

GETTING THE BEST OUT OF CYCLODEXTRINS

**Marketed drug products
containing SBECD (Dexolve)**

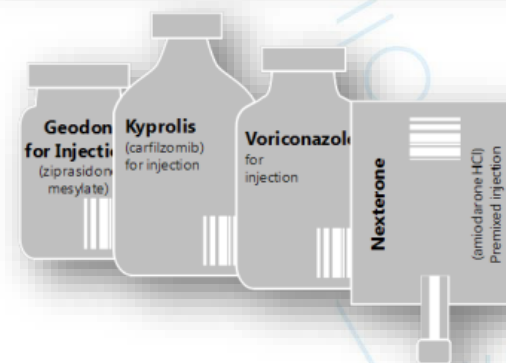
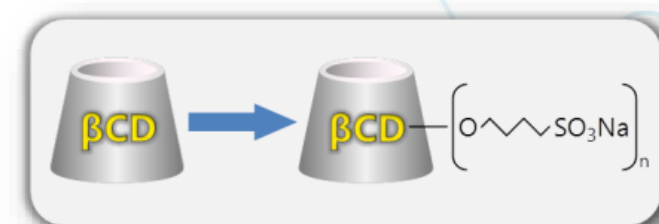


DEXOLVE™ FOR IMPROVED PHARMACEUTICAL FORMULATIONS



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



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

Marketed drug products containing SBECD

VFEND® (Pfizer)

Dexolve® → Sandoz generic

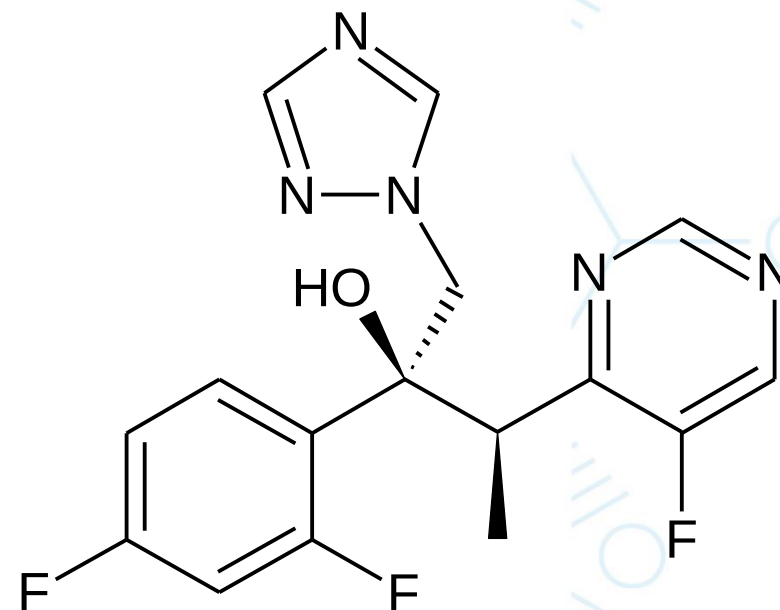
antifungal

intravenous

200 mg voriconazole / vial

3200 mg SBECD / vial

nDrug : nSBECD = 1 : 2.6



PATENT EXPIRED: 2019 (US6632803)



Marketed drug products containing SBECD

GEODON® IM

antipsychotic (anti-schizophrenic)

intramuscular

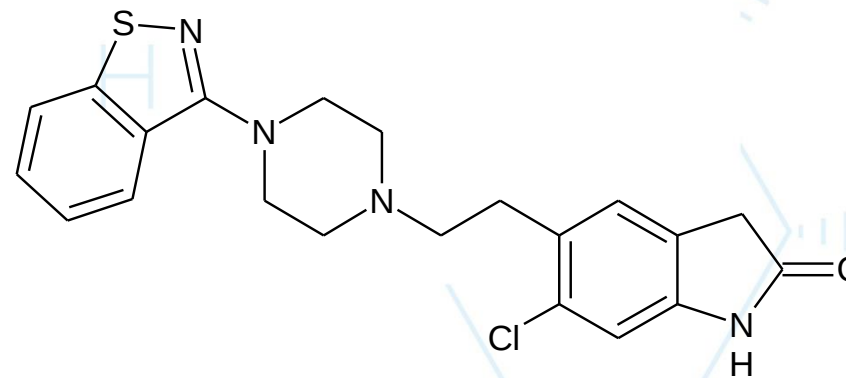
20 mg ziprasidone (mesylate) / vial

294 mg SBECD / vial

nDrug : nSBECD = 1 : 2.8



EXPECTED PATENT EXPIRY: May 7, 2021 (US6399777)



Marketed drug products containing SBECD

NEXTERONE®

antiarrhythmic

infusion

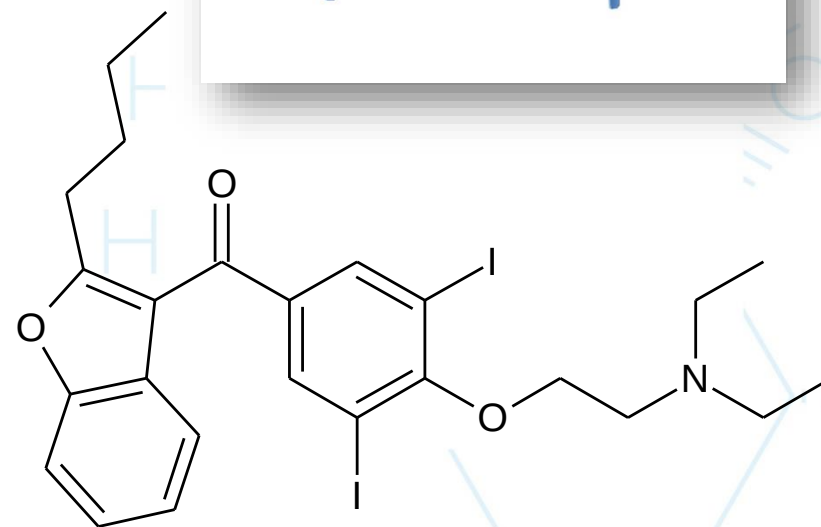
150 / 360 mg amiodarone·HCl / inf. bag

1500 / 3600 mg SBECD / inf. bag

nDrug : nSBECD = 1 : 3



EXPECTED PATENT EXPIRY: 2022 (US6869939)



Marketed drug products containing SBECD

KYPROLIS®

anticancer (Multiple Myeloma)

intravenous

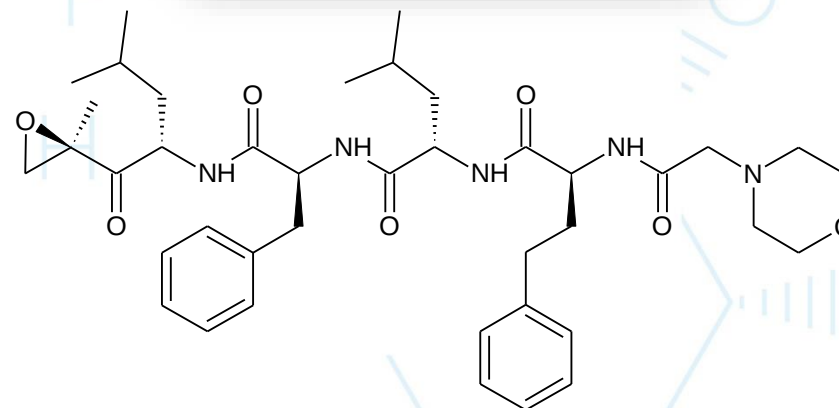
60 mg carfilzomib / vial

3000 mg SBECD / vial

nDrug : nSBECD = 1 : 16.6



EXPECTED PATENT EXPIRY: 2025 (US7737112)



Marketed drug products containing SBECD

CERENIA™

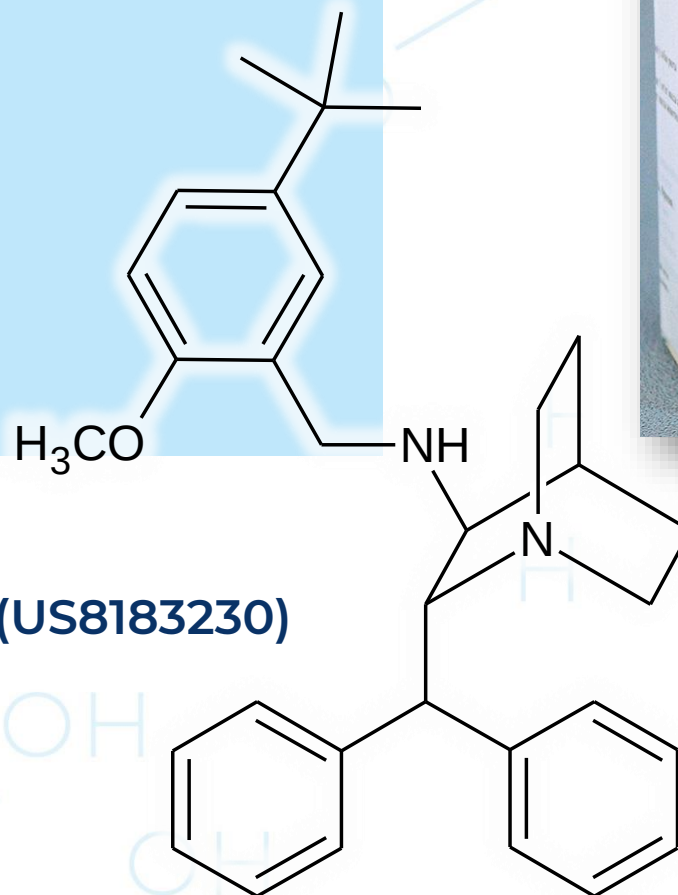
canine and feline anti-nausea

subcutaneous injection

200 mg maropitant (citrate) / vial

1260 mg SBECD / vial

nDrug : nSBECD = 1 : 1.4



EXPECTED PATENT EXPIRY: 2026 (US8183230)

Marketed drug products containing SBECD

NOXAFIL®

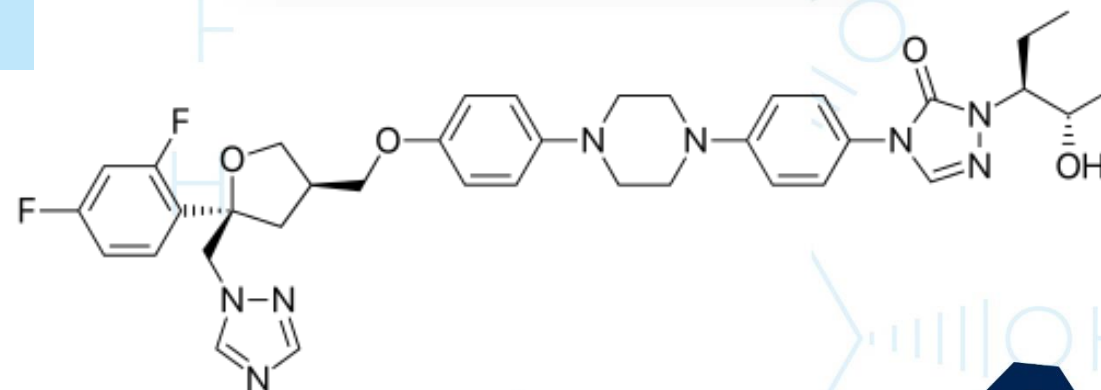
antifungal

intravenous

300 mg posaconazole / vial

6680 mg SBECD / vial

nDrug : nSBECD = 1 : 7.2



EXPECTED PATENT EXPIRY: 2032 (US9023790)

Marketed drug products containing SBECD

ABILIFY® IM

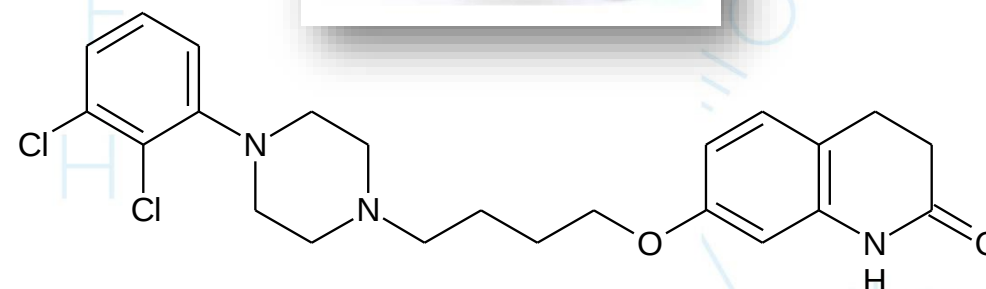
antipsychotic (anti-schizophrenic)

intramuscular

9.75 mg aripiprazole / vial

195 mg SBECD / vial

nDrug : nSBECD = 1 : 4.1



EXPECTED PATENT EXPIRY: 2033 (US8999952)

Marketed drug products containing SBECD

CARNEXIV®

antiepilepsy

intravenous

200 mg carbamazepine / vial

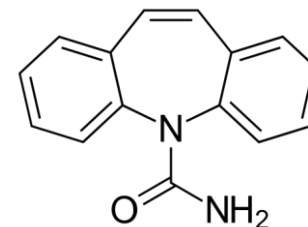
5000 mg SBECD / vial

nDrug : nSBECD = 1 : 2.7

EXPECTED PATENT EXPIRY: 2033 (US9770407)



Carnexiv™
(carbamazepine) injection
Continuity counts.



Marketed drug products containing SBECD

EVOMELA®

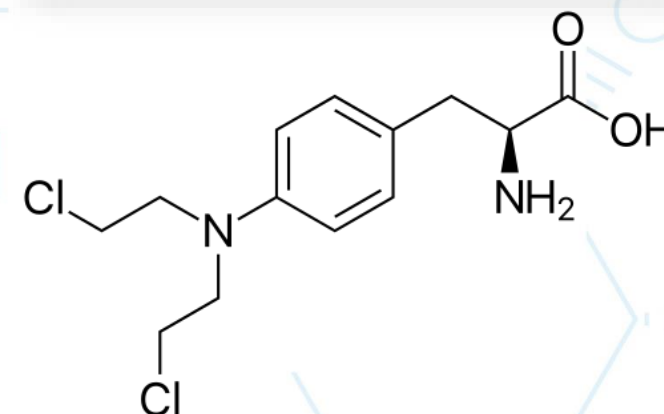
conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation

intravenous

50 mg melphalan / vial

2700 mg SBECD / vial

nDrug : nSBECD = 1 : 7.6



EXPECTED PATENT EXPIRY: no patent granted so far, orphan drug exclusivity until 2023, US Patent Appl: 14/108,169 (patent term: 2030 - expected)

Marketed drug products containing SBECD

BAXDELA®

for the treatment of acute bacterial skin and skin structure infections

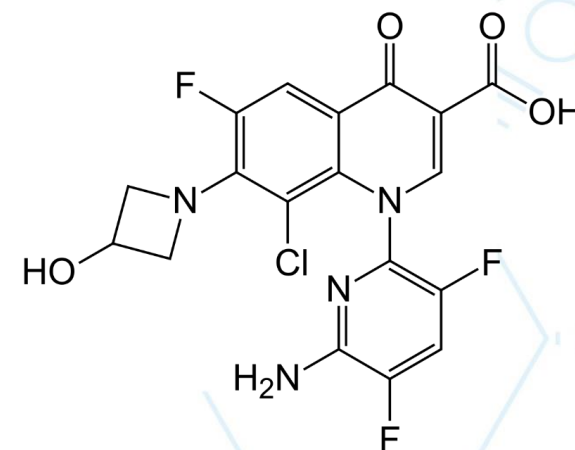
intravenous

300 mg delafloxacin / vial

2400 mg SBECD / vial

nDrug : nSBECD = 1 : 1.6

EXPECTED PATENT EXPIRY: US Patent Appl: 15/042,886 (patent term: 2029 - expected) – status: final rejection (27-11-2018, USPTO)



Marketed drug products containing SBECD

ZULRESSO®

for the treatment of
postpartum depression

intravenous infusion

25 mg brexanolone / vial

1250 mg SBECD / vial

nDrug : nSBECD = 1 : 7.4

EXPECTED PATENT EXPIRY: 2036 (US10246482)

PHARMACEUTICAL NEWS

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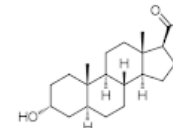
ZULRESSO (BREXANOLONE) IS THE FIRST DRUG APPROVED BY THE FDA SPECIFICALLY FOR POSTPARTUM DEPRESSION (PPD)



Zulresso

What is Zulresso?

Zulresso (brexanolone) is a gamma-aminobutyric acid A (GABAA) receptor positive allosteric modulator indicated for the treatment of postpartum depression (PPD).



Brexanolone

1-(3-Hydroxy-10,13-dimethyl-2,3,4,5,6,7,8,9,11,12,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl)ethanone

Marketed drug products containing SBECD

Levosimendan

intravenous infusion

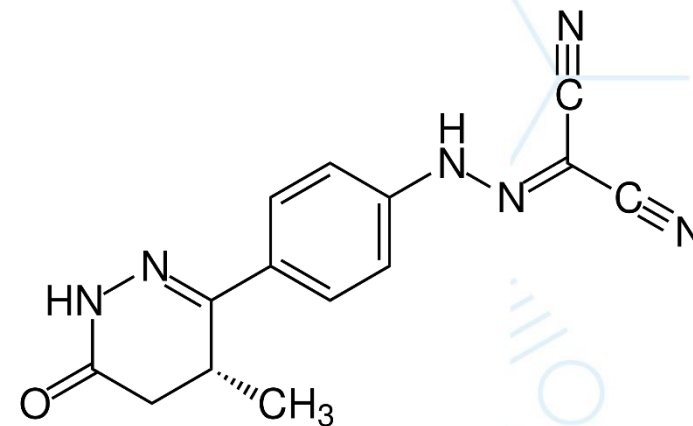
management of acutely
decompensated congestive
heart failure

12.5 mg levosimendan / vial

875 mg SBECD / vial*

nDrug : nSBECD = 1 : 9.1

*Calculated data from Example 2 of WO2017077032 but exactly
consistent with
60.5 mg Na-content noted in the package insert of the product



EXPECTED PATENT EXPIRY: 2036
(WO2017077032, US10507179)

Marketed drug products containing SBECD

VEKLURY® 100 mg concentrate for solution for infusion
treatment of coronavirus disease 2019 (COVID-19) in adults and adolescents with pneumonia requiring supplemental oxygen
intravenous infusion

100 mg remdesivir + 6000 mg SBECD / vial

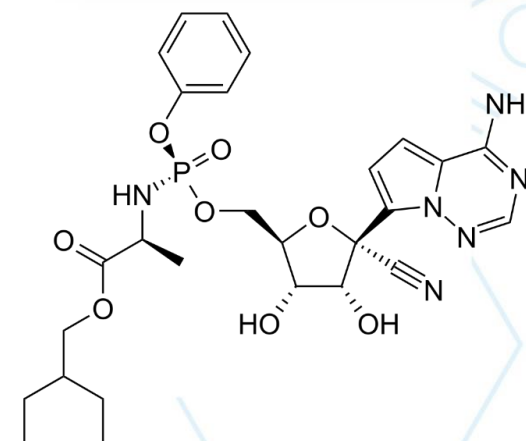
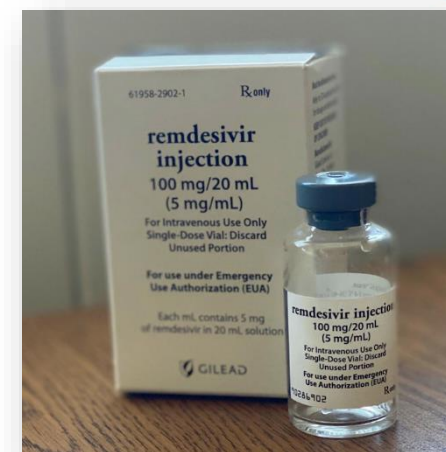
nDrug : nSBECD = 1 : 16.7

VEKLURY® 100 mg powder for concentrate for solution for infusion
intravenous infusion

100 mg remdesivir + 3000 mg SBECD / vial

nDrug : nSBECD = 1 : 8.3

EXPECTED PATENT EXPIRY: 2038 (WO2019014247)



Marketed drug products containing SBECD

SESQUIENT

intravenous anticonvulsant

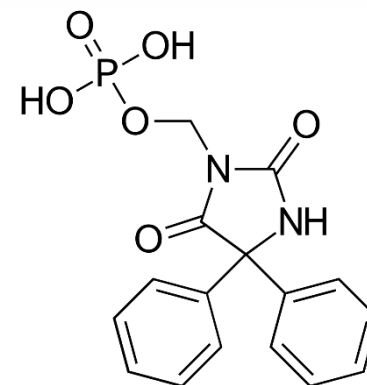
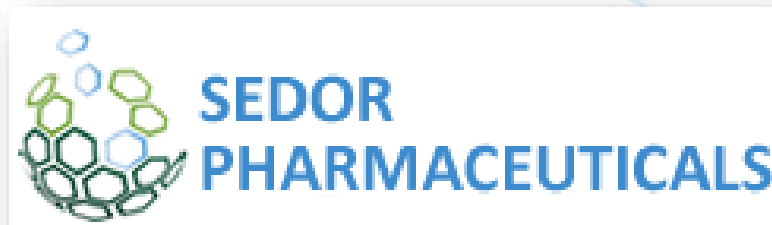
75 mg fosphenytoin Na / ml

100 mg SBECD / ml

(2 and 10 ml vials are available)

nDrug : nSBECD = 4 : 1*

SBECD is used in substoichiometric amount applied for chemical stabilization



EXPECTED PATENT EXPIRY:
expired (WO1998056422)

DEXOLVE™
FOR IMPROVED PHARMACEUTICAL FORMULATIONS

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DEXOLVE™