キネレット皮下注 100 mg シリンジ

＜アナキンラ（遺伝子組換え）＞

第 2 部（モジュール 2）
CTD の概要（サマリー）

2.6　非臨床試験の概要文及び概要表

2.6.3　薬理試験概要表

Swedish Orphan Biovitrum Japan 株式会社

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2.6.3 薬理試験概要表

2.6.3.1 薬理試験：一覧表 test article: anakinra

Type of study	Test system	Method of administration	Duration of dosing (frequency)	Doses (mg/kg/day)	Testing facility	Study no.	eCTD location
Primary pharmacodynamics							
	All primary pharmacodynamic studies were taken from the literature and reported in Module [2.6.2]; no data are tabulated here.						
Secondary pharmacodynamics							
	No secondary pharmacodynamic studies were reported in Module [2.6.2]						
Safety pharmacology							
A general pharmacology study of anakinra *in vivo* in mice, rats, and dogs; *ex vivo* using guinea pig ileum. The study included safety pharmacology endpoints. (GLP)	Mouse	i.v.	10 mL/kg (q.d. × 1)	0, 70, 200, 720; General activity and behavior 0, 20, 70, 200; CNS and GI assessments	[redacted] Japan	[redacted]66-80]	[4.2.1.3]
	Rat	i.v.	5 mL/kg (q.d. × 1)	0, 20, 70, 200			
	Dog	i.v.	1 mL/kg at 2 mL/min (q.d. × 1)	0 (vehicle), followed by 10, 30, or 90			
	Guinea pig ileum	*Ex vivo*	q.d. × 1	0, 0.1, 0.3, 0.9 mg/mL			
Pharmacodynamic drug interactions							
	All Pharmacodynamic drug interaction studies were taken from the literature and reported in Module [2.6.2]; no data are tabulated here.						

Abbreviations: CNS, Central nervous system; eCTD, Electronic Common Technical Document; GI, Gastrointestinal; GLP, Good Laboratory Practice; i.v., Intravenous; no., Number; q.d., Once daily.

2.6.3.2 効力を裏付ける試験

Primary pharmacodynamics				**Test article: Anakinra**		
All primary pharmacodynamic studies are presented in Module 2.6.2, Section [2.6.2.2] The details of these studies were taken from the literature; results are not tabulated here.						
Type of study	**Species/strain**	**Method of administration**	**Doses/concentrations**	**Sex/ no. per group**	**Noteworthy findings**	**Study no.**
N/A	N/A	N/A	N/A	N/A	N/A	N/A

Abbreviations: N/A, Not applicable; no., Number.

2.6.3.3 副次的薬理試験

Secondary pharmacodynamics				**Test article**: Anakinra		
No secondary pharmacodynamic studies conducted with anakinra were summarized in Module [2.6.2] or tabulated in this document.						
Type of study	**Species/strain**	**Method of administration**	**Doses/ concentrations**	**Sex/ no. per group**	**Noteworthy findings**	**Study no.**
N/A	N/A	N/A	N/A	N/A	N/A	N/A

Abbreviations: N/A, Not applicable; no., Number.

2.6.3.4 安全性薬理試験

Safety pharmacology					Test article: Anakinra		
Organ systems evaluated	**Species/strain**	**Method of administration**	**Doses[a] (mg/kg)**	**Sex/no. per group**	**Noteworthy findings**	**GLP compliance**	**Study no.**
General activity and behavior	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 70, 200, 720	M/6	No salient findings	Yes	[redacted]66-80]
CNS (locomotor activity)	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	
CNS (effects on thiopental-induced sleep)	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	
CNS (effects on acetic acid-induced writhing)	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	
CNS (effects on maximal electroconvulsions)	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	
CNS (effects on pentetrazol-induced convulsions)	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 20, 70, 200	M/6	No effects on pentetrazol-induced convulsions and death	Yes	
CNS (convulsive activity)	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	
GI (effects on intestinal transport of charcoal meal)	Mouse/Crj:CD-1 (ICR)	i.v. (10 mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	
CNS (effects on body temperature)	Rat/Crj:Wistar	i.v. (5mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	
Water and metabolic electrolytes (effects on urinary volume, electrolytes, creatinine clearance, and urinary NAG)	Rat/Crj:Wistar	i.v. (5mL/kg)	0, 20, 70, 200	M/6	No salient findings	Yes	

Safety pharmacology					**Test article:** Anakinra		
Organ systems evaluated	**Species/strain**	**Method of administration**	**Doses[a] (mg/kg)**	**Sex/no. per group**	**Noteworthy findings**	**GLP compliance**	**Study no.**
Autonomic nervous system and smooth muscle (effects on spontaneous movements and contraction of isolated ileum induced by acetylcholine, histamine, and barium)	Guinea pig/ Crj:Hartley (ileum)	Ileum immersed in bathing solution Anakinra added to tissue bath	0, 0.1, 0.3, 0.9 mg/mL	M/4	No salient findings	Yes	[redacted] 66-80]
Respiratory and cardiovascular systems (effects on respiration, BP, femoral artery blood flow, HR, and ECG)	Dog/Beagle	i.v.	0 (vehicle), followed by 10, 30, or 90	M/3	Respiration rate increase during the first i.v. administration (vehicle) of each dose group BP decrease during the first i.v. administration (vehicle) of each group Blood flow increase in the 30 g/kg group, n=1, and subsequent decrease in all groups HR increase in the 30 g/kg group, n=1, and subsequent decrease in all groups Decrease in R-wave amplitude in all groups T-wave appearance in all groups	Yes	

Abbreviations: BP, Blood pressure; CNS, Central nervous system; ECG, Electrocardiogram; GI, Gastrointestinal; GLP, Good Laboratory Practice; HR, Heart rate; i.v., Intravenous; M, Male; NAG, N-acetyl-β-D-glucosaminidase; n, Sample size; no., Number.

a. Single dose unless specified otherwise

2.6.3.5 薬力学的薬物相互作用

Pharmacodynamic drug interactions				Test article: Anakinra		
No pharmacodynamic drug interaction studies conducted with anakinra were summarized in Module [2.6.2] or tabulated in this document.						
Type of study	**Species/strain**	**Method of administration**	**Doses/ concentrations**	**Sex/ no. per group**	**Noteworthy findings**	**Study no.**
N/A	N/A	N/A	N/A	N/A	N/A	N/A

Abbreviations: N/A, Not applicable; no., Number.