# PRODUCT INFORMATION

## PF-06650833

*Item No. 28397*

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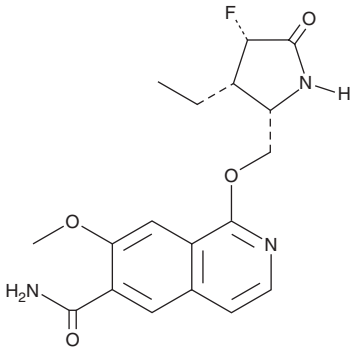
| **CAS Registry No.:** | 1817626-54-2 |
| **Formal Name:** | 1-[[(2S,3S,4S)-3-ethyl-4-fluoro-5-oxo-2-pyrrolidinyl]methoxy]-7-methoxy-6-isoquinolinecarboxamide |
| **Synonyms:** | Interleukin-1 Receptor-associated Kinase 4 Inhibitor, IL-1 Receptor-associated Kinase 4 Inhibitor, IRAK4 Inhibitor |
| **MF:** | $C_{18}H_{20}FN_3O_4$ |
| **FW:** | 361.4 |
| **Purity:** | ≥98% |
| **UV/Vis.:** | $\lambda_{max}$: 230, 348, 495 nm |
| **Supplied as:** | A solid |
| **Storage:** | -20°C |
| **Stability:** | ≥2 years |




*Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.*

### Laboratory Procedures

PF-06650833 is supplied as a solid. A stock solution may be made by dissolving the PF-06650833 in the solvent of choice, which should be purged with an inert gas. PF-06650833 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of PF-06650833 in ethanol is approximately 2 mg/ml and approximately 30 mg/ml in DMSO and DMF.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of PF-06650833 can be prepared by directly dissolving the solid in aqueous buffers. PF-06650833 is slightly soluble in PBS, pH 7.2. We do not recommend storing the aqueous solution for more than one day.

### Description

PF-06650833 is an inhibitor of IL-1 receptor-associated kinase 4 (IRAK4; $IC_{50}$ = 0.2 nM).[1] It is selective for IRAK4 over a panel of 268 kinases at 200 nM but also inhibits IRAK1, MAP kinase-interacting serine/threonine protein kinase 2 (MNK2), leucine-rich repeat kinase 2 (LRRK2), CDC-like kinase 4 (Clk4), and casein kinase 1γ1 (CK1γ1) by greater than 70% at 200 nM. PF-06650833 (100 nM) reduces secretion of DNA from primary human neutrophils stimulated by the toll-like receptor 7 (TLR7) agonist R-837 (imiquimod; Item No. 14956) and decreases IFN regulatory factor 5 (IRF5) nuclear translocation induced by the synthetic TLR7/8 ligand R-848 (Item No. 14806) in primary human peripheral blood mononuclear cells (PMBCs).[2] It decreases paw volume in a rat model of collagen-induced arthritis when administered at a dose of 100 mg/kg once per day.[1] Dietary administration of PF-06650833 reduces serum levels of the autoantibodies anti-dsDNA, anti-SSA, and anti-RNP and decreases kidney glomerular tuft area in a mouse model of systemic lupus erythematosus (SLE) induced by the isoprenoid alkane pristane.[2]

### References


1. Lee, K.L., Ambler, C.M., Anderson, D.R., *et al.* Discovery of clinical candidate 1-{[(2S,3S,4S)-3-ethyl-4-fluoro-5-oxopyrrolidin-2-yl]methoxy}-7-methoxyisoquinoline-6-carboxamide (PF-06650833), a potent, selective inhibitor of interleukin-1 receptor associated kinase 4 (IRAK4), by fragment-based drug design. *J. Med. Chem.* **60(13)**, 5521-5542 (2017).
2. Winkler, A., Sun, W., De, S., *et al.* The interleukin-1 receptor-associated kinase 4 inhibitor PF-06650833 blocks inflammation in preclinical models of rheumatic disease and in humans enrolled in a randomized clinical trial. *Arthritis Rheumatol.* **73(12)**, 2206-2218 (2021).





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