

(19) (KR)
(12) (A)

(51) . Int. Cl.7 (11) 2003-0097611
A61K 31/66 (43) 2003 12 31

(21) 10-2002-7013595 ()
(22) 2002 10 10
(62) 2000-7000680
: 2000 01 21 2001 04 04
2002 10 10
(86) PCT/US1998/14796 (87) WO 1999/04773
(86) 1998 07 17 (87) 1999 02 04

(30)	60/053,351	1997	07	22	(US)
	60/053,535	1997	07	23	(US)
	9717590.5	1997	08	20	(GB)
	9717850.3	1997	08	22	(GB)

(71) 07065 126

168 SK 11

(72) 07065 126

2
07065 126

07065 126

(74)

(54)

1

, , , , H2 ,

1 5		50ml 5		(270X) .	(
,)			
2 5		0.20mg/ml		50ml 5	(
	(,)	
270X)	.				
3	0.80mg/ml	50ml 1		(24 270X) .	(
(,)			
4	0.80mg/ml	50ml 1		(7 270X) .	(
(,)			
5 1 , 7 1		0.80mg/ml		50ml 4)
7 270X)	.	,			
6 2 , 3 4 1		0.40mg/ml		50ml 8)
(270X)	.	,			
7 5		0.20mg/ml		50ml 5	(
(270X)	.	,)	
8 5		4.0mg/ml		50ml 5	(
(270X)	.	,)	

, 1 1 , 1 2 , 2 1 , 1 2

, , (periprosthetic) , ,

가

가

가

가

[: H. Fleisch, Bisphosphonates In Bone Disease, From The Laboratory To The Patient, 2nd Edition, Parthenon Publishing(1995):].

가
가
가

(mineralization)

[: Boyce, B. F. Fogelman, I., Ralston, S. et al. (1984) Lancet 1(8381), pp. 821-824, and Gibbs, C. J., Aaron, J.E.; Peacock, M.(1986) Br. Med. J.292, p p. 1227-1229(1986):].

가

[: B.J. Gertz et al., Clinical Pharmacology of Alendronate Sodium, Osteoporosis Int., Suppl. 3: S13-16(1993) and B.J. Gertz et al., Studies of the oral bioavailability of alendronate, Clinical Pharmacology and Therapeutics, vol. 58, number 3, pp.288-298 (September 1995):].

가

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[: Fleisch, Id].

[: E.G. Lufkin et al., Pamidronate: An Unrecognized Problem in Gastrointestinal Tolerability, Osteoporosis International, 4: 320-322(1994):].

() [: P.C. De Groen, et al., Esophagitis Associated With The Use Of Alendronate, New England Journal of Medicine, vol. 335, no. 124, pp. 1016-1021(1996), D.O. Castell, Pill Esophagitis - The Case of Alendronate, New England Journal of Medicine, vol. 335, no. 124, pp. 1058-1059(1996), and U.A. Liberman et al., Esophagitis and Alendronate, New England Journal of Medicine, vol. 335, no. 124, pp. 1060-1070(1996):].

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가

(2)

가 : (1)

, 30

가

761,406 (Flora et al. 1988 8 2)

4,

가
 [: L. Morthensen, et al., Prevention Of Early Postmenopausal Bone Loss By Risedronate, Journal of Bone and Mineral Research, vol. 10, supp. 1, p.s 140(1995):]

가 5,366,965 (Stein. 1994 11 22)

, 20 120
 WO 95/30421 (Goodship et al. 1995 11 16

)
 . 1 1

가

1 2

, 1 1 , 1 2 , 2 1

가 (, 'GERD': gastrointestinal reflux disease), (, 가),

30
 가

(, 'GERD'), (, 가)

1 1 , 1 2 , 2 1 , 1 2

3 1 16 1

가

< >

, 1 2 , 1 1 , 1 2 , 2 1

가

, 3 1 16 1

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< >

, 1 2 , 2 1 , 1 2

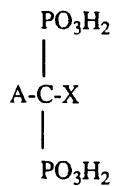
1 1

$$\begin{array}{ccccccccc}
 1 & 1 & & & 1 & 1 & , & 7 & 1 & , \\
 & . & 1 & 1 & , & & & & 7 & . & 1 & 1 \\
 & & , & 1 & 1 & & & & 2 & & 2
 \end{array}$$

1 2
2 1 2
. 1 2
. 1 2
. .
1 2
1 2 , 7
2 , 3 4
1 2
1

2 1 . 2 1 , 2 1 , 14 1 , 14 2 . 2 1 , 2 1 , 2 2 . 2

WO 95/30421(Goodship et al. 1995 11 16
())



A X H, OH, , NH₂, SH, , C1-C30 , C1-C30 , C1-C10
 NH₂, C1-C10 , C1-C10 , C1-C10 , ,

C1-C30, NH₂, C1-C10, NH₂, OH, SH C1-C10, 가

, A X , X A , 가

A가 H, OH
C1-C10 , X C1-C30 , C1-C30
C1-C10 .

가 A가 OH , X 3- , 4- - 1 -
- 1,1 - , .

-C1-C30-

가 ,

%

70mg
70mg

, 4 - - 1 - - 1,1 -

), 4 - - 1 -

2000 μ g/kg()

1.5

6000 μ g/kg()

10

,

8.75mg

140mg

1 1

1 1

17.5mg

70mg

35mg

70mg

1 2

1 2

8.75mg

35mg

17.5mg

35mg

2 1 1 2

140mg

70mg

,

35mg

140mg

H2

()

H2

(,) ()

pH 가

[: L.J. Hixson, et al., Current Trends in the Pharmacotherapy for Peptic Ulcer Disease, Arch. Intern. Med., vol. 152, pp.726-732(April 1992);].

H2

)

H2

30

24

30

12

H2

()

H2

()

(blister pack)'

가,

H2 ()

< >

가

1

가

4), 4 1 1 (2), 5 : (1), 1 (5), 4 1 (3
 (7) 5 (6), 5 (8). 2

:

(1) (pH 2),

(2) , 0.20mg/ml (pH 2).

(3) , 0.80mg/ml (pH 2).

(4) , 0.40mg/ml (pH 2).

(5) , 0.20mg/ml (pH 2).

(6) , 0.40mg/ml (pH 2).

0.90(%) NaCl() 147ml (L-585, 228000B003, Fisher Chemical) 960mg , 1.
 0M HCl() 3ml 가 , 1.0M HCl() 1.0M NaOH() pH 2

0ml , 30 5

1: 4 [(1) 50ml 5

2: 4 [(2) 50ml 5 0.20mg/ml

3: 5 [(3) 50ml 1 1 24 0.80mg/ml

4: 5 [(3) 50ml 1 1 7 0.80mg/ml

5: 6 0.80mg/ml [
 (3)] 50ml 4 1 1 , 7 4

6: 6 0.40mg/ml [
 (4)] 50ml 4 1 2 , 3 4 8

7: 8 0.20mg/ml [
 (5)] 50ml 5

8: 4 4.0mg/ml [
 (5)] 50ml 5

1

1 (1 1), 가 가

2 , 2 2

3 , 3 3

4 , 가 4 (5 2) (5
 3) . 4 4

5 , 가 가 5

6 , 6 6

7 , 7 7

8 , 8 8

(, 2) , 1 1 (1 (5) 1 3) 4) 가
 , (7) 2 (8) 2 , 6) , 가 ,

[1]

mg/ml				
1 (n=4) 0	5 1			

2 (n=4)	0.20	5 1			
3 (n=5)	0.80	1	24		
4 (n=5)	0.80	1	7	(5 2)	(5 3)
5 (n=6)	0.80	1 4 1 ,	7		
6 (n=6)	0.40	4 2 1			
7 (n=8)	0.20	5 1		(8 4)	
8 (n=4)	4.0	5 1	24	1	(4 3 ,

21 1

7 ((7 8). ,) 1 . . . 1 , 1 , ,

((7 8). ,) 1 . . . 1 , 1 , , 7

31 2

(4 7 8). ,) 1 . . . 1 , 2 , , 3

17.5mg
 (4 7 8). ,
 () 1 1 . 1 2 , , 3

4

2 1

140mg
 (14 7 8). ,
 () 1 1 . 2 1 , ,

5

1 2

70mg
 (4 7 8). ,
 (14 16) 1 1 . 2 1 , ,

6

2 5

2 5

7

5,358,941 (Bechard et al. 1994 1

0 24)

35mg

	1	4000
	45.48mg	182.72g
, NF	71.32mg	285.28g
, NF	80.0mg	320.0g
, NF	1.0mg	4.0g
, NF	2.0mg	8.0g

8.75, 17.5, 70 140mg.

70mg

8

75ml

	91.35mg
	22.5mg
	7.5mg
	1500mg
	56.25mg
	7.5mg
	75ml
1N ()	pH 6.75

, 75ml

8.75, 17.5, 35 140mg.

$$1, 2, 1, 1, 2, 1, 2, 1$$

가 ('GERD': gastrointestinal reflux disease), (가),

(57)

1. H_2 , , , H_2 , 3 , 1 ,

$$3. \quad \begin{matrix} 3 & 1 & 16 & 1 & & H_2 \\ , & & , & & & , \\ & & & & & H_2 \end{matrix}$$

$$4. \quad \begin{matrix} 1 & 1 & , & 1 & 2 & , & 2 & 1 & & 1 & & 2 \\ H2 & & & & H2 & & & & & & & , \\ , & & & & H2 & & & & & & & \end{matrix}$$

5.

(b) 1 H2

7.

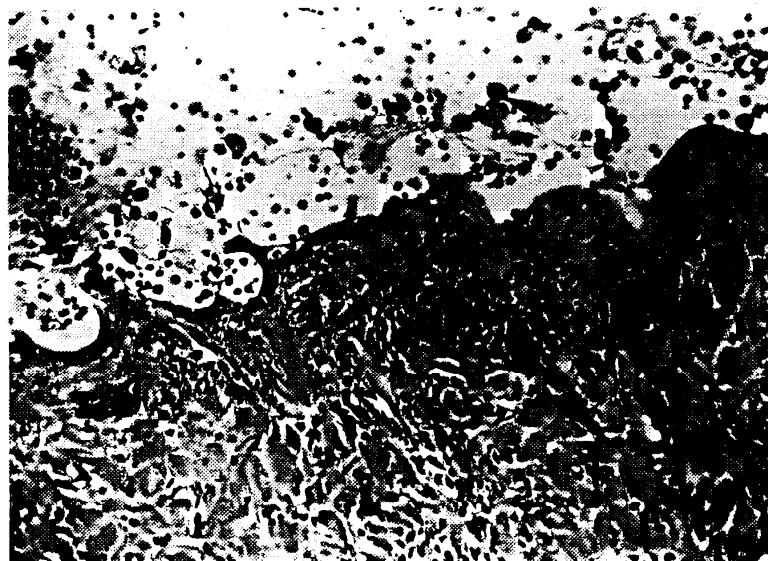
5 6

H2

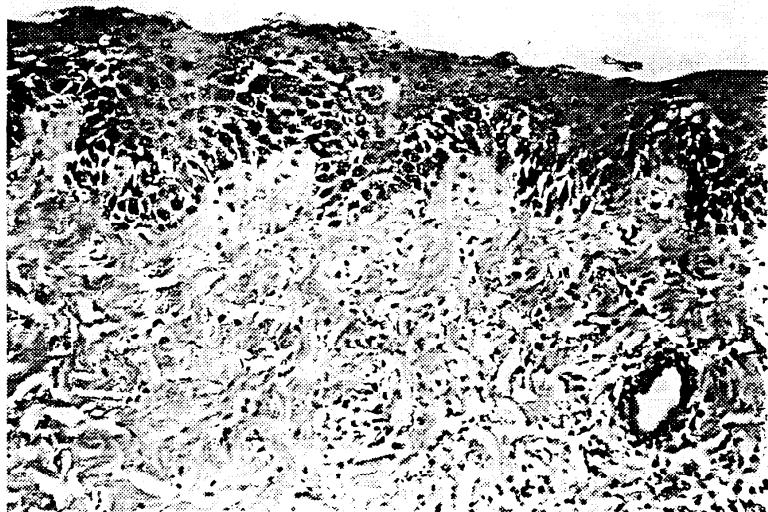
가



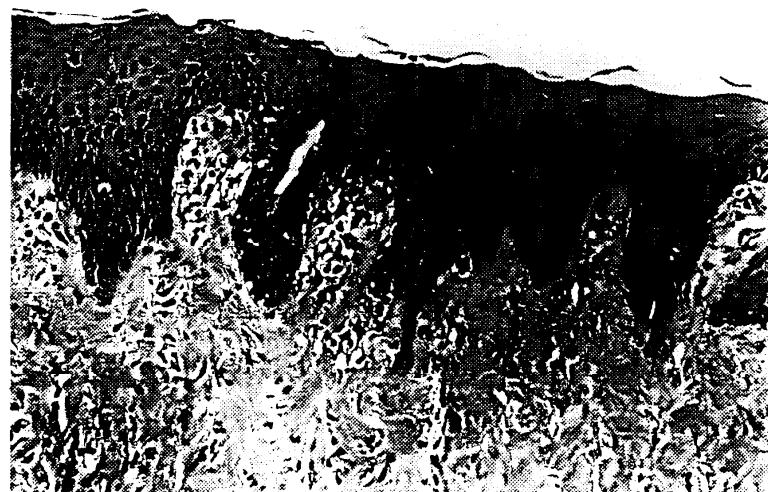
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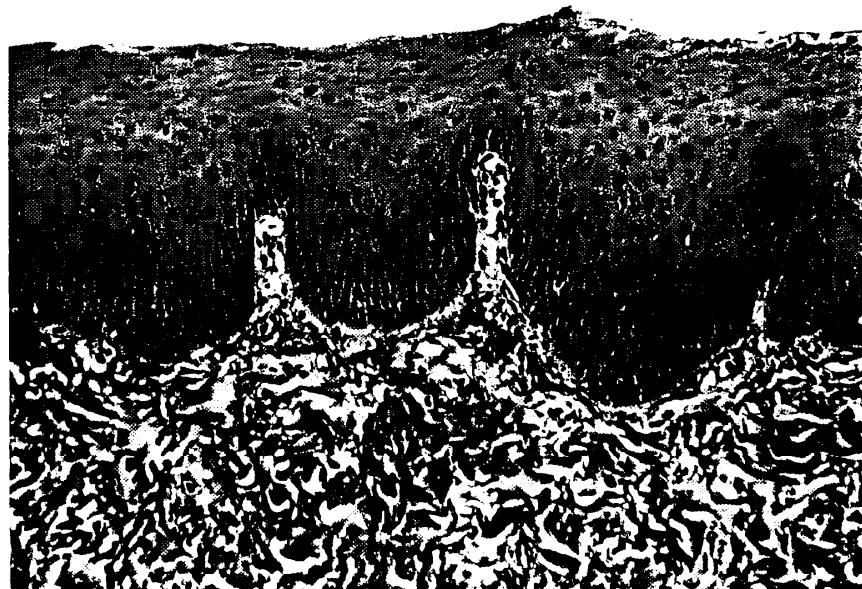
3



4



5



6



7



