

PRODUCT DATA SHEET

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Umifenovir powered by Lipodisq™ Sterile Solution

Nano-formulated aqueous solution: Ready-to-use

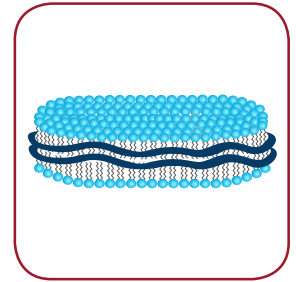
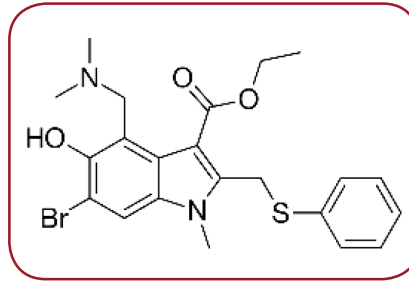
Cat. No.: IAX-700-106

Lot. No.:

Synonyms	Ethyl 6-bromo-4-[(dimethylamino)methyl]-5-hydroxy-1-methyl-2(phenylsulfanylmethyl)indole-3-carboxylate, arbidol in a detergent-free nano-formulation made of styrene-maleic acid lipid particles (SMALP)
Empirical Formula	C ₂₂ H ₂₅ BrN ₂ O ₃ S · HCl
Concentration	1 mg/ml (0.1% w/vol)
Size	1 ml
MW	477.4 · 36.5
CAS	131707-23-8
Purity	≥ 95% (HPLC)
Solution pH	7.00 - 7.50
Solubility	Soluble in water, PBS, Tris and other physiological solutions as formulated in a proprietary, thermostable, aqueous lipid nanoparticulate formulation (Lipodisq™, Malvern Cosmeceutics Ltd., Malvern UK). Avoid the use of buffers with divalent ions such as Ca or Mg or pH <6.5 or >8.0, which can cause particle instability. Unformulated umifenovir is soluble in DMF, DMSO or ethanol.
Formulation	Lipodisq™ are nanosized lipid-based discoidal particles that can be manufactured to incorporate hydrophobic, poorly water-soluble compounds, such as lipids, lipoproteins and glycolipids.
Appearance	Light yellow coloured clear aqueous solution
Handling	Keep sterile. Avoid skin and eye contact. If the solution is not clear, then pre-warm (~40°C) solution.
Activity	Cell culture tested (human macrophage cell line) (MTT). Recommended starting dilution: 1:200 or higher. Optimal working concentrations depend on the applications and need to be determined. Published procedures using Lipodisq™ formulations (Curcumin and IAXO TLR4 antagonists) <i>in vivo</i> rodent models at 3-10mg/kg. Recommended route of administration is subcutaneous (s.c.) with oral or nasal application as a possible alternative, which needs to be optimised. Carrier only control: Lipodisq™ Control Sterile Solution (Cat. No.: IAX-700-100).
Shipping	Ambient
Storage	2-8°C. For long-term storage between -15 and -25°C.
Stability	12 months after receipt (unopened and as supplied)
MSDS	Available on request

Document No.: IAX-700-106-TDS | **Version:** 1.2 | **Issue Date:** 16/09/2022

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General Information

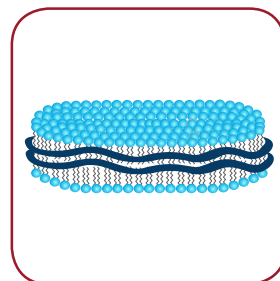
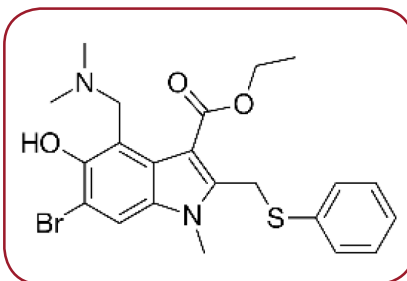
- Umifenovir (Arbidol) is known to have broad-spectrum anti-viral activity and has earlier been approved in China and Russia for treating influenza, SARS, and Lassa viruses. It has been tested in multiple clinical studies as a candidate for use as an anti-COVID19 therapeutic and has been suggested to act at the entry stage and at the post-entry stages by preventing viral attachment and inhibiting the release of virus particles from intracellular vesicles, respectively.
- In a recent phase III, clinical study Umifenovir met the primary and secondary endpoint criteria. It has been shown to be efficacious, safe and well-tolerated at the tested dosage.

Umifenovir References

- [1] *Arbidol as a broad-spectrum antiviral: an update.* Blaising, J, et al. *Antivir. Res.* (2014); 107:84
- [2] *Arbidol: a broad-spectrum antiviral compound that blocks viral fusion.* Boriskin YS, et al. *Curr. Med. Chem.* (2008); 15:997
- [3] *Potential treatment methods targeting 2019-nCoV infection.* Zheng LU, et al. *Eur. J. Med. Chem.* (2020); 205:112687
- [4] *Phase III, Randomized, Double-blind, Placebo controlled trial of Efficacy, Safety and Tolerability of Antiviral drug Umifenovir vs Standard care of therapy in non-severe COVID-19 patients.* Ramachandran R, et al. *Int. J. Infect. Dis.* (2022); 115:62

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Lipodisq™ Technology

- A nanoparticle (11-40nm) drug delivery system comprising a discoidal phospholipid bilayer membrane stabilised by a chaperone molecule annulus.
- Internal properties of the phospholipid membrane support the disposition and stabilisation of drug molecule candidates and preserve the native conformation of membrane molecules.
- The resulting encapsulated actives are rendered water-soluble and specialised for intra-cellular penetration/delivery via endosomal uptake mechanisms.
- Lipodisq™ solutions show a good safety profile and are suitable for *in vitro* and *in vivo* investigations.
- For a customizable biodegradable Lipodisq™ version with a higher concentration of actives or an alternative lipid option, contact Innaxon.

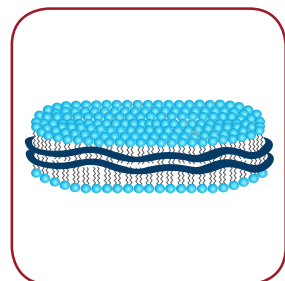
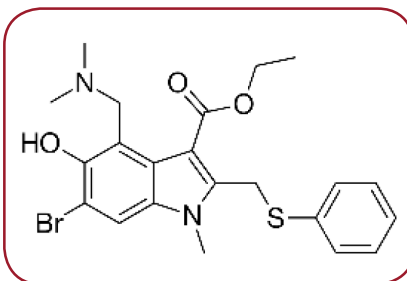
Component	Concentration	CAS #	EC #
Water (sterile)	QS	7732-18-5	231-791-2
Poly(styrene maleic acid)	25mg/ml	26762-29-8	607-996-1
Lecithin	9mg/ml	92128-87-5	295-786-7
Umifenovir hydrochloride	1 mg/ml	131707-23-8	680-680-9

Lipodisq™ References

- [1] *Mechanisms of Formation, Structure, and Dynamics of Lipoprotein Discs Stabilized by Amphiphilic Copolymers: A Comprehensive Review.* Orekhov PS, et al. *Nanomaterials* (2022); 12:361
- [2] *Applications of Synthetic Polymer Discoidal Lipid Nanoparticles to Biomedical Research.* Tanaka M. *Chem. Pharm. Bull.* (2022); 70:507
- [3] *Understanding the Structural Pathways for Lipid Nanodisc Formation: How Styrene Maleic Acid Copolymers Induce Membrane Fracture and Disc Formation.* Bjørnstad VA, et al. *Langmuir* (2021); 37:6178
- [4] *Physicochemical Characterization, Toxicity and In Vivo Biodistribution Studies of a Discoidal, Lipid-Based Drug Delivery Vehicle: Lipodisq Nanoparticles Containing Doxorubicin.* Torgersen ML, et al. *J. Biomed. Nanotechnol.* (2020); 16:41
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- [9] Nano-size uni-lamellar lipodisq improved in situ auto-phosphorylation analysis of *E. coli* tyrosine kinase using (19)F nuclear magnetic resonance. Li D, et al. Protein Cell (2015); 6:229
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- [11] Advances in the use of nanoscale bilayers to study membrane protein structure and function. Malhotra K and Alder NN. Biotechnol. Genet. Eng. Rev. (2014); 30:79
- [12] DEER EPR measurements for membrane protein structures via bifunctional spin labels and lipodisq nanoparticles. Sahu ID, et al. Biochemistry (2013); 52:6627
- [13] Detergent-free formation and physicochemical characterization of nanosized lipidpolymer complexes: lipodisq. Orwick MC, et al. Angew. Chem. (2012); 51:4653
- [14] Detergent-free incorporation of a seven-transmembrane receptor protein into nanosized bilayer lipodisq particles for functional and biophysical studies. Orwick-Rydmark M, et al. Nano Lett. (2012); 12:4687
- [15] In vitro and in vivo evaluation of tumor targeting styrene-maleic acid copolymer-pirarubicin micelles: survival improvement and inhibition of liver metastases. Daruwalla, J, et al. Cancer Sci. (2010); 101:1866
- [16] Poly(styrene-alt-maleic anhydride) derivatives as potent anti-HIV microbicide candidates. Fang W, et al. Bioorg. Med. Chem. Lett. (2009); 19:1903
- [17] SMA-doxorubicin, a new polymeric micellar drug for effective targeting to solid tumours. Greish K, et al. J. Control. Release (2004); 97:219
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