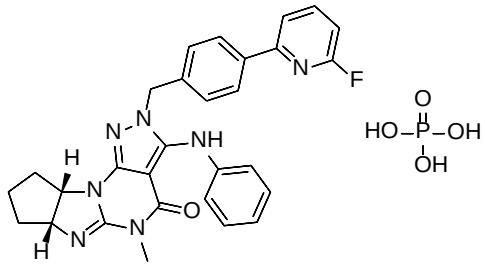
Product data sheet

MedKoo Cat#: 522622 Name: ITI-214 phosphate CAS#: 1642303-38-5 (phosphate) Chemical Formula: $C_{29}H_{29}FN_7O_5P$ Molecular Weight: 605.57	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

ITI-214 is an orally active, potent and Selective Inhibitors of Phosphodiesterase 1 for the Treatment of Cognitive Impairment Associated with Neurodegenerative and Neuropsychiatric Diseases. ITI-214 exhibited picomolar inhibitory potency for PDE1, demonstrated excellent selectivity against all other PDE families, and showed good efficacy in vivo. Currently, this investigational new drug is in Phase I clinical development and being considered for the treatment of several indications including cognitive deficits associated with schizophrenia and Alzheimer's disease, movement disorders, attention deficit and hyperactivity disorders, and other CNS and non-CNS disorders.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	30.0	49.54

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.65 mL	8.26 mL	16.51 mL
5 mM	0.33 mL	1.65 mL	3.30 mL
10 mM	0.17 mL	0.83 mL	1.65 mL
50 mM	0.03 mL	0.17 mL	0.33 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Snyder GL, Prickaerts J, Wadenberg ML, Zhang L, Zheng H, Yao W, Akkerman S, Zhu H, Hendrick JP, Vanover KE, Davis R, Li P, Mates S, Wennogle LP. Preclinical profile of ITI-214, an inhibitor of phosphodiesterase 1, for enhancement of memory performance in rats. Psychopharmacology (Berl). 2016 Sep;233(17):3113-24. doi: 10.1007/s00213-016-4346-2. Epub 2016 Jun 24. PMID: 27342643; PMCID: PMC4980415.

In vivo study

1. Snyder GL, Prickaerts J, Wadenberg ML, Zhang L, Zheng H, Yao W, Akkerman S, Zhu H, Hendrick JP, Vanover KE, Davis R, Li P, Mates S, Wennogle LP. Preclinical profile of ITI-214, an inhibitor of phosphodiesterase 1, for enhancement of memory performance in rats. Psychopharmacology (Berl). 2016 Sep;233(17):3113-24. doi: 10.1007/s00213-016-4346-2. Epub 2016 Jun 24. PMID: 27342643; PMCID: PMC4980415.

2. Golshiri K, Ataei Ataabadi E, Rubio-Beltran E, Dutheil S, Yao W, Snyder GL, Davis RE, van der Pluijm I, Brandt R, van den Berg-Garrelds IM, MaassenVanDenBrink A, de Vries R, Danser AHJ, Roks AJM. Selective PDE1 inhibition ameliorates vascular function, reduces inflammatory response, and lowers blood pressure in ageing animals. J Pharmacol Exp Ther. 2021 Jun 7:JPET-AR-2021-000628. doi: 10.1124/jpet.121.000628. Epub ahead of print. PMID: 34099502.

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7. Bioactivity

Biological target: ITI-214 is a PDE1 inhibitor with Ki of 58 pM.

In vitro activity

ITI-214 was found to potently inhibit the activity of full-length recombinant r-hPDE1A (Ki = 34 pM), r-hPDE1B (Ki = 380 pM), and r-hPDE1C (Ki = 37 pM) enzymes transiently expressed in HEK cells. The compound expressed >1000-fold greater activity toward PDE1 isoforms compared with the next nearest PDE family enzyme, PDE4D (Ki = 33 nM) and 10,000–300,000-fold selectivity toward all other PDE enzyme families (Table 1).

Reference: Psychopharmacology (Berl). 2016 Sep;233(17):3113-24. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4980415/

In vivo activity

To evaluate drug effects on the early consolidation of memory, ITI-214 was administered orally to groups of rats at a range of doses (1–10 mg/kg) shortly after the completion of the T1 period. ITI-214 administration resulted in an intermediate increase in d2, i.e., different from chance level, in animals that had received a 3 mg/kg dose within 4 min after T1 (Fig. 2, top panel). In this case, the d2 did not differ from vehicle ($F(3,92) = 1.88$, n.s.). Drug effects on the late phase of memory consolidation were studied by administering ITI-214 (0.1–3 mg/kg) 3 h after the T1 period. Twenty-one hours later, during T2, animals that had been treated with doses of 1 or 3 mg/kg ITI-214 displayed increases in d2 scores compared with chance performance and significantly different from vehicle ($F(4,67) = 4.18$, $p < 0.01$) with a full effective dose of 1 mg/kg. The results indicate that ITI-214 improved late consolidation of memory (Fig. 2).

Reference: Psychopharmacology (Berl). 2016 Sep;233(17):3113-24. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4980415/