Population pharmacokinetic analyses support the concept that Oxycodone, like other opioid analgesics, produces linear absorption (AUC) (see Figure 1). It takes approximately 18 hours for the drug to be absorbed. Most ROXICODONE™ tablets are bioequivalent to the 5 mg ROXICODONE™ tablets.

Table 1: Pharmacokinetic Parameters of Oxycodone Compared to Other Dose Forms

<table>
<thead>
<tr>
<th>Dose Form</th>
<th>Cmax (μg/mL)</th>
<th>Tmax (h)</th>
<th>AUC (μg*h/mL)</th>
<th>Vd (L)</th>
<th>CL (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROXICODONE™ 5 mg</td>
<td>12.9±3.1</td>
<td>1.0±0.3</td>
<td>7.2±2.3</td>
<td>9.7±2.6</td>
<td>n/a</td>
</tr>
<tr>
<td>ROXICODONE™ 15 mg</td>
<td>17.7±3.0</td>
<td>2.54±1.2</td>
<td>n/a</td>
<td>n/a</td>
<td>3.3±0.5</td>
</tr>
<tr>
<td>ROXICODONE™ 30 mg</td>
<td>19.0±3.7</td>
<td>1.0±0.5</td>
<td>n/a</td>
<td>n/a</td>
<td>2.9±0.4</td>
</tr>
<tr>
<td>ROXICODONE™ Intensol 130.6±34.7</td>
<td>21.1±6.1</td>
<td>1.9±1.5</td>
<td>n/a</td>
<td>n/a</td>
<td>3.71±0.8</td>
</tr>
<tr>
<td>ROXICODONE™ Intensol 133±25.2</td>
<td>22.3±8.2</td>
<td>1.8±1.8</td>
<td>n/a</td>
<td>n/a</td>
<td>3.73±0.9</td>
</tr>
</tbody>
</table>

The pharmacokinetics of ROXICODONE™ tablets are independent of food intake (see Food Effect section).

The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency. ROXICODONE™ is approximately 10 times more potent than morphine on this basis.

The activity of ROXICODONE™ is dependent on hepatic metabolism. The water partition coefficient is 0.7.

The formation of oxymorphone, but not noroxycodone, is enhanced through the administration of drugs with opioid agonist activity. If ROXICODONE™ is administered concomitantly with an opioid antagonist, the analgesic response will depend on the patient's opioid tolerance as well as the degree of agonist antagonist interaction.

The analgesic ingredient, oxycodone, is a semi-synthetic opioid with few therapeutic actions. The chief pharmacological action of oxycodone is analgesia. The therapeutic efficacy is related to the degree of tolerance to the analgesic effects of opioids.

The analgesic effect of opioids is usually paralleled by tolerance. Chronic use of opioids may cause a decrease in the secretion of gastrointestinal and pancreatic secretions, spasm of the sphincter of Oddi, and transient elevations in serum amylase. The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle.

Oxycodone depresses the cough reflex by direct effect on the bronchial musculature. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

Oxycodone may cause a decrease in the secretion of gastrointestinal and pancreatic secretions, spasm of the sphincter of Oddi, increased gastric acid secretion, constipation, and transient elevations in serum amylase.

Caution should also be used in patients with cor pulmonale, intracranial lesions or a pre-existing increase in intracranial pressure, Addison’s disease, and hypersensitivity to oxydodine, or in any situation in which increased intracranial pressure or intracranial lesions are suspected.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.

The primary actions of opioids on the gastrointestinal tract are probably related to their depressant effects on the central nervous system and organs composed of smooth muscle. The respiratory depressant effects of narcotics and their ability to produce physical dependence and tolerance are related to the ratio of the oral to intravenous (OIT) potency.

The mechanism of the analgesic action is unknown. However, specific opioid receptors for pain are found throughout the CNS.
Patients receiving narcotic analge-
sics during labor, should be observed closely for signs
of respiratory depression. A specific narcotic antagonist,
should not be administered in the absence of clinically
needed to adequately relieve pain.

Opioid-Tolerant Individuals

As with any potent opioid, it is critical to adjust the dos-
ing regimen for each patient individually, taking into account
needed, 3) the degree of opioid tolerance, 4) the general
ative potency estimate to calculate the dose of oxycodone
neither recommended nor intended for use in:

- Patients 65 years of age or older
- Patients with respiratory or cardiovascular disease
- Patients with a history of alcohol or drug abuse
- Patients with a history of epilepsy

Cardiovascular

- Cardiovascular collapse
- Bradycardia
- Cardiac arrest or arrhythmias
- Migraine
- Palpitation
- Tachycardia

Musculoskeletal

- Abdominal pain
- Accidental injury
- Allergic reaction
- Asthma
- Conjunctivitis

Gastrointestinal

- Abdominal pain
- Vomiting

Respiratory

- Asthma
- Chest pain
- Dyspnea
- Hypoxia

Psychiatric

- Anxiety
- Confusion
- Irritability
- Nervousness

Neurological

- Seizure
- Tremor

Miscellaneous

- Rash
- Sweating
- Vision disturbances

Adverse Reactions

1. Physical dependence, psychological dependence, and addiction may develop with chronic use of oxycodone, a full-agonist opioid. The potential for abuse, dependency, and addiction increase with the duration of therapy. All patients, including those who have used opioids, should be cautioned about the risk of addiction.

2. Physical dependence usually does not occur to a clinically

3. Patients should be advised that ROXICODONE

4. ROXICODONE

5. ROXICODONE

6. The potential for respiratory depression, hypotension, profound sedation, or additive CNS depression. Interactive effects resulting in respiratory depression. Gastric emptying may be useful in performance of potentially hazardous tasks (e.g. driving, operating machinery).

7. In all patients for whom dosing information was available

8. NURSING MOTHERS: ROXICODONE

9. Drug Interactions:

10. ROXICODONE

11. ROXICODONE

12. ROXICODONE

13. ROXICODONE

14. ROXICODONE

15. ROXICODONE

16. ROXICODONE

17. ROXICODONE

18. ROXICODONE

19. ROXICODONE

20. ROXICODONE

21. ROXICODONE

22. ROXICODONE

23. ROXICODONE

24. ROXICODONE

25. ROXICODONE

26. ROXICODONE

27. ROXICODONE

28. ROXICODONE

29. ROXICODONE

30. ROXICODONE

31. ROXICODONE

32. ROXICODONE

33. ROXICODONE

34. ROXICODONE

35. ROXICODONE

36. ROXICODONE

37. ROXICODONE

38. ROXICODONE

39. ROXICODONE

40. ROXICODONE

41. ROXICODONE

42. ROXICODONE

43. ROXICODONE

44. ROXICODONE

45. ROXICODONE

46. ROXICODONE

47. ROXICODONE

48. ROXICODONE

49. ROXICODONE

50. ROXICODONE

51. ROXICODONE

52. ROXICODONE

53. ROXICODONE

54. ROXICODONE

55. ROXICODONE

56. ROXICODONE

57. ROXICODONE

58. ROXICODONE

59. ROXICODONE

60. ROXICODONE

61. ROXICODONE

62. ROXICODONE

63. ROXICODONE

64. ROXICODONE

65. ROXICODONE

66. ROXICODONE

67. ROXICODONE

68. ROXICODONE

69. ROXICODONE

70. ROXICODONE

71. ROXICODONE

72. ROXICODONE

73. ROXICODONE

74. ROXICODONE

75. ROXICODONE

76. ROXICODONE

77. ROXICODONE

78. ROXICODONE

79. ROXICODONE

80. ROXICODONE

81. ROXICODONE

82. ROXICODONE

83. ROXICODONE

84. ROXICODONE

85. ROXICODONE

86. ROXICODONE

87. ROXICODONE

88. ROXICODONE

89. ROXICODONE

90. ROXICODONE

91. ROXICODONE