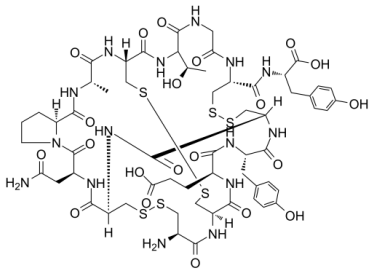
Data Sheet

Product Name:	Linaclotide
Cat. No.:	CS-3577
CAS No.:	851199-59-2
Molecular Formula:	$C_{59}H_{79}N_{15}O_{21}S_6$
Molecular Weight:	1526.74
Target:	Guanylate Cyclase
Pathway:	GPCR/G Protein
Solubility:	DMSO : 50 mg/mL (32.75 mM; Need ultrasonic); H2O : 16.67 mg/mL (10.92 mM; ultrasonic and adjust pH to 2 with HCl)



BIOLOGICAL ACTIVITY:

Linaclotide is a potent and selective **guanylate cyclase C** agonist; developed for the treatment of constipation-predominant irritable bowel syndrome (IBS-C) and chronic constipation. **In Vitro:** Linaclotide inhibits in vitro [^{125}I]-STa binding to intestinal mucosal membranes from wt mice in a concentration-dependent manner. In contrast, [^{125}I]-STa binding to these membranes from GC-C null mice is significantly decreased. After incubation in vitro in jejunal fluid for 30 min, linaclotide is completely degraded[1]. Linaclotide acts on guanylate cyclase-C receptors on the luminal membrane to increase chloride and bicarbonate secretions into the intestine and inhibit the absorption of sodium ions, thus increasing the secretion of water into the lumen and improving defecation; the drug is minimally absorbed into the systemic circulation[2]. **In Vivo:** Pharmacokinetic analysis shows very low oral bioavailability (0.10%). In intestinal secretion and transit models, linaclotide exhibits significant pharmacological effects in wt, but not in GC-C null mice: induction of increased fluid secretion into surgically ligated jejunal loops is accompanied by the secretion of elevated levels of cyclic guanosine-3',5-monophosphate and accelerated gastrointestinal transit[1]. Linaclotide significantly increases weekly spontaneous bowel movements and complete spontaneous bowel movements (CSBMs) while reducing abdominal pain in patients with chronic constipation[2].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: [1]Mouse: To determine oral bioavailability, three groups (n=3) of female CD-1 mice receive linaclotide (8 mg/kg) intravenously (i.v.), while two groups (n=3) receive linaclotide (8 mg/kg) by gavage (p.o.). Blood is allowed to clot for 5 min, centrifuged at 13,000×g for 3 min, and the serum is collected and stored at −80 °C until sample preparation and analysis by LC-MS/MS[1].

References:

[1]. Bryant AP, et al. Linaclotide is a potent and selective guanylate cyclase C agonist that elicits pharmacological effects locally in the gastrointestinal tract. Life Sci. 2010 May 8;86(19-20):760-5.

[2]. Love BL, et al. Linaclotide: a novel agent for chronic constipation and irritable bowel syndrome. Am J Health Syst Pharm. 2014 Jul 1;71(13):1081-91.

CAIndexNames:

L-Tyrosine, L-cysteinyl-L-cysteinyl-L-α-glutamyl-L-tyrosyl-L-cysteinyl-L-cysteinyl-L-asparaginyl-L-prolyl-L-alanyl-L-cysteinyl-L-threonylglycyl-L-cysteinyl-, cyclic (1→6),(2→10),(5→13)-tris(disulfide)

SMILES:

O=C([C@@H](NC([C@@](CSSC[C@@H]1N)([H])NC([C@@](CSSC[C@H](N2)C(N[C@H](C(O)=O)CC3=CC=C(O)C=C3)=O)([H])NC([C@@H](NC([C@@H](N4)CCC(O)=O)=O)CC5=CC=C(O)C=C5)=O)=O)CC(N)=O)N6[C@@](C(N[C@H](C(N[C@](CSSC[C@](C4=O)([H])NC1=O)([H])C(NC(C(NCC2=O)=O)[C@H](O)C)=O)=O)C)=O)([H])CCC6

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

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