

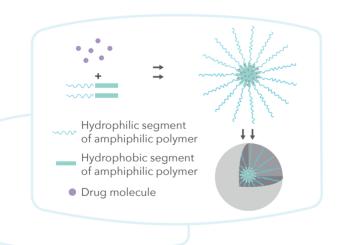
Apisolex™ Polymer

Solubility-enhancing polymer for use in bolus injections and IV infusions

Lubrizol Life Science Health's (LLS Health's) Apisolex[™] GMP, injectable-grade excipient is a safe, polyamino acid-based polymer that enhances the solubility of BSC Class II and IV APIs.

Formulation Benefits

- Increases the solubility of hydrophobic APIs by up to 50,000-fold.
- Allows high drug loading (up to 40:100 API:solubilizer ratio).
- Forms stable, lyophilized drug product that reconstitutes in saline in under 30 seconds.
- Enables IP protection and 505(b)(2) formulations/lifecycle management.





Processing Benefits

- Simple formulation techniques solution mixing or oil-in-water emulsion formation.
- Minimal API loss (recovery >90%).
- Standard, scalable formulation techniques.

Competitive Advantages

- **Higher drug loading** than other solubility-enhancing excipients.
- Substantially increases achievable concentration of API in water.
- Non-toxic, non-immunogenic, biocompatible, and biodegradable alternative to PEG.





Putting Apisolex™ Polymer to the Test

- The solubilization properties of Apisolex polymer were evaluated in comparison with other excipients for a series of poorly water soluble active pharmaceutical ingredients.
- The experiments were conducted by non-optimized, standard dispersion techniques (mixing or homogenization), followed by dilution or lyophilization and reconstitution.
- Target API concentration in final product after dilution or reconstitution was 500 µg/ml. The criteria for solubilization were turbidity (NMT 100 NTU), particle diameter (NMT 150 nm), and drug recovery after filtration (NLT 80%).

Series A results

Compared to solubilizers that utilize a dissolution and dilution technique, only Apisolex polymer enabled successful solubilization of all APIs evaluated and at a much lower ratio of excipient to API.

API / Excipient	Polysorbate 20	Polysorbate 80	Cremophor®1	Apisolex™
Amphotericin B	Fail	Fail	Fail	Pass
Cyclosporin A	Pass	Pass	Pass	Pass
Etoposide	Pass	Pass	Pass	Pass
Melphalan	Fail	Fail	Fail	Pass
Paclitaxel	Pass	Pass	Pass	Pass
BI-001 ²	Pass	Pass	Pass	Pass
BI-002 ²	Pass	Pass	Pass	Pass
BI-003 ²	Pass	Pass	Pass	Pass
BI-004 ²	Pass	Fail	Fail	Pass
BI-005 ²	Pass	Pass	Pass	Pass
Excipient : API Ratio	100 : 1			100: 5 - 10

¹Polyethoxylated castor oil (Kolliphor® ELP or Kolliphor EL, formerly known as Cremophor **EL, is a registered trademark of BASF Corp)

*APIs for this study were provided by Boehringer Ingelheim Pharm. Inc.

Series C results

In additional experiments conducted for APIs, BI-001 - BI-005, Apisolex polymer increased the drug solubility up to 50,000-fold.

API	Solubility in Water (µg/ml)	Solubility in Formulation with Apisolex Polymer (µg/ml)	Solubility Increase with Apisolex Polymer (Fold)
BI-001 ¹	20	2,000	100
BI-002 ¹	8	2,000	250
BI-003 ¹	0.4	20,000	50,000
BI-004 ¹	1.2	10,000	8,333
BI-0051	4	5,000	1,250

 $^{^{1}\}mbox{APIs}$ for this study were provided by Boehringer Ingelheim Pharm. Inc.

Series B results

Compared to solubilizers processed using the same lyophilization and reconstitution technique, only Apisolex polymer enabled successful solubilization of all APIs evaluated.

API / Excipient	TPGS ¹	Captisol®2	PEG-PLGA ³	Apisolex™
Amphotericin B	Fail	Fail	Fail	Pass
Cyclosporin A	Pass	Fail	Fail	Pass
Etoposide	Pass	Fail	Pass	Pass
Melphalan	Pass	Pass	Pass	Pass
Paclitaxel	Fail	Fail	Pass	Pass
BI-001 ⁴	Fail	Fail	Fail	Pass
BI-002 ⁴	Fail	Fail	Fail	Pass
BI-003 ⁴	Pass	Fail	Fail	Pass
BI-004 ⁴	Fail	Fail	Fail	Pass
BI-005 ⁴	Fail	Fail	Fail	Pass

Safe for Parenteral Use

Polymeric excipient is constituted of biocompatible, biodegradable amino acid building blocks and has been tested for safety for parenteral use:

	Test	Results	
System	Tolerability (rats and mice)	Well tolerated at doses as high as 1,500 mg/kg	
toxicity	32-day IV injection 28-day recovery (rats)	No treatment-related side effects detected	
Pharmacokinetics	[14C] labelled Apisolex IV dose in male and female rats	- Can be distributed to distan organs without accumulation - Tissue: plasma AUC0-t ratios <1.0	

Request your sample today

Visit apisolex.com to learn more.





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¹D-a-tocopheryl polyethylene glycol succinate ²Cyclodextrin (Captisol® SBE-AE-Beta-CD is a registered trademark of Ligand Pharmaceuticals Incorporated)

Polyethylene glycol-poly lactic acid-co-glycolic acid

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