



ERRATUM 1 TO THE MARCH 2007 INVESTIGATOR'S BROCHURE

PF-0044687

June 2007

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Safety and Risk Management

Pfizer Inc and Affiliates

An error has been noticed in Table 3 of the March 2007 PF-00446687 Investigator's Brochure.

The following elements have been removed from the section of table entitled "PF-00446687 had $IC_{50} > 10 \mu M$ (4.7 mg/mL) for the following targets": the Histamine (H_2) receptor, the Melanocortin (human MC_1 & MC_4) receptors, the Muscarinic (M_2) receptor, the Opiate (κ) receptor, the sigma (non-selective) receptors, and the 5-HT transporter (human). These data are included in the table in the section entitled 'Summary of binding IC_{50} values (μM) for PF-00446687'.

An updated version of Table 3 is attached below.

Table 3. Summary of the In Vitro General and Safety Pharmacology Studies with PF-0044687

Receptors		Ion Channels	Enzymes / Uptake Transporters
PF-0044687 had IC ₅₀ >10 µM (4.7 mg/mL) for the following targets:			
Adenosine	A ₁ , A ₂ , A ₃ (human)	[³ H]-dofetilide binding to HEK293 cells expressing human recombinant hERG (I _{Kr}) See section 5.1.3.1.2.	Phosphodiesterase (human 2,3,4,5,6, and 11)
Adrenergic	α ₁ (non-selective, rat cerebral cortex), α _{2A} , α _{2B} , β ₁ , β ₂ , β ₃ (human)		
Angiotensin-II	AT ₁ AT ₂ (human)		Acetylcholinesterase (human)
Benzodiazepine	BDZ (rat cerebral cortex)		Choline transporter
Bradykinin	B ₂ (human)		Monoamine Oxidase –A (human)
Cannabinoid	CB ₁ , CB ₂ (human)		Monoamine Oxidase –B (rat brain)
Calcitonin gene-related peptide	CGRP (human)		Tyrosine hydroxylase (rat striatum)
Dopamine	D ₁ , D _{2s} , D ₃ , D _{4,4} (human)		Na ⁺ /K ⁺ ATPase (dog kidney)
Endothelin	ET _B (human)		
GABA	GABA _A , GABA _B		

n = 2, unless otherwise stated.

NMDA = N-methyl-D-aspartate; Na⁺/K⁺ = sodium/potassium ion ratio; ATPase = adenosine triphosphatase;

NE = norepinephrine; DA = dopamine; 5-HT = serotonin;

Table 3. Summary of the In Vitro General and Safety Pharmacology Studies with PF-0044687 (Continued)

Receptors		Ion Channels	Enzymes / Uptake Transporters
PF-0044687 had IC ₅₀ >10 µM (4.7 mg/mL) for the following targets:			
Glutamate	NMDA (rat cerebral cortex)	Action potentials recorded from dog isolated Purkinje fibres See section 5.1.3.1.2.	NE transporter (human)
Glycine	Strychnine-insensitive		DA transporter (human)
Histamine	H ₁ (guinea-pig cerebellum), H ₃		GABA transporter
L1	Peripheral		Choline transporter
Leukotriene	LTD4 (human)		Guanylate cyclase
Ghrelin	Human		GABA transaminase
ML	ML ₁ (chicken), ML ₂ (hamster)		Catechol-O-methyl transferase
Muscarinic	M ₁ , M ₃ (human)		NO synthase (iNOS)
Neurokinin	NK ₁		Metalloproteinase (1,2,3,7 and 9 human)
N	(neuronal) (alpha -BGTX-insensitive)		Neutral endopeptidase (human)
Opiate	mu, δ2 (human)		Angiotensin Converting Enzyme (human)
Nicotinic	Neuronal, non-selective (rat cerebral cortex)		HIV-1 protease
Nociceptin	ORL1 (human)		Tryptase (human)
Oxytocin	OT (human)		Elastase
Phencyclidine	PCP (rat)		Phosphatase 1B (human)
Purinoreceptors	P2X (rat)		ZAP70 kinase
Serotonin	5-HT _{1A} (human), 5-HT _{1B} (rat cerebral cortex), 5-HT _{1D} (bovine), 5-HT _{2A} , 5-HT _{2B} , 5-HT _{2C} , 5-HT ₃ , 5-HT _{4e} , 5-HT ₆ , 5-HT ₇ (human)		P55fyn kinase

n = 2, unless otherwise stated.

NMDA = N-methyl-D-aspartate; Na⁺/K⁺ = sodium/potassium ion ratio; ATPase = adenosine triphosphatase; NE = norepinephrine; DA = dopamine; 5-HT = serotonin.

Table 3. Summary of the In Vitro General and Safety Pharmacology Studies with PF-00446687(Continued)

Receptors		Ion Channels	Enzymes / Uptake Transporters
PF-00446687 had IC ₅₀ >10 µM (4.7 mg/mL) for the following targets:			
Somatostatin	Sst4, sst5		P56lyn kinase
Glucocorticoid	GR (human)		Abl kinase
Estrogen	ERalpha		MAP kinase
Tyrosine hydroxylase	TH		Calcium modulated kinase
Urotensin	UT-II		
Vasoactive intestinal peptide	VPAC1 (human)		
Vasopressin	V1a (human)		
Ryanodine	RY3		
Chemokines	CCR1 (human)		
Summary of binding IC ₅₀ values (µM) for PF-00446687:			
Receptor		IC ₅₀ µM	
Histamine	H ₂	3.8	
Melanocortin	MC1	3.9	
Melanocortin	MC4	1.2	
Muscarinic	M1	20.4	
Muscarinic	M2	1.1	
Opioid	Kappa	5.1	
Opioid	Mu	10.7	
Neurokinin	NK1	11.8	
Sigma	Sigma (non-selective)	0.43	
Amine transporter	Noradrenaline transporter	35.9	
Amine transporter	5-HT transporter	2.2	
Ca ²⁺ channels	L-type, verapamil site	28.5	
Na ⁺ channels	Site 2	0.76	

n = 2, unless otherwise stated.

NMDA = N-methyl-D-aspartate; Na⁺/K⁺ = sodium/potassium ion ratio; ATPase = adenosine triphosphatase; NE = norepinephrine; DA = dopamine; 5-HT = serotonin; DHP = dihydropyridine; K⁺ = potassium ion; ATP = adenosine triphosphate; Ca²⁺ = Calcium ion; Na⁺ = sodium ion; Cl⁻ = chloride ion ; nH = Hill slope.