<안전성·유효성 심사관련 제출자료 목록>

○ 관련조항 : 의약품등의안전성·유효성심사에관한규정 (식품의약품안전청고시 제2003-17호, 2003.4.14.) 제2조제1항제1호 (단일제 → 단일제) 및 주6, 제7조제3항

구분 \ 자료번호	1	2	3		4								5			6		7	8
			가	나	가	나	다	라	마	바	사	아	가	나	다	가	나		
1. 제출자료	○	○	○	○	○	○	○	○	△	△	△	△	○	○	○	○	○	○	○
2. 제출여부	○	○	○	○	X	X	×	×	×	×	×	X	X	X	X	○	X	○	○
3. 면제사유	동규정 제7조제2항 및 제7조제3항에 따른 비임상시험자료(독성 및 약리시험자료) 및 가교자료 제출면제가능																		

*주 : 자료번호 1 내지 8은 동규정 제5조제1항제1호 내지 제8호의 자료를 말한다.

○ 제출자료 목록

1. 기원 또는 발견 및 개발경위에 관한 자료

2. 구조결정·물리화학적 성질에 관한 자료(기준 및 시험방법 포함)

3. 안정성에 관한 자료
   가. 36개월간의 장기보존시험자료 및 9개월간의 가속시험자료
   나. 가혹시험자료

4. 비임상시험성적에 관한 자료
1) An oral interaction study with bosentan and the immunosuppressant drugs cyclosporin A and tacrolimus in the rat

5. 임상시험성적에 관한 자료
가. 임상약리시험
1) Multiple ascending oral dose study of the tolerability, pharmacodynamics and pharmacokinetics of the endothelin receptor antagonist Ro 47-0203 in healthy male volunteers / B-159037 (BD14471)
2) Single and multiple dose pharmacokinetics of bosetan in patients with impaired liver function as compared to healthy subjects (AC-052-107)
3) A study to assess the pharmacokinetics of bosentan (Ro 47-0203) in subjects with

severe renal dysfunction compared to subjects with normal renal function (AC-052-104)

5) A single-dose study to investigate the relative bioavailability of an 125mg tablet of bosentan in comparison with an oral suspension of 125mg bosentan and to investigate the effect of food on the bioavailability of the 125mg tablet and 62.5mg tablet, given as 2×62.5mg, in healthy male subjects (AC-052-106)
6) A study to investigate the pharmacokinetics of bosentan in healthy subjects when given concomitantly with ketoconazole (AC-052-108)
7) A study to investigate the possible drug-drug interaction between bosentan and simvastatin in healthy subjects (AC-052-109)
8) A study on the possible interaction between the endothelin receptor antagonist bosentan and the anti-diabetic glibenclamide in healthy volunteers. (AC-052-103)
9) The effect of bosentan on the pharmacokinetics of digoxin in healthy male subject (B-159044)
10) The effect of bosentan on the pharmacokinetics and pharmacodynamics of warfarin in healthy male subjects (B-159043)
11) A Renal Hemodynamic and Pharmacokinetic Study of Bosentan(Ro 47-0203) and Cyclosporine A (Sandimmun Neoral) in Health Volunteers (BD15083).
12) Excretion Balance, Pharmacokinetic and Metabolism Study after a Single P.O. and a Single I.V. Dose of [^{14}C]-Labeled Ro 47-0203 in Healthy Male Volunteers(B-159041)
13) The effect of multiple oral dose treatment with Ro 47-0203 on the elimination and absorption of Ro 47-0203 in healthy male subjects (B-159038)
14) A single ascending oral dose study of the tolerability, safety, pharmacodynamics and pharmacokinetics of the endothelin receptor antagonist Ro 47-0203 in young healthy male volunteers (B-162282)
15) A comparative investigation of the tolerability, safety, and pharmacokinetics of single-dose bosentan in Japanese and caucasian healty subjects (AC-052-110)
16) A comparative investigation of the pharmacokinetics of multiple-dose bosentan in japanese and caucasian healthy subjects (AC-052-111)

나. 치료적 탐색시험

1) A phase II, multicenter, randomized, double-blind, parallel-group, dose-resposne study comparing the efficacy and safety of 100, 500, 1000mg QD, and 1000mg BID of bosentan with placebo in patients with mild to modeate essential hypertension (B-165230)

다. 치료적 확증시험

1) A double-blind, randomized, placebo-controlled study to assess the effects of Ro 47-0203(bosentan) on exercise capacity in patients with pulmonary arterial hypertension (B-01.023)
2) A pilot double-blind, randomized, placebo-controlled study to assess the effects of Ro 47-0203(bosentan) on exercise capacity, hemodynamics, and quality of life of patients with primary pulmonary hypertension or pulmonary hypertension due to scleroderma (B-00.028)
3) Multicenter, open-label, single-arm, safety study of bosentan in patients with pulmonary arterial hypertension (B-02.010)
4) A double-blind, randomized, placebo-controlled study to assess the effect of Tracleer(bosentan) in combination with the initiation of epoprostenol therapy on cardiopulmonary hemodynamics in patients with severe pulmonary arterial hypertension (AC-052-355)
5) Pharmacokinetics and tolerability of Tracleer(bosentan) in pediatric patients with pulmonary arterial hypertension: Single and muliple oral doses (AC-052-356)
6) A double-blind, randomized, placebo-controlled trial to assess the effects of Ro 47-0203(Bosentan) on the clinical status of patients with advanced chronic heart failure and the pharmacokinetics of Ro 47-0203 (Bosentan) (B-166849)
7) 폐고혈압증 환자에 대한 보센탄의 일반 임상 시험 (AC-052-363)
8) 폐고혈압증 환자에 대한 보센탄의 일반 임상 시험 - 추가보고서 (AC-052-363)

6. 국내 유사제품과의 비교검토 및 당해 의약품등의 특성에 관한 자료

1) 영국의약품집 수재 : Actelion pharmaceuticals UK "Tracleer 62.5, 125mg film-coated tablets"
2) 미국 PDR 수재 : Actelion pharmaceuticals US "Tracleer 62.5, 125mg film-coated tablets"

7. 국내 유사제품과의 비교표