Product Information

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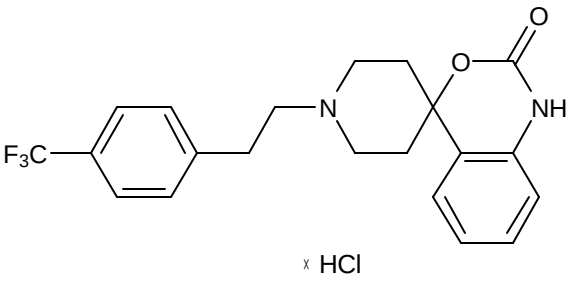
RS 102895 hydrochloride

Catalog Number **R1903**
Store at Room Temperature

CAS RN 300815-41-2 (free base)
Synonym: 1′-[2-[4-(Trifluoromethyl)phenyl]ethyl]-spiro[4H-3,1-benzoxazine-4,4′-piperidin]-2(1H)-one hydrochloride



x HCl

Product Description
Molecular Formula: $C_{21}H_{21}F_3N_2O_2$ x HCl
Molecular Weight: 426.86

Chemokine receptors and their ligands play major roles in asthma, atherosclerosis, cancer, inflammation (IBD, MS, RA), and infectious diseases such as AIDS. Chemokine receptors are seven-transmembrane G protein-coupled receptors. They have been the targets of intense drug discovery and development. Chemokine receptor classification is based on the spacing of the N-terminal cysteine residues and designated as CXC (α-subclass), CC (β-subclass), and CX_3C (minor subclass). CCR2 belongs to the β-subclass of chemokine receptors and is also known as monocyte chemoattractant protein-1 (MCP-1) after one of its major natural ligands (MCP-1, MCP-2, MCP-3, and MCP-4). CCR2 receptors are among the inducible (inflammatory) chemokine receptors in contrast to the constitutive (developmentally-regulated) chemokine receptors. Two subtypes of CCR2 receptors exist and are referred to as CCR2a and CCR2b. The CCR2b receptor isoform is five-fold more sensitive to chemotaxis-induction by MCP-1 and unlike CCR2a, results in calcium influx.

RS 102895 is chemokine receptor CCR2 antagonist, which belongs to the novel structural spiropiperidine class. It is potent and specific for the CCR2b receptor. The binding of RS 102895 to the CCR2b receptor has been carefully mapped through mutagenesis and binding studies using the cloned receptor. In Chinese hamster lung cells (ATCC CRL-1657) stably transfected and expressing human CCR2b receptor, RS 102895 displayed IC_{50} values of 360 nM and 17.8 mM, respectively, for MCP-1/CCR2 vs. MIP-1α/CCR1 binding. In chemotaxis studies using THP-1-5X cells, RS 102895 displayed an IC_{50} value of 1.7 mM for MCP-1, while achieving an IC_{50} value of 37 mM for RANTES, which acts through the CCR1. In calcium influx studies using ATCC CRL-1657 cells, RS 102895 displayed IC_{50} values of 31 nM and 130 nM, respectively, for MCP-1 vs. MCP-3.

Administration of CCR2 antagonists or neutralizing antibodies for its ligand, MCP-1, reduces inflammation in animal models including adjuvant arthritis, lung granuloma, and glomerulonephritis. Animals genetically deleted of CCR2 or MCP-1 are protected from inflammation and atherosclerosis induced by bacterial products and high fat diets. These findings make it important to have potent and selective antagonists for the further understanding of CCR2b post receptor signaling events that mediate these pathological conditions. RS 102895 exhibits the requisite selectivity and potency for the CCR2b receptor to be a valuable tool to further study these mechanisms.

Precautions and Disclaimer
This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Preparation Instructions
RS 102895 is soluble (>10 mg/ml) in DMSO.

Storage/Stability
Store at room temperature.

References

1. Proudfoot, A.E., Chemokine receptors: multifaceted therapeutic targets. Nature Rev. Immunol., **2**, 106-115 (2002).
2. Mirzadegan, T., et al., Identification of the binding site for a novel class of CCR2b chemokine receptor antagonists. J. Biol. Chem., **275**, 25562-25571 (2000).
3. Onuffer, J.J., and Horuk, R., Chemokines, chemokine receptors and small-molecule antagonists: recent developments. Trends in Pharm. Sciences, **23**, 459-467 (2002).

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