

## PRODUCT DATA SHEET

Page 1 / 4

### Umifenovir powered by Lipodisq™ Sterile Solution

Nano-formulated aqueous solution: Ready-to-use

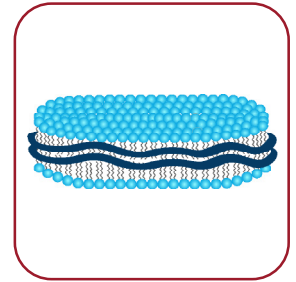
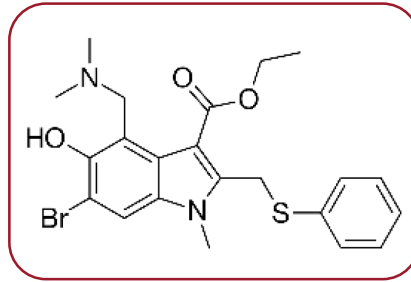
**Cat. No.:** IAX-700-106

**Lot. No.:**

<b>Synonyms</b>	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)
<b>Empirical Formula</b>	C <sub>22</sub> H <sub>25</sub> BrN <sub>2</sub> O <sub>3</sub> S · HCl
<b>Concentration</b>	1 mg/ml (0.1% w/vol)
<b>Size</b>	1 ml
<b>MW</b>	477.4 . 36.5
<b>CAS</b>	131707-23-8
<b>Purity</b>	≥ 95% (HPLC)
<b>Solution pH</b>	7.00 - 7.50
<b>Solubility</b>	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.
<b>Formulation</b>	Lipodisq™ are nanosized lipid-based discoidal particles that can be manufactured to incorporate hydrophobic, poorly water-soluble compounds, such as lipids, lipoproteins and glycolipids.
<b>Appearance</b>	Light yellow coloured clear aqueous solution
<b>Handling</b>	Keep sterile. Avoid skin and eye contact. If the solution is not clear, then pre-warm (~40°C) solution.
<b>Activity</b>	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).
<b>Shipping</b>	Ambient
<b>Storage</b>	2-8°C. For long-term storage between -15 and -25°C.
<b>Stability</b>	12 months after receipt (unopened and as supplied)
<b>MSDS</b>	Available on request

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Page 2 / 4

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#### General Information

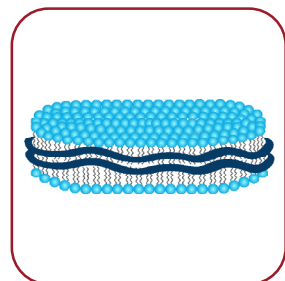
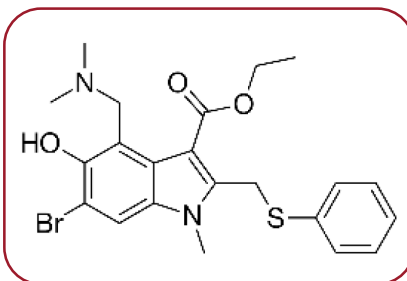
- Umifenovir (Arbidol) is known to have broad-spectrum anti-viral activity and has earlier been approved in China and Russia for treating influenza, SARS, and Lassa viruses. It has been tested in multiple clinical studies as a candidate for use as an anti-COVID19 therapeutic and has been suggested to 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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Page 3 / 4

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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.

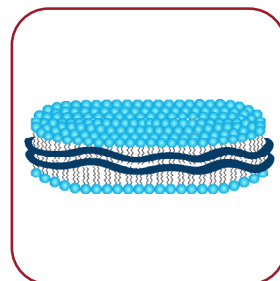
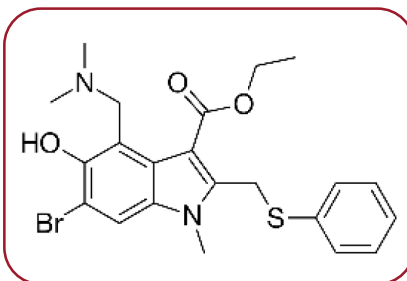
Component	Concentration	CAS #	EC #
Water (sterile)	QS	7732-18-5	231-791-2
Poly(styrene maleic acid)	25mg/ml	26762-29-8	607-996-1
Lecithin	9mg/ml	92128-87-5	295-786-7
Umifenovir hydrochloride	1 mg/ml	131707-23-8	680-680-9

#### 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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- [6] *From polymer chemistry to structural biology: The development of SMA and related amphipathic polymers for membrane protein extraction and solubilization.* Bada Juarez JF, et al. *Chem. Phys. Lipids.* (2019); 221:167
- [7] *The styrene–maleic acid copolymer: a versatile tool in membrane research.* Dörr JM, et al. *Eur. Biophys. J.* (2016); 45:3
- [8] *Reconstitution of membrane proteins: a GPCR as an example.* Goddard AD, et al. *Methods Enzymol.* (2015); 556:405

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Page 4 / 4

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#### Lipodisq™ References

- [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
- [10] Characterizing the structure of lipodisq nanoparticles for membrane protein spectroscopic studies. Zhang R, et al. Biochim. Biophys. Acta. (2015); 1848:329
- [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
- [18] Responsive Hydrophobically Associating Polymers: A Review of Structure and Properties. Tonge, SR and Tighe, BJ. Adv. Drug Deliv. Rev. (2001); 53:109

Lipodisq™ technology is covered by one or more of the following patents owned by Malvern Cosmeceutics Limited: AU2006253886, CA2611144, CN101184473B, EP1890675, GB2426703, IN261468, JP5142898, US8623414 and WO/2021/005340A1 pending.

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