

# GETTING THE BEST OUT OF CYCLODEXTRINS

Company Introduction



The world's only all-round **CYCLODEXTRIN** company with over

**40-year experience of CD-technology**

**in pharmaceutical-, cosmetics-, food-, environmental- and analytical applications**

### Experience

over 490 technical/scientific papers  
and 950 technical reports to customers

200 different cyclodextrin derivatives  
130 patents/applications  
40 products on the market

Drug Master Files (USA type IV) and eCTD

Over 20,000 citations to CYCLOLAB's papers

### Expertise & Technology

Custom synthesis

Drug solubilization, and stabilization

Further industrial applications

Cyclodextrin-related analytics,

Stability testing

GMP-conform manufacturing

Feasibility studies

### Team

18 qualified cyclodextrin scientists

12 PhDs

3 MBAs

2 members in the QA

By profession

Chemists

Chemical engineers

Biologists

Pharmacists

18 qualified technicians and operators

Sales, business dev, logistics, admin

### Resources

2,000 m<sup>2</sup> (own property) facility

2 galenic/technology labs

4 analytical labs (GC, HPLC, MS and CZE)

2 synthetic chemistry labs

350 m<sup>2</sup> cGMP compliant production area  
(Spray-drying unit)

Freeze-drying units

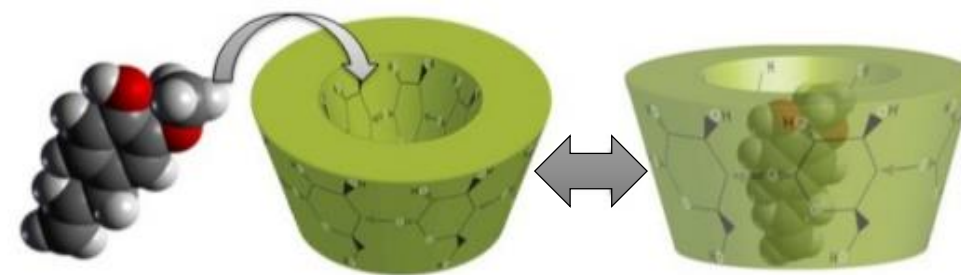
**Quality systems**

**ISO 9001:2015**

**cGMP (OGYÉI/57792-7/2018)**

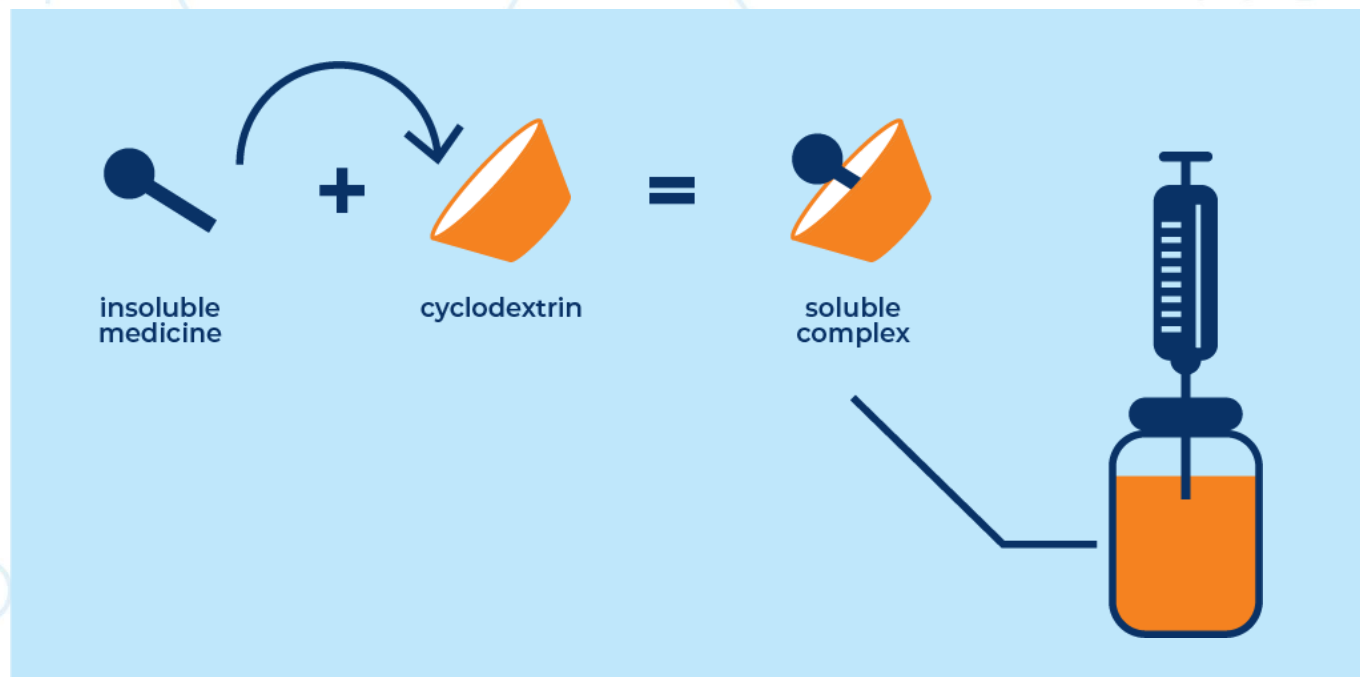
## WHAT ARE CYCLODEXTRINS?

- Composed of sugars
- Cyclic molecules
- Naturally occurring compounds
- Used in food, pharmaceuticals, drug delivery, chemical industries, agriculture, etc.
- **Sub-nanometer** sized molecular containers with hydrophilic outer phase and hydrophobic interior properties
- Reversible inclusion complex formation



## MAIN FUNCTIONAL PROPERTIES OF CDs

They form **NON-COVALENT** „host-guest” type inclusion complexes in a **reversible** manner (Szejtli,1980)



**Cyclodextrins may increase**



- Drug solubility
- Wetting, dissolution rate
- Drug stability
- Absorbed quantity

**Cyclodextrins may decrease**



- API's dose for same efficacy
- Taste
- Side effects
- Smell

## WHY USE CYCLODEXTRINS? POSSIBILITIES

- Significant solubility enhancement (10 to 100,000 fold)
- Improvement of **chemical stability**
- Increased bioavailability, facilitated delivery
- Reduced aggregation
- Moderate irritation or reduced side-effects
- Maximized patient safety, complete renal elimination
- **ENABLES** formulation of water-insoluble APIs in all dosage forms
- Lower API doses can be achieved



## CDs USED IN PHARMACEUTICALS

### Parent Native Unsubstituted

$\alpha$ -CD (Alfadex)

EP, USP

$\beta$ -CD (Betadex)

EP, USP

$\gamma$ -CD (Gammadex)

EP, USP, JPC

### Derivatives Substituted

2-hydroxypropyl  $\beta$ -CD (HP- $\beta$ -CD,  
hydroxypropyl betadex)

EP, USP

Sulfobutylether  $\beta$ -CD (SBE- $\beta$ -CD, betadex  
sulfobutyl ether sodium)

EP, USP

Random methylated  $\beta$ -CD (RM- $\beta$ -CD)  
rare: nasal/ocular

2-hydroxypropyl  $\gamma$ -CD (HP- $\gamma$ -CD)

# CDs USED IN PHARMACEUTICALS

**>100 pharma products on the market containing cyclodextrins**



	$\alpha$ -CD	$\beta$ -CD	$\gamma$ -CD	HP- $\beta$ -CD	SBE- $\beta$ -CD	RM- $\beta$ -CD	HP- $\gamma$ -CD
ORAL		X	X	X	X		
NASAL						X	
RECTAL		X		X			
DERMAL		X	X	X			
OCULAR		X		X	X	X	X
PARENTERAL	X			X	X		X

European Medicinal Agency EMA/CHMP/333892/2013, Committee for Human Medicinal Products (CHMP)  
Background review for cyclodextrins used as excipients



# CDs USED IN PHARMACEUTICALS

## Oral solution

Itraconazole (Janssen)

HP- $\beta$ -CD



## Eye drops

Indomethacin (Bausch&Lomb)

HP- $\beta$ -CD



Diclofenac (Novartis)

HP- $\gamma$ -CD



## Nasal

Estradiol (Servier)

RM- $\beta$ -CD



## Oral tablets/capsules

Piroxicam (Chiesi)

$\beta$ -CD



Cladribine (Merck)

HP- $\beta$ -CD



Ethinylestradiol/Drospirenon (Bayer)

$\beta$ -CD



# CDs USED IN PHARMACEUTICALS

## Intravenous

Voriconazole (Sandoz)  
SBE- $\beta$ -CD



Carfilzomib (Amgen)  
SBE- $\beta$ -CD



Amiodarone (Baxter)  
SBE- $\beta$ -CD



## Topical

Minoxidil (Pierre Fabre)  
 $\gamma$ -CD



## Taste masking

Cetirizine (J&J)  
 $\beta$ -CD

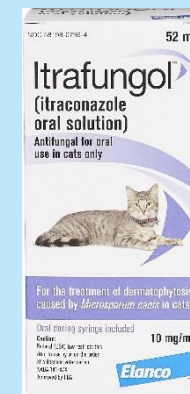


Nicotine (J&J)  
 $\beta$ -CD



## Veterinary

Maropitant for dogs (Pfizer)  
SBE- $\beta$ -CD



Itraconazole for cats (Elanco)  
HP- $\beta$ -CD



## GMP Manufacturing

Betadex Sulfobutyl Ether Sodium  
**Dexolve™**

Custom cGMP synthesis  
of CDs, CD complexes,  
investigational medicinal  
products

Preparation/filing of  
regulatory dossier

## Products

- Pharma grade CDs
- Fine chemical grade CDs
- Standard grade CDs
- Single isomer CDs
- Fluorescent derivatives
- Maltooligomers
- CD complexes
- Analytical standards
- Sugammadex impurities
- CD polymers
- Special HPLC columns



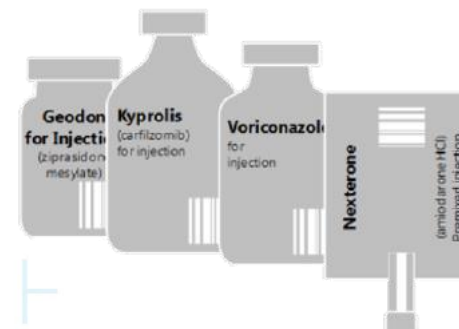
# CYCLOLAB PRODUCT PORTFOLIO DEXOLVE™



**>350 kg/batch USP N.F. / EP**

Global presence and distribution  
cGMP certified OGYÉI/57792-7/2018  
48 months stability data  
>200 batches manufactured  
Annual capacity over 30,000 kgs  
2<sup>nd</sup> manufacturing site established

**No down payment**  
**no royalty**  
**no milestone payment**



SAMPLES  
**FREE**  
SAMPLES



# CYCLOLAB SERVICE PORTFOLIO

## RELATED SERVICES – R&D



### Early phase drug development

Customization of CD enabled formulations

Investigation of changes in physico-chemical properties

Life cycle management

### IP services and consultation

30 years of experience in compilation of CD related patents (synthesis, application, etc.), patent claim analysis, consultancy in CD related projects

Over 62.000 CD related papers

### Custom cyclodextrin synthesis

Exclusive manufacture, unique synthetic routes

self-tailored products and characteristics

### In vitro bioequivalence studies

Design and performance of in vitro studies to support bioequivalence of a CD enabled formulation.

### Analytical services

Method development, validation; cGMP release testing of pharma grade CDs

HPLC, GC, CE, UV, MS, NMR, IR, Micro and BET content methods

Stability studies

CD-guest interaction studies

CD-based chiral separations

Assay, impurity tests

Bioanalytical investigations



## CYCLOLAB SERVICE PORTFOLIO

### Feasibility study

Running a short feasibility study with your molecule free of charge

Proof of concept to consider CD based formulations



### CycloLab Grant

CycloLab offers a unique possibility to collaborate on creating novel and interesting cyclodextrins under the terms of the CycloLab Grant

The proposal after application is thoroughly evaluated by CycloLab

If the application is approved, the cyclodextrin is provided free of charge for the beneficiary

## Formulations

Pediatric and geriatric reformulation  
Injectable panobinostat – various types of cancer  
Injectable lonafarnib – progeria  
Injectable repurposing: oral drugs reformulated as injectables

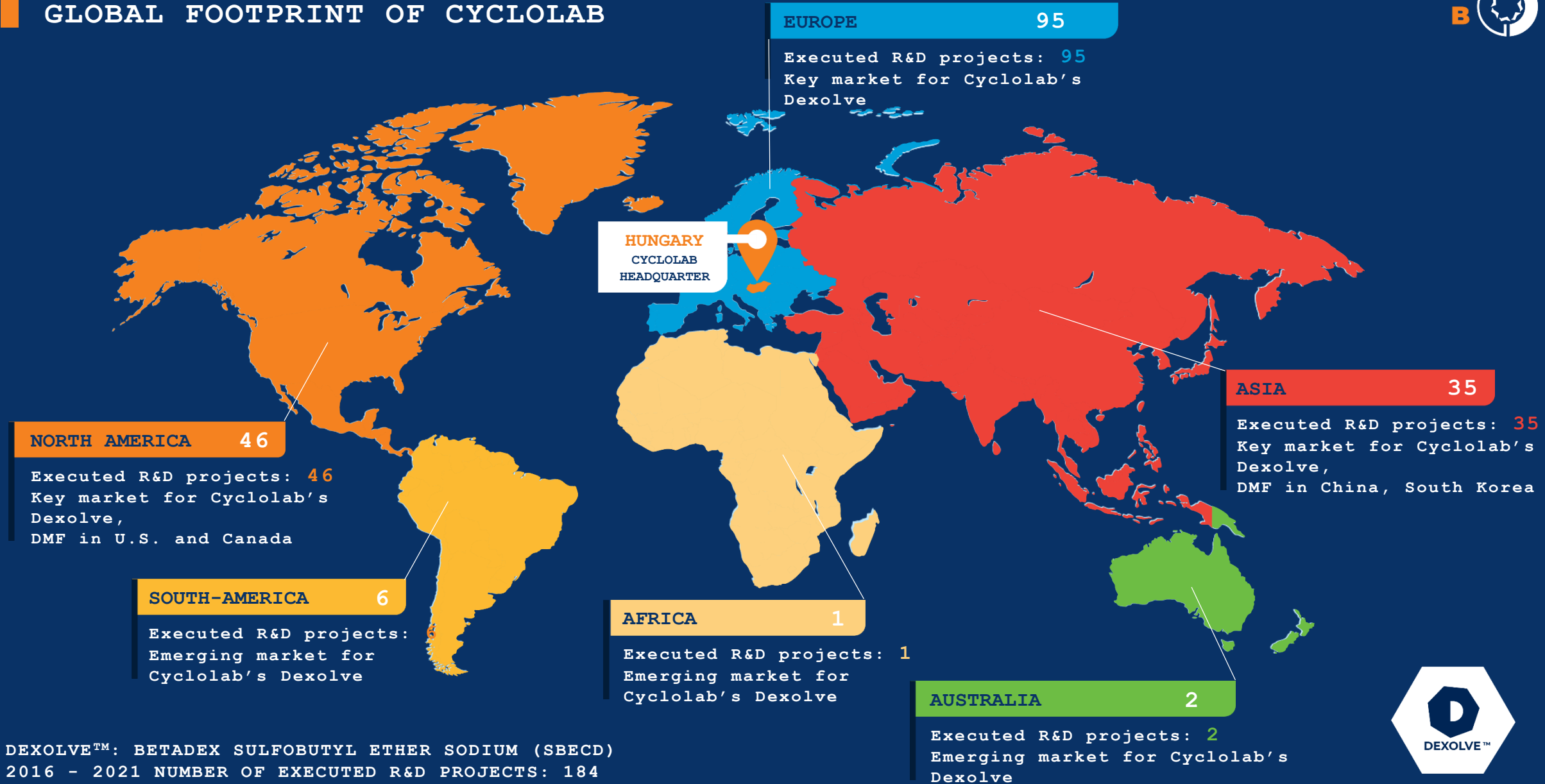
## Cyclodextrins as NCEs

Antivirals (SARS-CoV-2, Zika, Dengue), protective gear  
Lysosomal storage diseases (Niemann Pick C)  
Neurodegenerative diseases (Alzheimer's)  
Antibacterials (Quorum quenching)  
Sugammadex (technology, analytical support and impurity supply)

## Drug delivery systems

Platform for selective and targeted anticancer therapy with unmodified APIs  
Platform for improving BBB penetration

# GLOBAL FOOTPRINT OF CYCLOLAB



DEXOLVE™: BETADEX SULFOBUTYL ETHER SODIUM (SBECD)  
2016 - 2021 NUMBER OF EXECUTED R&D PROJECTS: 184





# CYCLOLAB GETTING THE BEST OUT OF CYCLODEXTRINS

## COMPANY CONTACTS

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