740 | 744 | 748 | 752 | 756 | 760 | 764 | 768 | 772 | 776 | 780 | 784 | 788 | 792 | 796 | 800 | 804 | 808 | 812 | 816 | 820 | 824 | 828 | 832 | 836 | 840 | 844 | 848 | 852 | 856 | 860 | 864 | 868 | 872 | 876 | 880 | 884 | 888 | 892 | 896 | 900 | 904 | 908 | 912 | 916 | 920 | 924 | 928 | 932 | 936 | 940 | 944 | 948 | 952 | 956 | 960 | 964 | 968 | 972 | 976 | 980 | 984 | 988 | 992 | 996 | 1000 | 1004 | 1008 | 1012 | 1016 | 1020 | 1024 | 1028 | 1032 | 1036 | 1040 | 1044 | 1048 | 1052 | 1056 | 1060 | 1064 | 1068 | 1072 | 1076 | 1080 | 1084 | 1088 | 1092 | 1096 | 1100 | 1104 | 1108 | 1112 | 1116 | 1120 | 1124 | 1128 | 1132 | 1136 | 1140 | 1144 | 1148 | 1152 | 1156 | 1160 | 1164 | 1168 | 1172 | 1176 | 1180 | 1184 | 1188 | 1192 | 1196 | 1200 | 1204 | 1208 | 1212 | 1216 | 1220 | 1224 | 1228 | 1232 | 1236 | 1240 | 1244 | 1248 | 1252 | 1256 | 1260 | 1264 | 1268 | 1272 | 1276 | 1280 | 1284 | 1288 | 1292 | 1296 | 1300 | 1304 | 1308 | 1312 | 1316 | 1320 | 1324 | 1328 | 1332 | 1336 | 1340 | 1344 | 1348 | 1352 | 1356 | 1360 | 1364 | 1368 | 1372 | 1376 | 1380 | 1384 | 1388 | 1392 | 1396 | 1400 | 1404 | 1408 | 1412 | 1416 | 1420 | 1424 | 1428 | 1432 | 1436 | 1440 | 1444 | 1448 | 1452 | 1456 | 1460 | 1464 | 1468 | 1472 | 1476 | 1480 | 1484 | 1488 | 1492 | 1496 | 1500 | 1504 | 1508 | 1512 | 1516 | 1520 | 1524 | 1528 | 1532 | 1536 | 1540 | 1544 | 1548 | 1552 | 1556 | 1560 | 1564 | 1568 | 1572 | 1576 | 1580 | 1584 | 1588 | 1592 | 1596 | 1600 | 1604 | 1608 | 1612 | 1616 | 1620 | 1624 | 1628 | 1632 | 1636 | 1640 | 1644 | 1648 | 1652 | 1656 | 1660 | 1664 | 1668 | 1672 | 1676 | 1680 | 1684 | 1688 | 1692 | 1696 | 1700 | 1704 | 1708 | 1712 | 1716 | 1720 | 1724 | 1728 | 1732 | 1736 | 1740 | 1744 | 1748 | 1752 | 1756 | 1760 | 1764 | 1768 | 1772 | 1776 | 1780 | 1784 | 1788 | 1792 | 1796 | 1800 | 1804 | 1808 | 1812 | 1816 | 1820 | 1824 | 1828 | 1832 | 1836 | 1840 | 1844 | 1848 | 1852 | 1856 | 1860 | 1864 | 1868 | 1872 | 1876 | 1880 | 1884 | 1888 | 1892 | 1896 | 1900 | 1904 | 1908 | 1912 | 1916 | 1920 | 1924 | 1928 | 1932 | 1936 | 1940 | 1944 | 1948 | 1952 | 1956 | 1960 | 1964 | 1968 | 1972 | 1976 | 1980 | 1984 | 1988 | 1992 | 1996 | 2000 | 2004 | 2008 | 2012 | 2016 | 2020 | 2024 | 2028 | 2032 | 2036 | 2040 | 2044 | 2048 | 2052 | 2056 | 2060 | 2064 | 2068 | 2072 | 2076 | 2080 | 2084 | 2088 | 2092 | 2096 | 2100 | 2104 | 2108 | 2112 | 2116 | 2120 | 2124 | 2128 | 2132 | 2136 | 2140 | 2144 | 2148 | 2152 | 2156 | 2160 | 2164 | 2168 | 2172 | 2176 | 2180 | 2184 | 2188 | 2192 | 2196 | 2200 | 2204 | 2208 | 2212 | 2216 | 2220 | 2224 | 2228 | 2232 | 2236 | 2240 | 2244 | 2248 | 2252 | 2256 | 2260 | 2264 | 2268 | 2272 | 2276 | 2280 | 2284 | 2288 | 2292 | 2296 | 2300 | 2304 | 2308 | 2312 | 2316 | 2320 | 2324 | 2328 | 2332 | 2336 | 2340 | 2344 | 2348 | 2352 | 2356 | 2360 | 2364 | 2368 | 2372 | 2376 | 2380 | 2384 | 2388 | 2392 | 2396 | 2400 | 2404 | 2408 | 2412 | 2416 | 2420 | 2424 | 2428 | 2432 | 2436 | 2440 | 2444 | 2448 | 2452 | 2456 | 2460 | 2464 | 2468 | 2472 | 2476 | 2480 | 2484 | 2488 | 2492 | 2496 | 2500 | 2504 | 2508 | 2512 | 2516 | 2520 | 2524 | 2528 | 2532 | 2536 | 2540 | 2544 | 2548 | 2552 | 2556 | 2560 | 2564 | 2568 | 2572 | 2576 | 2580 | 2584 | 2588 | 2592 | 2596 | 2600 | 2604 | 2608 | 2612 | 2616 | 2620 | 2624 | 2628 | 2632 | 2636 | 2640 | 2644 | 2648 | 2652 | 2656 | 2660 | 2664 | 2668 | 2672 | 2676 | 2680 | 2684 | 2688 | 2692 | 2696 | 2700 | 2704 | 2708 | 2712 | 2716 | 2720 | 2724 | 2728 | 2732 | 2736 | 2740 | 2744 | 2748 | 2752 | 2756 | 2760 | 2764 | 2768 | 2772 | 2776 | 2780 | 2784 | 2788 | 2792 | 2796 | 2800 | 2804 | 2808 | 2812 | 2816 | 2820 | 2824 | 2828 | 2832 | 2836 | 2840 | 2844 | 2848 | 2852 | 2856 | 2860 | 2864 | 2868 | 2872 | 2876 | 2880 | 2884 | 2888 | 2892 | 2896 | 2900 | 2904 | 2908 | 2912 | 2916 | 2920 | 2924 | 2928 | 2932 | 2936 | 2940 | 2944 | 2948 | 2952 | 2956 | 2960 | 2964 | 2968 | 2972 | 2976 | 2980 | 2984 | 2988 | 2992 | 2996 | 3000 | 3004 | 3008 | 3012 | 3016 | 3020 | 3024 | 3028 | 3032 | 3036 | 3040 | 3044 | 3048 | 3052 | 3056 | 3060 | 3064 | 3068 | 3072 | 3076 | 3080 | 3084 | 3088 | 3092 | 3096 | 3100 | 3104 | 3108 | 3112 | 3116 | 3120 | 3124 | 3128 | 3132 | 3136 | 3140 | 3144 | 3148 | 3 |

7.9 Propofol

The use of propofol for induction and maintenance of anesthesia does not alter the clinical duration or recovery characteristics following recommended doses of rocuronium bromide.

7.10 Quinidine

Injection of quinidine during recovery from use of muscle relaxants is associated with recurrent paralysis. This possibility must also be considered for rocuronium bromide [See *Warnings and Precautions* (5.9)].

7.11 Succinylcholine

The use of rocuronium bromide before succinylcholine, for the purpose of attenuating some of the side effects of succinylcholine, has not been studied.

If rocuronium bromide is administered following administration of succinylcholine, it should not be given until recovery from succinylcholine has been observed. The median duration of action of rocuronium bromide 0.6 mg/kg administered after a 1 mg/kg dose of succinylcholine when T_1 returned to 75% of control was 36 minutes (range 14 to 57, n=12) vs. 28 minutes (17 to 51, n=12) without succinylcholine.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Developmental toxicology studies have been performed with rocuronium bromide in pregnant, conscious, nonventilated rabbits and rats. Inhibition of neuromuscular function was the endpoint for high-dose selection. The maximum tolerated dose served as the high-dose and was administered intravenously three times a day to rats (0.3 mg/kg, 15 to 30% of human intubation dose of 0.6 to 1.2 mg/kg based on the body surface unit of mg/m²) from day 6 to 17 and to rabbits (0.02 mg/kg, 25% human dose) from day 6 to 18 of pregnancy. High-dose treatment caused acute symptoms of respiratory dysfunction due to the pharmacological activity of the drug. Teratogenicity was not observed in these animal species. The incidence of late embryonic death was increased at the high-dose in rats most likely due to oxygen deficiency. Therefore, this finding probably has no relevance for humans because immediate mechanical ventilation of the intubated patient will effectively prevent embryo-fetal hypoxia. However, there are no adequate and well-controlled studies in pregnant women. Rocuronium bromide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.2 Labor and Delivery

The use of rocuronium bromide in Cesarean section has been studied in a limited number of patients [see *Clinical Studies* (14.5)]. Rocuronium bromide is not recommended for rapid sequence induction in Cesarean section patients.

8.4 Pediatric Use

The use of rocuronium bromide has been studied in pediatric patients 3 months to 14 years of age under halothane anesthesia. Of the pediatric patients anesthetized with halothane who did not receive atropine for induction, about 80% experienced a transient increase (30% or greater) in heart rate after intubation. One of the 19 infants anesthetized with halothane and fentanyl who received atropine for induction experienced this magnitude of change. [See *Dosage and Administration* (2.5) and *Clinical Studies* (14.3)].

The overall analysis of ECG data in pediatric patients indicates that the concomitant use of rocuronium bromide with general anesthetic agents can prolong the QTc interval. The data also suggest that rocuronium bromide may increase heart rate. However, it was not possible to conclusively identify an effect of rocuronium bromide independent of that of anesthesia and other factors. Additionally, when examining plasma levels of rocuronium bromide in correlation to QTc interval prolongation, no relationship was observed [See *Dosage and Administration* (2.5), *Warnings and Precautions* (5.8) and *Clinical Studies* (14.3)].

Rocuronium bromide is not recommended for rapid sequence intubation in pediatric patients. Recommendations for use in pediatric patients are discussed in other sections [see *Dosage and Administration* (2.5) and *Clinical Pharmacology* (12.2)].

Due to Organon USA Inc.'s marketing exclusivity rights, this drug product is not approved with certain pediatric use information. Labeling describing additional information for pediatric use is approved for Organon USA Inc.'s rocuronium bromide injection.

8.5 Geriatric Use

Rocuronium bromide was administered to 140 geriatric patients (65 years or greater) in U.S. clinical trials and 128 geriatric patients in European clinical trials. The observed pharmacokinetic profile for geriatric patients (n=20) was similar to that for other adult surgical patients [see *Clinical Pharmacology* (12.3)]. Onset time and duration of action were slightly longer for geriatric patients (n=43) in clinical trials. Clinical experiences and recommendations for use in geriatric patients are discussed in other sections [see *Dosage and Administration* (2.5), *Clinical Pharmacology* (12.2), and *Clinical Studies* (14.2)].

8.6 Patients with Hepatic Impairment

Since rocuronium bromide is primarily excreted by the liver, it should be used with caution in patients with clinically significant hepatic impairment. Rocuronium bromide 0.6 mg/kg has been studied in a limited number of patients (n=9) with clinically significant hepatic impairment under steady-state isoflurane anesthesia. After rocuronium bromide 0.6 mg/kg, the median (range) clinical duration of 60 (35 to 166) minutes. The median recovery time to 42 minutes in patients with normal hepatic function. The median prolonged time of 53 minutes was also prolonged in patients with cirrhosis compared to 20 minutes in patients with normal hepatic function. Four of eight patients with cirrhosis, who received rocuronium bromide 0.6 mg/kg under opioid/nitrous oxide/oxygen anesthesia, did not achieve complete block. These findings are consistent with the increase in volume of distribution at steady state observed in patients with significant hepatic impairment [see *Clinical Pharmacology* (12.3)]. If used for rapid sequence induction in patients with ascites, an increased initial dosage may be necessary to assure complete block. Duration will be prolonged in these cases. The use of doses higher than 0.6 mg/kg has not been studied [see *Dosage and Administration* (2.5)].

8.7 Patients with Renal Impairment

Due to the limited role of the kidney in the excretion of rocuronium bromide, usual dosing guidelines should be followed. In patients with renal dysfunction, the duration of neuromuscular blockade was not prolonged; however, there was substantial individual variability (range, 22 to 90 minutes). [see *Clinical Pharmacology* (12.3)].

10 OVERDOSAGE

Overdosage with neuromuscular blocking agents may result in neuromuscular block beyond the time needed for surgery and anesthesia. The primary treatment is maintenance of a patent airway, controlled ventilation and adequate sedation until recovery of normal neuromuscular function is assured. Once evidence of recovery from neuromuscular block is observed, further recovery may be facilitated by administration of an anticholinesterase agent in conjunction with an appropriate anticholinergic agent.

Reversal of Neuromuscular Blockade

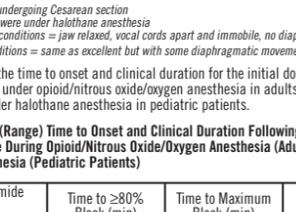
Anticholinesterase agents should not be administered prior to the demonstration of some spontaneous recovery from neuromuscular blockade. The use of a nerve stimulator to document recovery is recommended.

Patients should be evaluated for adequate clinical evidence of neuromuscular recovery, e.g., 5 second head lift, adequate phonation, ventilation, and upper airway patency. Ventilation must be supported while patients exhibit any signs of muscle weakness. Recovery may be delayed in the presence of debilitation, carcinomatosis, and concomitant use of certain drugs which enhance neuromuscular blockade or separately cause respiratory depression. Under such circumstances the management is the same as that of prolonged neuromuscular blockade.

11 DESCRIPTION

Rocuronium bromide injection is a nondepolarizing neuromuscular blocking agent with a rapid to intermediate onset depending on dose and intermediate duration. Rocuronium bromide is chemically designated as 1-[17 β -(acetylxylo)-3 α -hydroxy-2 β -(4-morpholinyl)-5 α -androstane-16 β -yl]-1-(2-propenyl)pyrrolidinium bromide.

The structural formula is:



The chemical formula is C₂₉H₄₃BrN₃O₄ with a molecular weight of 609.70. The partition coefficient of rocuronium bromide in n-octanol/water is 0.5 at 20°C.

Rocuronium bromide is supplied as a sterile, nonpyrogenic, isotonic solution that is clear, colorless to yellow/orange, for intravenous injection only. Each mL contains 10 mg rocuronium bromide, 2 mg sodium acetate, and 3.3 mg sodium chloride. The aqueous solution is adjusted to a pH of 4 with acetic acid and/or sodium hydroxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Rocuronium bromide is a nondepolarizing neuromuscular blocking agent with a rapid to intermediate onset depending on dose and intermediate duration. It acts by competing for cholinergic receptors at the motor end-plate. This action is antagonized by acetylcholinesterase inhibitors, such as neostigmine and edrophonium.

12.2 Pharmacodynamics

The ED₉₅ (dose required to produce 95% suppression of the first [T₁] mechanomyographic [MMG] response of the adductor pollicis muscle [thumb]) to indirect supramaximal train-of-four stimulation of the ulnar nerve) during opioid/nitrous oxide/oxygen anesthesia is approximately 0.3 mg/kg. Patient variability around the ED₉₅ dose suggests that 50% of patients will exhibit T₁ depression of 91 to 97%.

Table 4 presents intubating conditions in patients with intubation initiated at 60 to 70 seconds.

Table 4: Percent of Excellent or Good Intubating Conditions and Median (Range) Time to Completion of Intubation in Patients with Intubation Initiated at 60 to 70 Seconds

| Rocuronium Bromide Dose (mg/kg) Administered over 5 sec | Percent of Patients With Excellent or Good Intubating Conditions | Time to Completion of Intubation (min) |
|---|--|--|
| Adults* 18 to 64 yrs 0.45 (n=43) 0.6 (n=51) | 86% 96% | 1.6 (1.0 to 7.0) 1.6 (1.0 to 3.2) |
| Infants** 3 mo to 1 yr 0.6 (n=18) Pediatric** 1 to 12 yrs 0.6 (n=12) | 100% 100% | 1.0 (1.0 to 1.5) 1.0 (0.5 to 2.3) |

* Excludes patients undergoing Cesarean section

** Pediatric patients were under halothane anesthesia

Excellent intubating conditions = jaw relaxed, vocal cords apart and immobile, no diaphragmatic movement
Good intubating conditions = as excellent but with some diaphragmatic movement

Table 5 presents the time to onset and clinical duration for the initial dose of rocuronium bromide injection under opioid/nitrous oxide/oxygen anesthesia in adults and geriatric patients, and under halothane anesthesia in pediatric patients.

TABLE 5: Median (Range) Time to Onset and Clinical Duration Following Initial (Intubating) Dose During Opioid/Nitrous Oxide/Oxygen Anesthesia (Adults) and Halothane Anesthesia (Pediatric Patients)

| Rocuronium Bromide Dose (mg/kg) Administered over 5 sec | Time to $\geq 80\%$ (min) | Time to Maximum (min) | Clinical Duration (min) |
|--|--|---|--|
| Adults 18 to 64 yrs 0.45 (n=50) 0.6 (n=142) 0.9 (n=20) 1.2 (n=18) | 1.3 (0.8 to 6.2) 1.0 (0.4 to 6.0) 1.1 (0.3 to 3.8) 0.7 (0.4 to 1.7) | 3.0 (1.3 to 8.2) 1.8 (0.6 to 13.0) 1.4 (0.8 to 6.2) 1.0 (0.6 to 4.7) | 22 (12 to 31) 31 (15 to 85) 58 (27 to 111) 67 (38 to 160) |
| Geriatric ≥ 65 yrs 0.6 (n=31) 0.9 (n=5) 1.2 (n=7) | 2.3 (1.0 to 8.3) 2.0 (1.0 to 3.0) 1.0 (0.8 to 3.5) | 3.7 (1.3 to 11.3) 2.5 (1.2 to 5.0) 1.3 (1.2 to 4.7) | 46 (22 to 73) 62 (49 to 75) 94 (64 to 138) |
| Infants 3 mo to 1 yr 0.6 (n=17) 0.8 (n=9) Pediatric 1 to 12 yrs 0.6 (n=27) 0.8 (n=18) | — — 0.8 (0.4 to 2.0) | 0.8 (0.3 to 3.0) 0.7 (0.5 to 0.8) 1.0 (0.5 to 3.3) 0.5 (0.3 to 1.0) | 41 (24 to 68) 40 (27 to 70) 26 (17 to 39) 30 (17 to 56) |

n = the number of patients who had time to maximum block recorded

Clinical duration = time until return to 25% of control T₁. Patients receiving doses of 0.45 mg/kg who achieved less than 90% block (16% of these patients) had about 12 to 15 minutes to 25% recovery.

Due to Organon USA Inc.'s marketing exclusivity rights, this drug product is not approved with certain pharmacodynamic information. Labeling describing additional pharmacodynamics in pediatric populations is approved for Organon USA Inc.'s rocuronium bromide injection.

The time to 80% or greater block and clinical duration as a function of dose are presented in Figures 1 and 2.

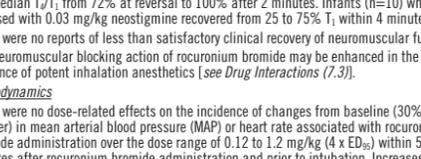


FIGURE 1: Time to 80% or greater Block vs. Initial Dose of Rocuronium Bromide by Age Group (Median, 25th and 75th percentile, and individual values)

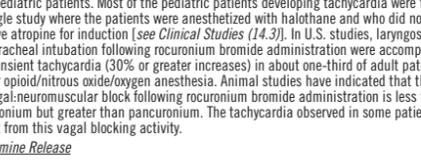


FIGURE 2: Duration of Clinical Effect vs. Initial Dose of Rocuronium Bromide by Age Group (Median, 25th and 75th percentile, and individual values)

The clinical durations for the first five maintenance doses, in patients receiving five or more maintenance doses are represented in Figure 3 [see *Dosage and Administration* (2.3)].



FIGURE 3: Duration of Clinical Effect vs. Number of Rocuronium Bromide Maintenance Doses, by Dose

Once spontaneous recovery has reached 25% of control T₁, the neuromuscular block produced by rocuronium bromide is readily reversed with anticholinesterase agents, e.g., edrophonium or neostigmine.

The median spontaneous recovery from 25 to 75% T₁ was 13 minutes in adult patients. When neuromuscular block was reversed in 36 adults at a T₁ of 22 to 27%, recovery to a T₁ of 89 (50 to 132%) and T₁/T₁ of 69 (38 to 92%) was achieved within 5 minutes. Only five of 320 adults reversed received an additional dose of reversal agent. The median (range) dose of reversal agent was 0.04 (0.01 to 0.09) mg/kg and the median (range) dose of edrophonium was 0.5 (0.3 to 1.0) mg/kg.

In geriatric patients (n=51) reversed with neostigmine, the median T₁/T₁ increased from 40 to 88% in 5 minutes.

In clinical trials with halothane, pediatric patients (n=27) who received 0.5 mg/kg edrophonium had increases in the median T₁/T₁ from 37% at reversal to 93% after 2 minutes. Pediatric patients (n=58) who received 1 mg/kg edrophonium had increases in the median T₁/T₁ from 72% at reversal to 100% after 2 minutes. Infants (n=10) who were reversed with 0.03 mg/kg neostigmine recovered from 25 to 75% T₁ within 4 minutes.

There were no reports of less than satisfactory clinical recovery of neuromuscular function. The neuromuscular blocking action of rocuronium bromide may be enhanced in the presence of potent inhalation anesthetics [see *Drug Interactions* (7.3)].

Hemodynamics

There were no dose-related effects on the incidence of changes from baseline (30% or greater) in mean arterial blood pressure (MAP) or heart rate associated with rocuronium bromide administration over the dose range of 0.12 to 1.2 mg/kg (4 x ED₉₅) within 5 minutes after rocuronium bromide administration and prior to intubation. Increases or decreases in MAP were observed in 2 to 5% of geriatric and other adult patients, and in about 1% of pediatric patients. Heart rate changes (30% or greater) occurred in 0 to 2% of geriatric and other adult patients. Tachycardia (30% or greater) occurred in 12 of 127 pediatric patients. Most of the pediatric patients developing tachycardia were from a single study where the patients were anesthetized with halothane and who did not receive atropine for induction [see *Clinical Studies* (14.3)]. In U.S. studies, laryngoscopy and tracheal intubation following rocuronium bromide administration were accompanied by transient tachycardia (30% or greater increases) in about one-third of adult patients under opioid/nitrous oxide/oxygen anesthesia. Animal studies have indicated that the ratio of vagal:neuromuscular block following rocuronium bromide administration is less than vecuronium but greater than pancuronium. The tachycardia observed in some patients may result from this vagal blocking activity.

Histamine Release

In studies of histamine release, clinically significant concentrations of plasma histamine occurred in 1 of 88 patients. Clinical signs of histamine release (flushing, rash, or bronchospasm) associated with the administration of rocuronium bromide were assessed in clinical trials and reported in 9 of 1137 (0.8%) patients.

12.3 Pharmacokinetics

Adult and Geriatric Patients

In an effort to maximize the information gathered in the *in vivo* pharmacokinetic studies, the data from the studies was used to develop *population estimates* of the parameters for the subpopulations represented (e.g., geriatric, pediatric, renal and hepatic impairment). These population based estimates and a measure of the estimate variability are contained in the following section.

Following intravenous administration of rocuronium bromide, plasma levels of rocuronium follow a three compartment open model. The rapid distribution half-life is 1 to 2 minutes and the slower distribution half-life is 14 to 18 minutes. Rocuronium is approximately 30% bound to human plasma proteins. In geriatric and other adult surgical patients undergoing either opioid/nitrous oxide/oxygen or inhalational anesthesia, the observed pharmacokinetic profile was essentially unchanged.

TABLE 7: Mean (SD) Pharmacokinetic Parameters in Adults (n=22; Age 27 to 58 yrs) and Geriatric (n=20; 65 yrs or greater) During Opioid/Nitrous Oxide/Oxygen Anesthesia

| PK Parameters | Adults (Ages 27 to 58 yrs) | Geriatrics (≥ 65 yrs) |
|---|----------------------------|-----------------------------|
| Clearance (L/kg/hr) | 0.25 (0.08) | 0.21 (0.06) |
| Volume of Distribution at Steady State (L/kg) | 0.25 (0.04) | 0.22 (0.03) |
| t _{1/2} β Elimination (hr) | 1.4 (0.4) | 1.5 (0.4) |

In general, studies with normal adult subjects did not reveal any differences in the pharmacokinetics of rocuronium due to gender.

Studies of distribution, metabolism, and excretion in cats and dogs indicate that rocuronium is eliminated primarily by the liver. The rocuronium analog 17-desacetyl-rocuronium, a metabolite, has been rarely observed in the plasma or urine of humans administered single doses of 0.5 to 1 mg/kg with or without a subsequent infusion (for up to 12 hr) of rocuronium. In the cat, 17-desacetyl-rocuronium has approximately one-twentieth the neuromuscular blocking potency of rocuronium. The effects of renal failure and hepatic disease on the pharmacokinetics and pharmacodynamics of rocuronium in humans are consistent with these findings.

TABLE 8: Mean (SD) Pharmacokinetic Parameters in Adults with Normal Renal and Hepatic Function (n=10, ages 23 to 65), Renal Transplant Patients (n=10, ages 21 to 45) and Hepatic Dysfunction Patients (n=9, ages 31 to 67) During Isoflurane Anesthesia

| PK Parameters | Normal Renal and Hepatic Function | Renal Transplant Patients | Hepatic Dysfunction Patients |
|---|-----------------------------------|---------------------------|------------------------------|
| Clearance (L/kg/hr) | 0.16 (0.05)* | 0.13 (0.04) | 0.13 (0.06) |
| Volume of Distribution at Steady State (L/kg) | 0.26 (0.03) | 0.34 (0.11) | 0.53 (0.14) |
| t _{1/2} β Elimination (hr) | 2.4 (0.8)* | 2.4 (1.1) | 4.3 (2.6) |

* Differences in the calculated t_{1/2} β and Cl between this study and the study in young adults vs. geriatrics (≥ 65 years) is related to the different sample populations and anesthetic techniques

The net result of these findings is that subjects with renal failure have clinical durations that are similar to but somewhat more variable than the duration that one would expect in subjects with normal renal function. Hepatically impaired patients, due to the large increase in volume, may demonstrate clinical durations approaching 1.5 times that of subjects with normal hepatic function. In both populations the clinician should individualize the dose to the needs of the patient [see *Dosage and Administration* (2.5)].

Tissue redistribution accounts for most (about 80%) of the initial amount of rocuronium administered. As tissue compartments fill with continued dosing (4 to 8 hours), less drug is redistributed away from the site of action and, for an infusion-only dose, the rate to maintain neuromuscular blockade falls to about 20% of the initial infusion rate. The use of a loading dose and a smaller infusion rate reduces the need for adjustment of dose.

Pediatric Patients

Under halothane anesthesia, the clinical duration of effects of rocuronium bromide did not vary with age in patients 4 months to 8 years of age. The terminal half-life and other pharmacokinetic parameters of rocuronium in these pediatric patients are presented in Table 9.

TABLE 9: Mean (SD) Pharmacokinetic Parameters of Rocuronium in Pediatric Patients (ages 3 to less than 12 mos, n=6; 1 to less than 3 yrs, n=5; 3 to less than 8 yrs, n=7) During Halothane Anesthesia

| PK Parameters | Patient Age Range | | |
|---|-------------------|-------------|-------------|
| | 3 to <12 mos | 1 to <3 yrs | 3 to <8 yrs |
| Clearance (L/kg/hr) | 0.35 (0.08) | 0.32 (0.07) | 0.44 (0.16) |
| Volume of Distribution at Steady State (L/kg) | 0.30 (0.04) | 0.26 (0.06) | 0.21 (0.03) |
| t _{1/2} β Elimination (hr) | 1.3 (0.5) | 1.1 (0.7) | 0.8 (0.3) |

Due to Organon USA Inc.'s marketing exclusivity right, this drug product is not approved with certain pediatric pharmacokinetic information. Labeling describing additional pharmacokinetics in pediatric populations is approved for Organon USA Inc.'s rocuronium bromide injection.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies in animals have not been performed with rocuronium bromide to evaluate carcinogenic potential or impairment of fertility. Mutagenicity studies (Ames test, analysis of chromosomal aberrations in mammalian cells, and micronucleus test) conducted with rocuronium bromide did not suggest mutagenic potential.

14 CLINICAL STUDIES

In U.S. clinical studies, a total of 1137 patients received rocuronium bromide, including 176 pediatric, 140 geriatric, 55 obstetric, and 766 other adults. Most patients (90%) were ASA physical status I or II, about 9% were ASA III, and 10 patients (undergoing coronary artery bypass grafting or valvular surgery) were ASA IV. In European clinical studies, a total of 1394 patients received rocuronium bromide, including 52 pediatric, 128 geriatric (65 years or greater) and 1214 other adults.

14.1 Adult Patients

Intubation using doses of rocuronium bromide 0.6 to 0.85 mg/kg was evaluated in 203 adults in 11 clinical studies. Excellent to good intubating conditions were generally achieved within 2 minutes and maximum block occurred within 3 minutes in most patients. Doses within this range provide clinical relaxation for a median (range) time of 33 (14 to 85) minutes under opioid/nitrous oxide/oxygen anesthesia. Larger doses (0.9 and 1.2 mg/kg) were evaluated in two studies with 19 and 16 patients under opioid/nitrous oxide/oxygen anesthesia and provided 58 (27 to 111) and 67 (38 to 160) minutes of clinical relaxation, respectively.

Cardiovascular Disease

In one clinical study, 10 patients with clinically significant cardiovascular disease undergoing coronary artery bypass graft received an initial dose of 0.6 mg/kg rocuronium bromide. Neuromuscular block was maintained during surgery with bolus maintenance doses of 0.3 mg/kg. Following intubation, continuous 8 mcg/kg/min infusion of rocuronium bromide produced relaxation sufficient to support mechanical ventilation for 6 to 12 hours in the surgical intensive care unit (SICU) while the patients were recovering from surgery.

Rapid Sequence Intubation

Intubating conditions were assessed in 230 patients in six clinical studies where anesthesia was induced with either thiopental (3 to 6 mg/kg) or propofol (1.5 to 2.5 mg/kg) in combination with either fentanyl (2 to 5 mcg/kg) or alfentanil (1 mg). Most of the patients also received a premedication such as midazolam or temazepam. Most patients had intubation attempted within 60 to 90 seconds of administration of rocuronium bromide 0.6 mg/kg or succinylcholine 1 to 1.5 mg/kg. Excellent or good intubating conditions were achieved in 119/120 (99% [95% confidence interval 95 to 99.9%]) patients receiving rocuronium bromide and in 108/110 (98% [94 to 99.8%]) patients receiving succinylcholine. The duration of action of rocuronium bromide 0.6 mg/kg is longer than succinylcholine and at this dose is approximately equivalent to the duration of other intermediate acting neuromuscular blocking drugs.

Obese Patients

Rocuronium bromide was dosed according to actual body weight (ABW) in most clinical studies. The administration of rocuronium bromide in the 47 of 330 (14%) patients who were at least 30% or more above their ideal body weight (IBW) was not associated with clinically significant differences in the onset, duration, recovery, or reversal of rocuronium bromide-induced neuromuscular block.

In one clinical study in obese patients, rocuronium bromide 0.6 mg/kg was dosed according to ABW (n=12) or IBW (n=11). Obese patients dosed according to IBW had a longer time to maximum block, a shorter median (range) clinical duration of 25 (14 to 29) minutes, and did not achieve intubating conditions comparable to those dosed based on ABW. These results support the recommendation that obese patients be dosed based on actual body weight. [See *Dosage and Administration* (2.5)]

Obstetric Patients

Rocuronium bromide 0.6 mg/kg was administered with thiopental, 3 to 4 mg/kg (n=13) or 4 to 6 mg/kg (n=42), for rapid sequence induction of anesthesia for Cesarean section. No neonate had APGAR scores greater than 7 at 5 minutes. The umbilical venous plasma concentrations were 18% of maternal concentrations at delivery. Intubating conditions were poor or inadequate in 5 of 13 women receiving 3 to 4 mg/kg thiopental when intubation was attempted 60 seconds after drug injection. Therefore, rocuronium bromide is not recommended for rapid sequence induction in Cesarean section patients.

14.2 Geriatric Patients

Rocuronium bromide was evaluated in 55 geriatric patients (ages 65 to 80 years) in six clinical studies. Doses of 0.6 mg/kg provided excellent to good intubating conditions in a median (range) time of 2.3 (1 to 8) minutes. Recovery times from 25 to 75% after these doses were not prolonged in geriatric patients compared to other adult patients. [See *Dosage and Administration* (2.5) and *Use in Specific Populations* (8.5)]

14.3 Pediatric Patients

Rocuronium bromide 0.6 or 0.8 mg/kg was evaluated for intubation in 75 pediatric patients (n=28; age 3 to 12 months, n=47; age 1 to 12 years) in three studies using halothane (1 to 5%) and nitrous oxide (60 to 70%) in oxygen. Doses of 0.6 mg/kg provided a median (range) time to maximum block of 1 (0.5 to 3.3) minutes(s). This dose provided a median (range) time of clinical relaxation of 41 (24 to 68) minutes in 3 month to 1 year-old infants and 26 (17 to 39) minutes in 1 to 12 year-old pediatric patients. [See *Dosage and Administration* (2.5) and *Use in Specific Populations* (8.4)]

Due to Organon USA Inc.'s marketing exclusivity rights, this drug product is not approved with a description of certain pediatric studies. Labeling describing additional pediatric studies is approved for Organon USA Inc.'s rocuronium bromide injection.

16 HOW SUPPLIED/STORAGE AND HANDLING

Rocuronium bromide injection is available in the following:

- Rocuronium bromide injection 5 mL multiple dose vials containing 50 mg rocuronium bromide (10 mg/mL)
Box of 10 **NDC 0703-2394-03**
- Rocuronium bromide injection 10 mL multiple dose vials containing 100 mg rocuronium bromide (10 mg/mL)
Box of 10 **NDC 0703-2395-03**

The packaging of this product contains no natural rubber (latex).

Rocuronium bromide should be stored in a refrigerator, 2° to 8°C (36° to 46°F). DO NOT FREEZE. Upon removal from refrigeration to room temperature storage conditions (25°C/77°F), use rocuronium bromide within 60 days. Use opened vials of rocuronium bromide within 30 days.