# SKI2852

**Cat. No.:** HY-19325

**CAS No.:** 1346554-47-9

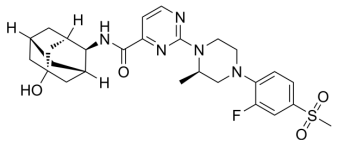
**Molecular Formula:** $C_{27}H_{34}FN_5O_4S$

**Molecular Weight:** 543.65

**Target:** 11β-HSD

**Pathway:** Metabolic Enzyme/Protease

**Storage:** Please store the product under the recommended conditions in the Certificate of Analysis.



## BIOLOGICAL ACTIVITY

**Description**

SKI2852 is a potent, selective and orally active 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor with $IC_{50}$s of 1.6 nM and 2.9 nM against mHSD1 and hHSD1, respectively[1].

**$IC_{50}$ & Target**

IC50: 1.6 nM (mHSD1), 2.9 nM (hHSD1)[1]

**In Vitro**

SKI2852 inhibits 11β-HSD1 with an $IC_{50}$ of 4.4 ± 0.5 nM in HEK293 cells stably transfected with human 11β-HSD1 cDNA[1].
The amide carbonyl group of SKI2852 established a central hydrogen bond interaction with the hydroxyl side chain of Ser170, one of the key residues (Ser170, Tyr183, and Lys 187) that define the catalytic triad for 11β-HSD1 activity[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**In Vivo**

SKI2852 (20 mg/kg; oral; once daily for 25 days) significantly reduces blood glucose and HbA1c levels and improved the lipid profiles in ob/ob mice[1].
In Vivo PK Data for SKI2852[1]

| species | iv[a] | | | | po[b] | | | |
|---|---|---|---|---|---|---|---|---|
| | CL (L/kg/h) | $V_{ss}$ (L/kg) | $t_{1/2}$ (h) | AUC (μg × h/mL) | $C_{max}$ (μg/mL) | $t_{max}$ (h) | AUC (μg × h/mL) | F (%) |
| mouse[c] | 0.42 | 1.1 | 1.7 | 2.35 | 2.21 | 1.0 | 11.26 | 96 |
| rat[c] | 0.93 | 2.1 | 1.8 | 1.12 | 1.02 | 1.3 | 3.39 | 60 |
| dog[d] | 0.36 | 2.4 | 4.7 | 1.47 | 1.12 | 2.1 | 11.52 | 98 |

[a]10% hydroxylpropyl-β-cyclodextrin was used as vehicle. [b]0.5% methylcellulose and 1% Tween80 was used as vehicle. [c] Dosed iv at 1 mg/kg, po at 5mg/kg. [d]Dosed iv at 0.5 mg/kg, po at 4 mg/kg.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| | |
|---|---|
| Animal Model: | ob/ob mice, diet-induced obesity (DIO) model[1] |
| Dosage: | 20 mg/kg |
| Administration: | Oral, once daily for 25 days |
| Result: | Efficiently reduced postprandial glucose and/or blood HbA1c levels and suppressed hepatic mRNA levels of gluconeogenic enzymes. Clearly enhanced hepatic and whole-body insulin sensitivities in a hyperinsulinemic-euglycemic clamp experiment in DIO mice. |

| | |
|---|---|
| Animal Model: | C57BL/6 mice, rats and dogs[1] |
| Dosage: | 0.5 or 4 mg/kg |
| Administration: | IV or PO (Pharmacokinetic Analysis) |
| Result: | Showed good pharmacokinetic profiles. |

## REFERENCES

[1]. Ryu JH, et al. Discovery of 2-((R)-4-(2-Fluoro-4-(methylsulfonyl)phenyl)-2-methylpiperazin-1-yl)-N-((1R,2s,3S,5S,7S)-5-hydroxyadamantan-2-yl)pyrimidine-4-carboxamide (SKI2852): A Highly Potent, Selective, and Orally Bioavailable Inhibitor of 11β-Hydroxysteroid Dehydrogenase Type 1 (11β-HSD1). J Med Chem. 2016 Nov 23;59(22):10176-10189.



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