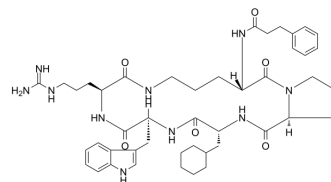


## PMX 205

Cat. No.:	HY-110136
CAS No.:	514814-49-4
Molecular Formula:	C <sub>45</sub> H <sub>62</sub> N <sub>10</sub> O <sub>6</sub>
Molecular Weight:	839.04
Target:	Complement System
Pathway:	Immunology/Inflammation
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



## BIOLOGICAL ACTIVITY

<b>Description</b>	PMX 205 is a potent complement C5a receptor (C5aR; CD88) antagonist.
<b>IC<sub>50</sub> &amp; Target</b>	C5aR <sup>[1]</sup>
<b>In Vitro</b>	<p>A complement activation product, C5a, is known to recruit and activate microglia and astrocytes in vitro by activation of a G protein-coupled cell-surface C5aR. In the MTT assay, in 24 h plate, it shows that all groups are significant when compared with negative control group. For PMX 205 (PMX205) group, the value recorded is in between 0.09893 to 0.2465, EP54 group, 0.02724 to 0.1748 and Tamoxifen group, the value recorded in between 0.09880 to 0.2464. For the 48 h plate of incubation time, only two groups show a significant result, which are PMX 205 and Tamoxifen. The values recorded are in between 0.04987 to 0.3273 and 0.5777 to 0.8551 respectively. For the 72 h plate, only one group shows a significant result, PMX 205 (antagonist group) with the value recorded in between 0.02136 to 0.5322<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>PMX 205 (PMX205) is an orally active, selective C5aR antagonist. Animals treated with PMX 205 (1 mg/kg/day, oral) displays a significant extension of survival time and a reduction in end-stage motor scores, as compared with vehicle-treated rats. PMX 205-treated animals also display reduced levels of astroglial proliferation in the lumbar spinal cord. SOD1<sup>G93A</sup> rats are orally dosed with PMX 205 (1 mg/kg/day) from two time points (days 28 and 70) before the onset of major clinical symptoms. Both treatment groups have a significant extension in survival time compared with untreated rats (p=0.022, day 28; p=0.015, day 70), with no clear differences in outcomes between the two treatment regimens<sup>[2]</sup>. Tg2576 mice are treated with PMX 205 (PMX205) at 20 µg/mL in the drinking water (n=17) from 12 to 15 mo of age, the time frame at which there is a rapid accumulation of amyloid deposits in these animals. Untreated Tg2576 animals (n=11) are used as controls. After 3 mo, animals treated with PMX 205 show significantly less fibrillar plaque load (thioflavine reactivity) than do untreated animals. In 3×Tg mice, PMX 205 also significantly reduces hyperphosphorylated tau (69%)<sup>[3]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## PROTOCOL

<b>Cell Assay <sup>[1]</sup></b>	<p>The mouse mammary tumor cell lines 4T1 are plated at a density 5.0×10<sup>4</sup> cells/ml/well of 96-multiwell plates in complete medium. After 24 h of incubation, the medium is changed with serum starve medium to synchronize the cell cycle and growth as to ensure that the cells reaches its plateau phase. After 24 h of serum-starving, cells are treated with 5 µL/well of 0.1 M of agonist, EP54, antagonist, PMX 205 and the positive control is treated with Tamoxifen drug. 5 µL/well of the 12 mM</p>
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ck solution is added 5 h before reading is taken and about 50 µL/well of the SDS-HCL solution is added and mixed thoroughly using pipette 3 h before reading is taken. The MTT assay is assessed at different time point; 0, 24, 48 and 72 h at wavelength 570 nm respectively by using ELISA plate reader Infinite M200<sup>[1]</sup>.

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**Animal Administration** <sup>[2][3]</sup>

**Rats**<sup>[2]</sup>

Transgenic SOD1<sup>G93A</sup> rats expressing human mutant G93A SOD1 (NTac:SD-Tg SOD1<sup>G93A</sup> L26H) are used. Three experimental groups are chosen: untreated, PMX 205 treats from day 28 onward, and PMX 205 treats from day 70 onward. Animals are administered PMX 205 via drinking water (1 mg/kg/day) , from day 28 or day 70 onward; controls receive water only<sup>[2]</sup>.

**Mice**<sup>[3]</sup>

Tg2576 mice are treated (starting at or after the initiation of plaque pathology) for 2-3 mo with PMX 205 given in the drinking water only (10-20 µg/mL, equivalent to ~3-6 mg/kg/day) or both in drinking water (10-20 µg/mL) and s.c. (1 mg/kg) twice weekly throughout the treatment period. Untreated transgenic animals of same age are used as controls. Nontransgenic littermates are similarly treated or not treated with the drug. 3×Tg mice are also treated with PMX 205 in the drinking water. Due to the low pathology of the males, only female mice of this strain are used for these studies<sup>[3]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Theranostics. 2019 Oct 12;9(25):7566-7582.
- Cell Mol Neurobiol. 2022 Aug 25.

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## REFERENCES

- [1]. Kosni NN, et al. Expression of complement C5a receptor and the viability of 4T1 tumor cells following agonist-antagonist treatment. J Cancer Res Ther. 2016 Apr-Jun;12(2):590-6.
- [2]. Woodruff TM, et al. The complement factor C5a contributes to pathology in a rat model of amyotrophic lateral sclerosis. J Immunol. 2008 Dec 15;181(12):8727-34.
- [3]. Fonseca MI, et al. Treatment with a C5aR antagonist decreases pathology and enhances behavioral performance in murine models of Alzheimer's disease. J Immunol. 2009 Jul 15;183(2):1375-83.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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