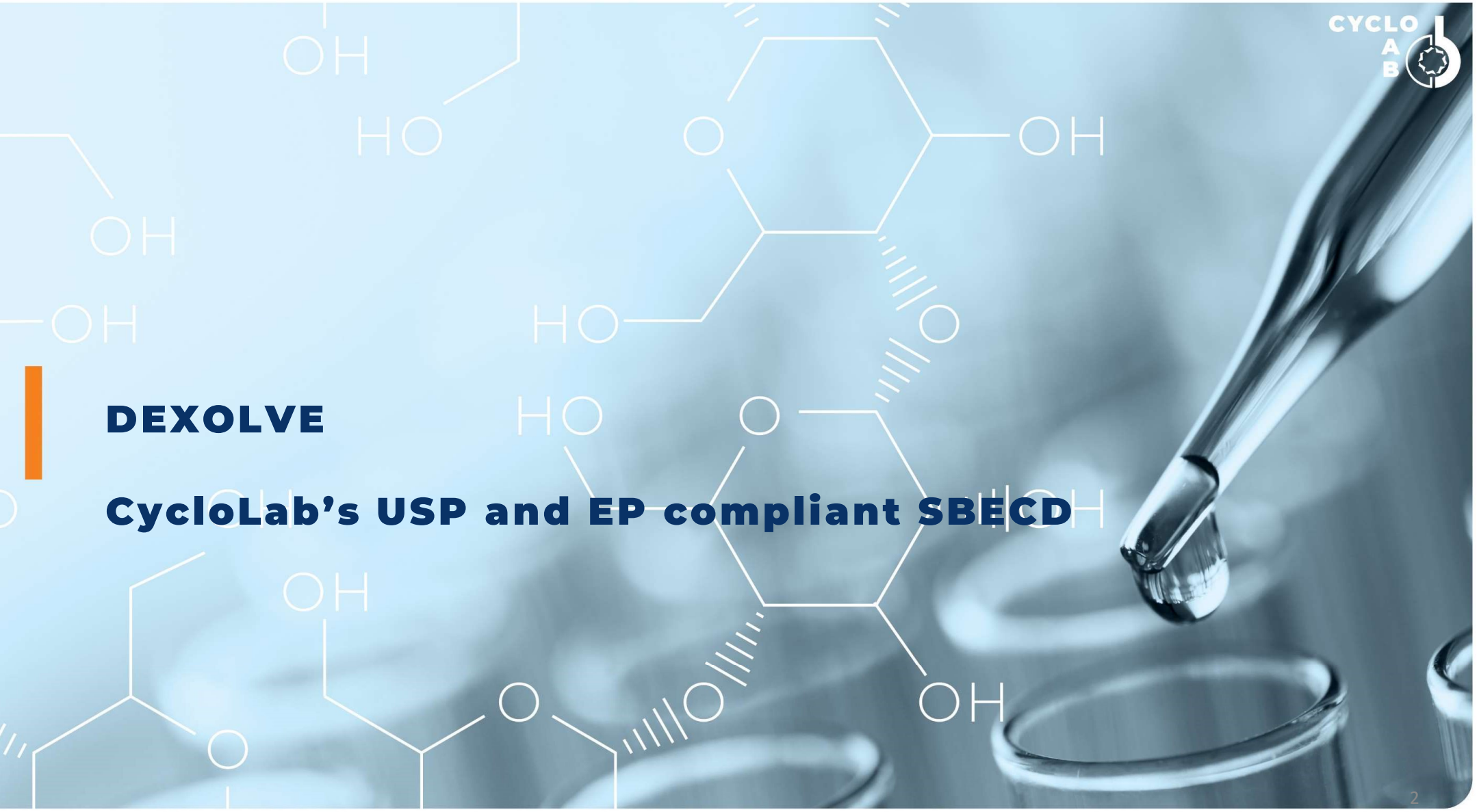
CYCLOLAB

PIONEERS IN CYCLODEXTRIN-BASED INNOVATION

GETTING THE BEST OUT OF CYCLODEXTRINS

CycloLab's Betadex Sulfobutyl Ether Sodium (Dexolve™)

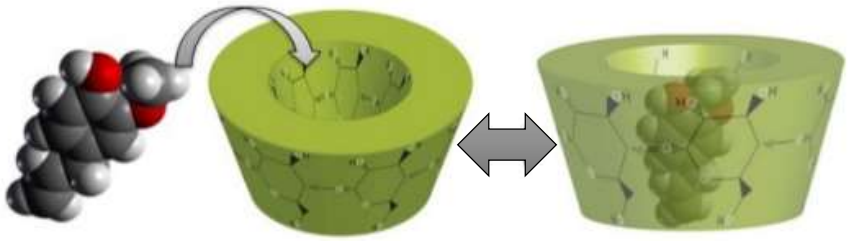


DEXOLVE

CycloLab’s USP and EP compliant SBECD

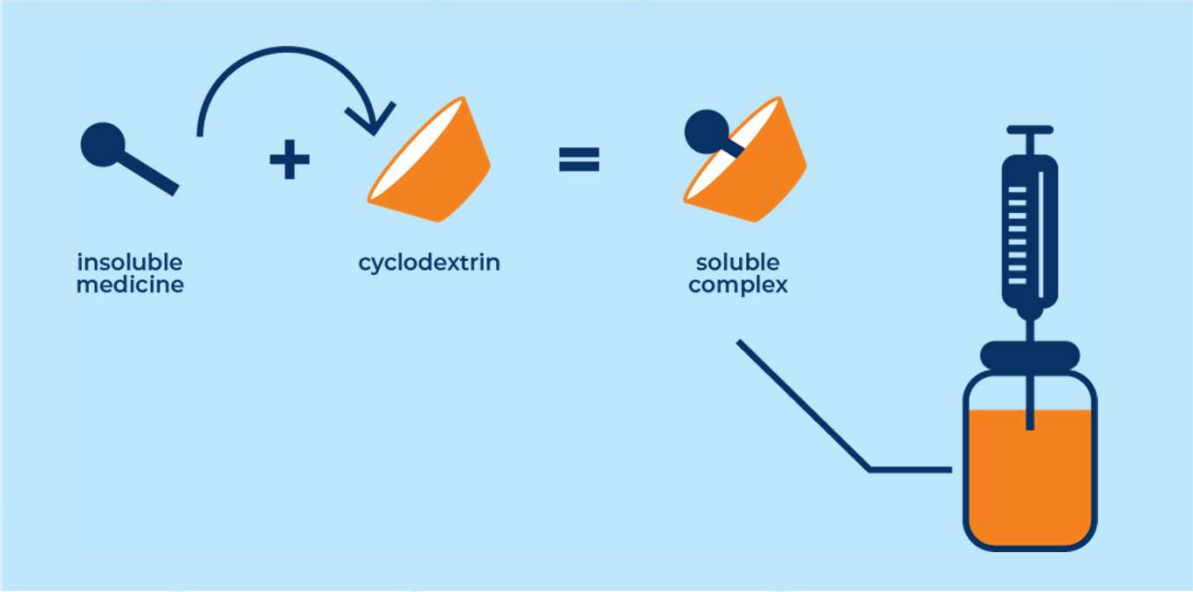
WHAT ARE CYCLODEXTRINS?

- 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

CDs USED IN PHARMACEUTICALS

>100 pharma products on the market containing cyclodextrins

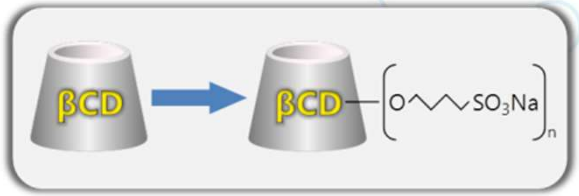
	α-CD	β-CD	γ-CD	HP-β-CD	SBE-β-CD	RM-β-CD	HP-γ-CD
ORAL		X	X	X	X		
NASAL						X	
RECTAL		X		X			
DERMAL		X	X	X			
OCULAR		X		X	X	X	X
PARENTERAL	X			X	X		X

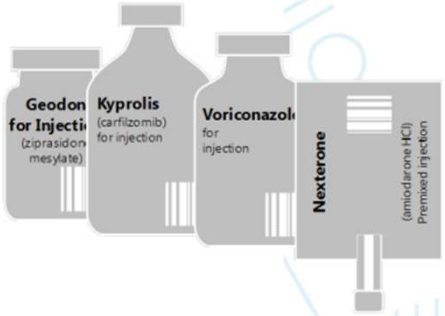
European Medicinal Agency EMA/CHMP/333892/2013, Committee for Human Medicinal Products (CHMP)
Background review for cyclodextrins used as excipients

DEXOLVE™ FOR IMPROVED PHARMACEUTICAL FORMULATIONS

CycloLab Ltd. is the producer of the first generic USP and EP-conform Betadex Sulfobutyl Ether Sodium (SBECD = Dexolve™)

- 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





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FOR IMPROVED PHARMACEUTICAL FORMULATIONS

	Solubility increase using 10 m/m % SBECD vs purified water
Piroxicam	20X
Carbamazipine	36X
Amiodarone	50X
Voriconazole	85X
Delafloxacin	340X
Ziprasidone*HCl	470X
Aripiprazole	3350X
Posaconazole pH 6	20X
Posaconazole pH 3	120X

Aqueous solubilities: Pubmed database (https://pubchem.ncbi.nlm.nih.gov)
solubility in SBECD solutions: CycloLab results

FDA REGISTERED
DMF No. 21922

GMP
OGYÉI/577 92-7/2018

CANADA HEALTH
DMF No. 2009-080

CFDA
DMF No. F20180001741

MFDS KOREA
In progress

EudraGMDP
OGYÉI/3039 1-2/2018

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CYCLO A B

There are 13 APIs on the market and at least 150 further in development in formulations containing SBECD including

- Voriconazole (Vfend, Pfizer)
- Carfilzomib (Kyprolis, Amgen)
- Amiodarone (Nexterone, Baxter)
- Ziprasidone (Geodon, Pfizer)
- Maropitant (vet., Cerenia, Zoetis)
- Aripiprazole (Abilify, BMS)
- Posaconazole (Noxafil, MSD)
- Carbamazepine (Carnexiv, Lundbeck)
- Melphalan (Evomela, Spectrum)
- Delafloxacin (Baxdela, Melinta)
- Brexanolone (Zulresso, Sage)
- Remdesivir (Veklury, Gilead)
- Fosphenytoin (Sesquient, Sedor)

- Mebendazol
- Topiramate
- Omeprazole
- Clopidogrel
- Docetaxel
- Meloxicam
- Allopregnanolone
- Iohexol
- Busulfan
- Alphaxalone

Several other nitrogen containing APIs are in various clinical phases

DEXOLVE™

DEXOLVE™ FOR IMPROVED PHARMACEUTICAL FORMULATIONS

Main regulatory / QA / sales aspects:

Maintained DMF Type IV for SBECD in US and Canada since 2008, in China since 2019

Prepared via a self-developed proprietary, patented technology with a process independent from any existing patents (expires in 2031)

60-month stability data

Successful production of over 250 subsequent USP compliant batches – no OOS result in the production

Dedicated production facility, with 30000+ kg annual capacity producing up to 720+ kg batches

Quality system compliant to ISO 9001 and GMP requirements (regularly audited)

Over 82 APIs of over 400 partners in development using Dexolve in commercial and development phases

Flexible business model, technical and regulatory support on development

GLOBAL FOOTPRINT OF CYCLOLAB

EUROPE 95

Executed R&D projects: 95
Key market for Cyclolab's Dexolve

HUNGARY
CYCLOLAB HEADQUARTER

NORTH AMERICA 46

Executed R&D projects: 46
Key market for Cyclolab's Dexolve,
DMF in U.S. and Canada

SOUTH-AMERICA 6

Executed R&D projects: 6
Emerging market for Cyclolab's Dexolve

AFRICA 1

Executed R&D projects: 1
Emerging market for Cyclolab's Dexolve

ASIA 35

Executed R&D projects: 35
Key market for Cyclolab's Dexolve,
DMF in China, South Korea

AUSTRALIA 2

Executed R&D projects: 2
Emerging market for Cyclolab's Dexolve

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

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