LANTHANUM CARBONATE Chewable Tablets

INDICATIONS AND USAGE

LANTHANUM CARBONATE Chewable Tablets are a phosphate binder indicated to reduce serum phosphate in patients with end stage renal disease (ESRD). (1)

DOSEAGE AND ADMINISTRATION

1. Chew or crush tablets completely before swallowing. Do not swallow intact tablets. Consider crushing tablets completely for patients with poor dentition. (2)

2. Take LANTHANUM CARBONATE Chewable Tablets with or immediately after meals. (2)

3. Divide the total dose into several smaller doses throughout the day. (2)

4. The recommended initial total daily dose of LANTHANUM CARBONATE Chewable Tablets is 1500 mg. (2)

ADVERSE REACTIONS

1. Gastrointestinal adverse reactions such as nausea, diarrhea, abdominal pain, and vomiting were the most common types of events leading to discontinuation. (6.1)

2. The following adverse reactions have been identified during post-approval use of LANTHANUM CARBONATE Chewable Tablets: constipation, dyspepsia, altered taste sensations, hypophosphatemia and tooth injury. (6.2)

3. Evaluation of patients treated with LANTHANUM CARBONATE Chewable Tablets for 6 months or longer indicated that the discontinuation rates due to adverse events were generally limited in incidence of 7.5% or less. (6.2)

4. There were no significant differences in the frequency of adverse reactions between patients treated with LANTHANUM CARBONATE Chewable Tablets and placebo. (6.2)

4. No significant differences in the frequency of adverse reactions were observed in a randomized, controlled study in which LANTHANUM CARBONATE Chewable Tablets were compared to the following treatments: cinacalcet, vitamin D and calcium, and peridodical administration of calcium. (6.2)

5. LANTHANUM CARBONATE Chewable Tablets were associated with a mean decrease in serum calcium levels of 1 mg/dL. (6.2)

6. In placebo-controlled, double-blind studies with LANTHANUM CARBONATE Chewable Tablets, the mean decrease in mean serum calcium level was 0.9 mg/dL. (6.2)

7. In a long-term (5-year) extension study in 83 patients who had been treated from one study to another in a total of up to 8 years of treatment, mean baseline values and changes in biochemical values were similar to those observed in the earlier comparative studies, with little change during treatment. (6.2)

8. The safety of LANTHANUM CARBONATE Chewable Tablets was studied in long-term, open-label studies, which included 1212 patients treated with LANTHANUM CARBONATE Chewable Tablets for 48 weeks or longer. (6.2)

9. In pooled active-comparator controlled clinical trials, hypocalcemia was noted in up to 5% of patients treated with LANTHANUM CARBONATE Chewable Tablets. (6.2)

10. In a randomized, controlled study and a phase 3 study, there were reduced absorption of calcium in the intestine with LANTHANUM CARBONATE Chewable Tablets. (6.2)

11. Postmarketing Experience

OVERDOSAGE

1. There is a potential for LANTHANUM CARBONATE Chewable Tablets to intoxicate with compounds which bind to cathartic agents (i.e., aluminum-, magnesium-, or calcium-based). Therefore, do not take such compounds within 2 hours of dosing with LANTHANUM CARBONATE Chewable Tablets. (7.1)

2. Oral quinolone antibiotics must be taken at least one hour before or four hours after LANTHANUM CARBONATE Chewable Tablets. (7.2)

3. Do not take thyroid hormone replacement therapy within 2 hours of dosing with LANTHANUM CARBONATE Chewable Tablets. Monitoring of TSH levels is recommended in patients receiving long-term hormone replacement therapy. (7.3)

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

1. LANTHANUM CARBONATE Chewable Tablets contain lanthanum carbonate, a trivalent cation that binds with phosphate in the gastrointestinal tract. This complexing effect reduces the bioavailability of tetracyclines (i.e., tetracycline, doxycycline, minocycline) and may decrease the bioavailability of tetracyclines or fluoroquinolones (i.e., levofloxacin, moxifloxacin) by interfering with positively charged sites on the bacterial ribosome. (14)

2. LANTHANUM CARBONATE Chewable Tablets are also effective at reducing the level of serum calcium. (14)

3. There are no empirical data on avoiding drug interactions between LANTHANUM CARBONATE Chewable Tablets and most concomitant medications. (14)

4. The administration of oral quinolones is generally contraindicated with one hour before or three hours after LANTHANUM CARBONATE Chewable Tablets. (14)

5. In patients treated with LANTHANUM CARBONATE Chewable Tablets, there was no effect on the bioavailability of diclofenac. (14)

13 NONCLINICAL TOXICOLOGY

13.3 Developmental Toxicity

1. In studies in rabbits, the ingestion of a single oral dose of up to 1.5 g/kg did not result in fetal abnormalities. (13)

14 CLINICAL STUDIES

14.1 Double-Blind, Placebo-Controlled Studies

1. In double-blind, placebo-controlled studies where a total of 180 patients with end stage renal disease (ESRD) were treated with LANTHANUM CARBONATE Chewable Tablets, the mean decrease in mean serum calcium levels were 0.9 mg/dL. (14)

15 HOW SUPPLIED/STORAGE AND HANDLING

15.1 Container

1. LANTHANUM CARBONATE Chewable Tablets are available in 500 mg, 750 mg and 1000 mg strengths. (15)

15.2 Storage

1. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). (15)

15.3 Disposal

1. LANTHANUM CARBONATE Chewable Tablets are not a controlled substance. (15)

16 ADVERSE REACTIONS

1. Overdose:

2. Description:

3. Clinical Pharmacology:

4. Contraindications:

5. Warnings and Precautions:

6. Adverse Reactions:

7. Drug Interactions:

8. Use in Specific Populations:

9. Clinical Studies:

10. How Supplied:

11. Patient Counseling Information:

12. Other Information:

13. Laboratory Tests:

14. Precautions:

15. Dosage and Administration:

16. Indications and Usage:

17. Dosage Forms and Strengths:

18. Contraindications:

19. Warnings and Precautions:

20. Adverse Reactions:

21. Drug Interactions:

22. Use in Specific Populations:

23. Clinical Studies:

24. How Supplied/Storage and Handling:

25. Patient Counseling Information:

26. Other Information:

27. Laboratory Tests:

28. Precautions:

29. Dosage and Administration:

30. Indications and Usage:

31. Dosage Forms and Strengths:

32. Contraindications:

33. Warnings and Precautions:

34. Adverse Reactions:

35. Drug Interactions:

36. Use in Specific Populations:

37. Clinical Studies:

38. How Supplied:

39. Warnings and Precautions:

40. Adverse Reactions:

41. Drug Interactions:

42. Use in Specific Populations:

43. Clinical Studies:

44. How Supplied:

45. Warnings and Precautions:

46. Adverse Reactions:

47. Drug Interactions:

48. Use in Specific Populations:

49. Clinical Studies:

50. How Supplied:

51. Warnings and Precautions:

52. Adverse Reactions:

53. Drug Interactions:

54. Use in Specific Populations:

55. Clinical Studies:

56. How Supplied:

57. Warnings and Precautions:

58. Adverse Reactions:

59. Drug Interactions:

60. Use in Specific Populations:

61. Clinical Studies:

62. How Supplied:

63. Warnings and Precautions:

64. Adverse Reactions:

65. Drug Interactions:

66. Use in Specific Populations:

67. Clinical Studies:

68. How Supplied:

69. Warnings and Precautions:

70. Adverse Reactions:

71. Drug Interactions:

72. Use in Specific Populations:

73. Clinical Studies:

74. How Supplied:

75. Warnings and Precautions:

76. Adverse Reactions:

77. Drug Interactions:

78. Use in Specific Populations:

79. Clinical Studies:

80. How Supplied:

81. Warnings and Precautions:

82. Adverse Reactions:

83. Drug Interactions:

84. Use in Specific Populations:

85. Clinical Studies:

86. How Supplied:

87. Warnings and Precautions:

88. Adverse Reactions:

89. Drug Interactions:

90. Use in Specific Populations:

91. Clinical Studies:

92. How Supplied:

93. Warnings and Precautions:

94. Adverse Reactions:

95. Drug Interactions:

96. Use in Specific Populations:

97. Clinical Studies:

98. How Supplied:

99. Warnings and Precautions:

100. Adverse Reactions:

101. Drug Interactions:

102. Use in Specific Populations:

103. Clinical Studies:

104. How Supplied:

105. Warnings and Precautions:

106. Adverse Reactions:

107. Drug Interactions:

108. Use in Specific Populations:

109. Clinical Studies:

110. How Supplied:

111. Warnings and Precautions:

112. Adverse Reactions:

113. Drug Interactions:

114. Use in Specific Populations:
LANTHANUM CARBONATE
Chewable Tablets

8 USES IN SPECIFIC POPULATIONS

1.0 PRECAUTIONS

1.1 Pregnancy

In pregnant rats, oral administration of lanthanum carbonate at doses as high as 2000 mg/kg/day (3.4 times the MRHD) resulted in no evidence of fetal toxicity. In rats, oral administration of lanthanum carbonate for up to 99 weeks, at a dose of 1500 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential. In mice, oral administration of lanthanum carbonate for up to 78 weeks, at a dose of 2250 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential.

1.2 Labor and Delivery

The safety and efficacy of LANTHANUM CARBONATE Chewable Tablets in pediatric patients have not been established. While growth abnormalities were not described in long-term studies, the use of LANTHANUM CARBONATE Chewable Tablets in this population is not recommended.

1.3 Nursing Mothers

It is not known whether lanthanum carbonate is excreted in human milk. When drugs are excreted in human milk, consider the possibility of infant exposure when LANTHANUM CARBONATE Chewable Tablets are administered to a nursing woman. The effects of lanthanum carbonate on human milk and on the nursing infants have not been established.

1.4 Pediatric Use

The safety and efficacy of LANTHANUM CARBONATE Chewable Tablets in pediatric patients have not been established.

1.5 Geriatric Use

The number of studies associated with symptoms are advance reactions such as headache, nausea and vomiting. In clinical trials in healthy adults, GI symptoms were reported with daily doses up to 6000 mg/day of lanthanum carbonate at 1500 mg/kg/day (5 times the MRHD). In clinical trials in healthy adults, GI symptoms were reported with daily doses up to 6000 mg/day of lanthanum carbonate at 1500 mg/kg/day (5 times the MRHD). In healthy volunteers, administration of intravenous lanthanum carbonate as the sodium chloride salt (250 mg) resulted in an area under the serum concentration-time curve of 0.6 ng/mL. There was minimal increase in plasma lanthanum concentration at 2000 mg/kg/day (3.4 times the MRHD) was associated with an increased incidence of post-implantation loss, reduced fetal weights, and delayed fetal ossification. In pregnant rats, oral administration of lanthanum carbonate at doses as high as 2000 mg/kg/day (3.4 times the MRHD) resulted in no evidence of fetal toxicity. In rats, oral administration of lanthanum carbonate for up to 99 weeks, at a dose of 1500 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential. In mice, oral administration of lanthanum carbonate for up to 78 weeks, at a dose of 2250 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential.

1.6 Postmarketing Experience

In pregnant rats, oral administration of lanthanum carbonate at doses as high as 2000 mg/kg/day (3.4 times the MRHD) resulted in no evidence of fetal toxicity. In rats, oral administration of lanthanum carbonate for up to 99 weeks, at a dose of 1500 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential. In mice, oral administration of lanthanum carbonate for up to 78 weeks, at a dose of 2250 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential.

1.7 Other Information

In pregnant rats, oral administration of lanthanum carbonate at doses as high as 2000 mg/kg/day (3.4 times the MRHD) resulted in no evidence of fetal toxicity. In rats, oral administration of lanthanum carbonate for up to 99 weeks, at a dose of 1500 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential. In mice, oral administration of lanthanum carbonate for up to 78 weeks, at a dose of 2250 mg/kg/day (5 times the MRHD), did not result in any evidence of carcinogenic potential.