

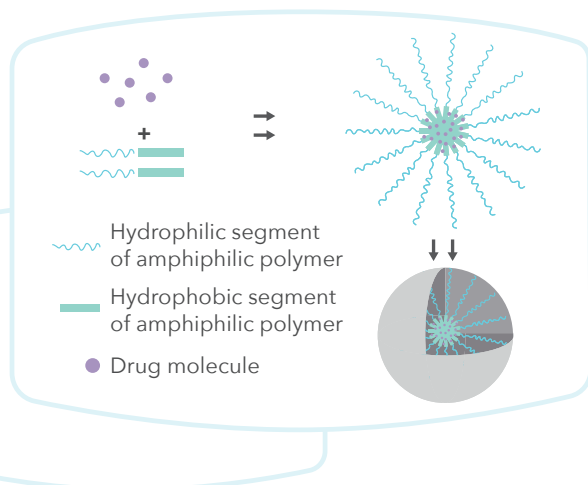
# Apisolex™ Polymer

## 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® <sup>1</sup>	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 <sup>2</sup>	Pass	Pass	Pass	Pass
BI-002 <sup>2</sup>	Pass	Pass	Pass	Pass
BI-003 <sup>2</sup>	Pass	Pass	Pass	Pass
BI-004 <sup>2</sup>	Pass	Fail	Fail	Pass
BI-005 <sup>2</sup>	Pass	Pass	Pass	Pass
Excipient : API Ratio	100 : 1			100: 5 - 10

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

<sup>2</sup>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 <sup>1</sup>	20	2,000	100
BI-002 <sup>1</sup>	8	2,000	250
BI-003 <sup>1</sup>	0.4	20,000	50,000
BI-004 <sup>1</sup>	1.2	10,000	8,333
BI-005 <sup>1</sup>	4	5,000	1,250

<sup>1</sup>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 <sup>1</sup>	Captisol® <sup>2</sup>	PEG-PLGA <sup>3</sup>	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 <sup>4</sup>	Fail	Fail	Fail	Pass
BI-002 <sup>4</sup>	Fail	Fail	Fail	Pass
BI-003 <sup>4</sup>	Pass	Fail	Fail	Pass
BI-004 <sup>4</sup>	Fail	Fail	Fail	Pass
BI-005 <sup>4</sup>	Fail	Fail	Fail	Pass

<sup>1</sup>D-α-tocopheryl polyethylene glycol succinate

<sup>2</sup>Cyclodextrin (Captisol® SBE-AE-Beta-CD is a registered trademark of Ligand Pharmaceuticals Incorporated)

<sup>3</sup>Polyethylene glycol-poly lactic acid-co-glycolic acid

<sup>4</sup>APIs for this study were provided by Boehringer Ingelheim Pharm. Inc.

## 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 toxicity	Tolerability (rats and mice)	Well tolerated at doses as high as 1,500 mg/kg
	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 distant organs without accumulation - Tissue: plasma AUC0-t ratios <1.0

Request your sample today

Visit [apisolex.com](http://apisolex.com) to learn more.

