Efinaconazole Co-crystal Oral tablet

■ Product Information

Product Name	Efinaconazole PEG6000 (Efinaconazole Co-crystal) Oral Tablet
Dosage & Administration	QD (once daily)
Efficacy & Indications	Onychomycosis caused by dermatophytes
Original Reference Drug	Jublia® topical solution
Competitive Products	Original reference drug and oral antifungal agents
Key Differentiation	1. Improved patient compliance by shifting from topical to oral administration 2. Reduced hepatotoxicity and minimized drug–drug interaction (DDI) risks

■ Technical Overview

Description	To enhance solubility and bioavailability while minimizing hepatotoxicity and drug–drug interaction commonly observed with existing oral antifungal agents, Efinaconazole was co-crystallized with PEG6000 at a 1:1 ratio. The resulting API is developed for the manufacture of oral solid dosage forms.
Key Differentiation	• At an oral dose of 30 mg, demonstrated approximately 13-fold higher AUClast and earlier Tmax compared with the original reference drug. • Maintained stable AST and ALT levels within the normal range even with dose escalation. • Exhibited a 21-fold higher NOAEL value compared with the original drug under repeated-dose conditions, indicating a significantly improved safety profile.
Development Status	• Mar 2024: Efficacy study in onychomycosis completed • Mar 2025: API process validation scheduled for completion • Sep 2025: Fina • 8lization of formulation composition • Nov 2025: KDMF listing planned • Sep 2025: Completion of GLP toxicity studies (4-week rodent, 4-week non-rodent DRF results secured)
Intellectual Property	• Co-crystal composition patent: KR Patent No. 10-2513523 (granted in Korea; also secured in major markets including the US, EU, Japan, and China) • Additional patents covering co-crystal manufacturing processes and formulation technologies • Patent term protection expected until 2039

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■ Scope and Conditions of Technology Transfer

Scope	**1. API Manufacturing and Process Technology**
	- Comprehensive documentation covering the co-crystal API manufacturing process (process flow diagrams, process parameters, and detailed methodologies)
	- Process reproducibility and consistency evaluation data
	2. API Analytical and Quality Control Data
	- Specifications, detailed test methods, and scientific justification for method establishment
	- Analytical methods and data for confirmation of co-crystal structure
	- Complete impurity profile
	3. Finished Dosage Form Development Data
	- Pre-formulation study results (solubility, pKa, particle size distribution, flowability, and other physicochemical properties)
	- Initial formulation design data (composition ratios, dissolution patterns, etc.)
	4. Efficacy and Toxicology Data
	- Efficacy results, including in vivo onychomycosis pharmacology models
	- Full set of GLP-compliant toxicology data required for Phase 1 initiation, including:
	  - 2-week and 4-week DRF studies (rodent and non-rodent)
	  - Recovery phase data and NOAEL interpretation
	  - Safety pharmacology and genetic toxicology studies

Conditions	**1. Exclusivity** - Technology transfer rights may be granted on an exclusive or non-exclusive basis, subject to negotiation. **2. Documentation Delivery** - All relevant documentation, analytical methods, and data sets will be transferred upon contract execution. **3. Technical Support** - On-site or remote technical support for process scale-up, validation, and regulatory filing will be provided within a defined period. **4. Intellectual Property** - License rights will be transferred under valid patent coverage, with protection until 2039. **5. Financial Terms** - Upfront fees, milestone payments, and royalties to be determined through mutual agreement.

■ Capability of Technology Provider

Organization Overview	- Daebong LS Co., Ltd.: Listed on KOSDAQ since 2005 - Engaged in the manufacturing and sales of Active Pharmaceutical Ingredients (APIs), functional cosmetic ingredients, and food additives - Operates a specialized clinical subsidiary, PNK Skin Clinical Research Center Co., Ltd., focusing on dermatological clinical trials

Organizational Capabilities	- Possesses a PIC/S GMP-certified API manufacturing plant (Incheon Plant 1)
	- Achieved manufacturing quality compliance approval from Japan PMDA for API production (Incheon Plant 1)
	- Operates three dedicated R&D centers:
	  - Convergence Technology Research Institute
	  - Natural Products Research Center (Incheon)
	  - Natural Products Research Center (Jeju)

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■ Comparative Analysis of Competitor Drugs

Category	Efinaconazole Co-crystal Oral Tablet	Julia® Topical Solution	Diflucan® Capsule	Lamisil® Table	Sporanox® Capsule
Active Ingredient	Efinaconazole (Co-crystal)	Efinaconazole	Fluconazole	Terbinafine	Itraconazole
Classification	Antifungal agent	Antifungal agent	Antifungal agent	Antifungal agent	Antifungal agent
Developer	Daebong LS	Kaken Pharmaceutical	Pfizer	Novartis	Janssen
Dosage & Administration	Oral, QD(once daily)	Once daily, applied topically at bedtime to the affected area	Once weekly oral administration	Twice daily or once daily oral administration	Twice daily oral administration
NOAEL (Rodents, 3-month adjusted)	210(API)	30	8.3	10	10

Note
NOAEL (No Observed Adverse Effect Level):
The highest dose at which no statistically or biologically significant adverse effects are observed compared with control groups in repeated-dose toxicity studies.
The adjustment basis follows *FDA Redbook 2000* ("study duration-based extrapolation").

Category	Efinaconazole Co-crystal Oral Tablet	Differentiation vs. Existing Products
Efficacy & Penetration	Enables systemic treatment via oral administration	Topical formulations are limited to local application and have difficulty reaching deep nail bed infections
Route of Administration	Superior penetration compared with topical agents	Oral antifungals (e.g., itraconazole, terbinafine) require high-dose, long-term administration with potential liver toxicity and DDI risks
Safety	Comparable efficacy at lower doses; repeat-dose toxicity studies showed no liver toxicity or specific adverse findings	Conventional oral antifungals are associated with hepatotoxicity and drug–drug interactions (DDI)
Patient Compliance	Designed for once-daily (QD) administration, improving adherence	Some oral antifungals require twice-daily dosing or drug holidays, leading to poor compliance
Cost-effectiveness	Co-crystal technology reduces API content, lowering manufacturing costs	Existing products often require higher doses or combination therapy, resulting in higher production costs

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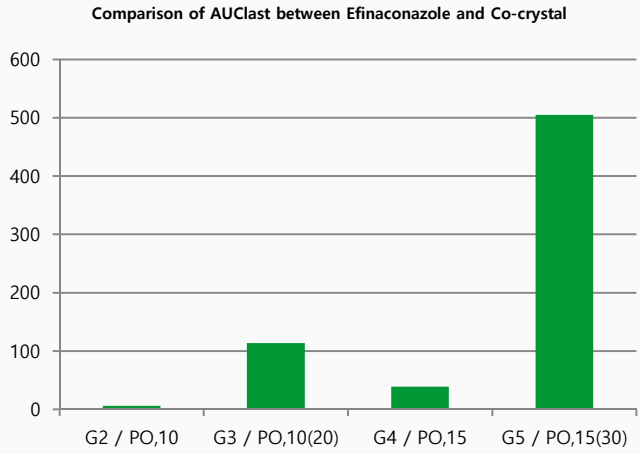
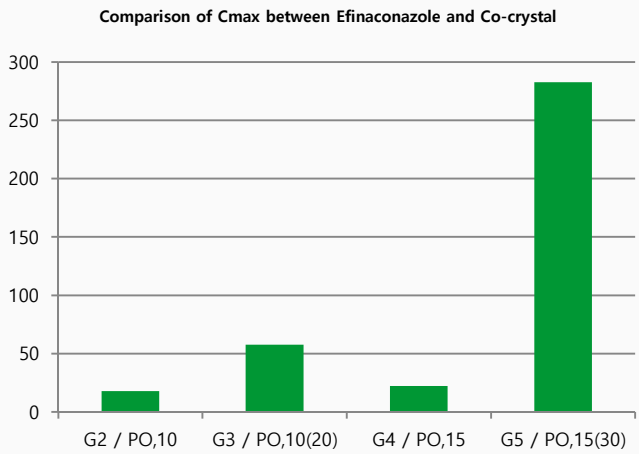
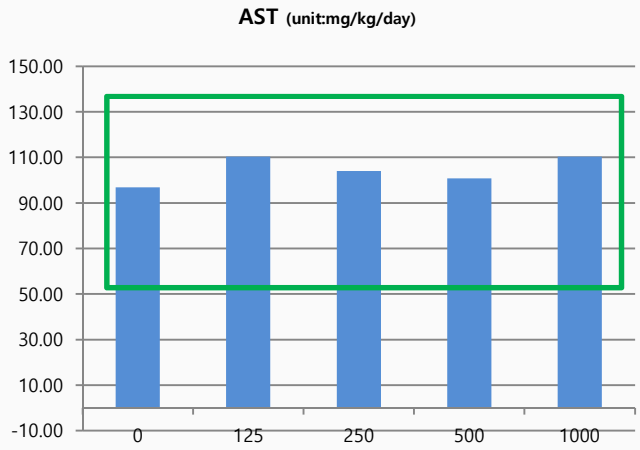
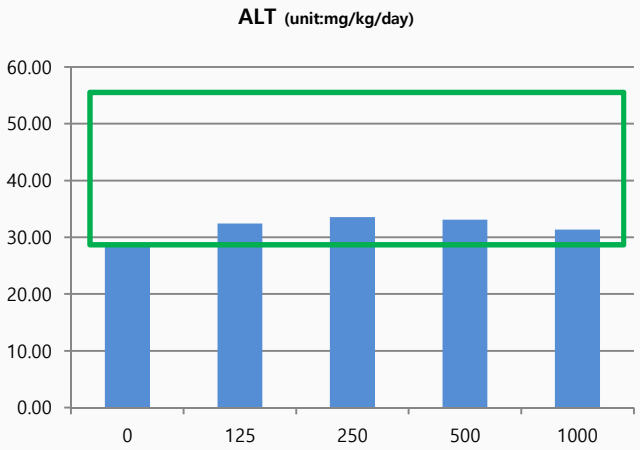
■ Preclinical Data



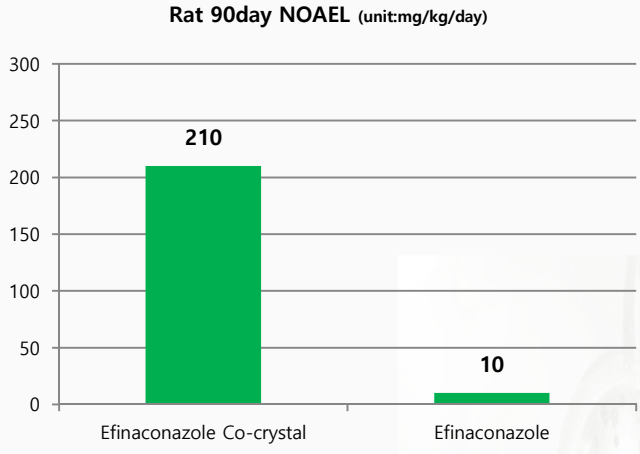


Following a 30 mg oral dose of Efinaconazole Co-crystal, AUClast and Tmax increased approximately 13-fold compared with efinaconazole alone (based on Sprague-Dawley rats).





Even with dose escalation, AST and ALT levels remained stable within the normal range after administration of Efinaconazole Co-crystal (Sprague-Dawley rats).



- NOAEL Comparison in DRF Studies

	Efinaconazole Co-crystal	Efinaconazole
Rat 90day NOAEL	210	10

* The estimated 6-month NOAEL of Efinaconazole Co-crystal was calculated based on the conservative adjustment approach (1/3 rule) described in *FDA Redbook 2000*.

In a 90-day repeated-dose study, the NOAEL of Efinaconazole Co-crystal was 21-fold higher than that of the original drug, indicating a significantly lower toxicity profile (Sprague-Dawley rats).