FOLEY & LARDNER LLP

FOLEY & LARDNER LLP
ATTORNEYS AT LAW
WASHINGTON HARBOUR
3000 K STREET, N.W., SUITE 600
WASHINGTON, D.C. 20007-5143
202.672.5300 TEL
202.672.5399 FAX
www.foley.com
WRITER'S DIRECT LINE
202.672.5430
drosen@foley.com EMAIL

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VIA REGULATIONS.GOV

Division of Dockets Management
U.S. Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

ANDA SUITABILITY PETITION

Dear Sir/Madam:

The undersigned submits this petition under Sections 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FDCA, or the "Act") and 21 CFR § 314.93 to request that the Commissioner of Food and Drugs determine that an Abbreviated New Drug Application (ANDA) may be submitted for a drug product that is not identical to the Reference Listed Drug (RLD) for Busulfan Injection.

A. Action Requested

The Petitioner seeks a determination from the Commissioner of Food and Drugs that an ANDA may be submitted for Busulfan Injection, USP 5 mg/mL.

B. Statement of Grounds

Our client is requesting to file an ANDA for Busulfan Injection, USP 5 mg/mL. The RLD product, Busulfex™ (busulfan) Injection, is approved in 6mg/mL strength (NDA 20924). Please refer to Attachment 1 for a copy of the pertinent page from the "Approved Drug Products with Therapeutic Equivalence Evaluations" (Orange Book) which lists the approved RLD product referenced in this petition.

Our client is proposing to provide Busulfan Injection, USP 5 mg/mL without using the solubilizing agent N,N-dimethylacetamide (DMA) for safety purposes. During the review of the Busulfex™ (busulfan) Injection, the FDA pharmacology/toxicology reviewer stated the following, even though recommending approval of the NDA:

> **The doses of DMA are high enough to cause significant toxicities. The use of DMA in other drug products should be carefully evaluated**.
>
> https://www.accessdata.fda.gov/drugsatfda_docs/nda/99/20954_phrmr_P3.pdf

Our client will be seeking the identical indications and dosing as currently approved for the Busulfex™ (busulfan) Injection.

> **Indications for Use**: Busulfan Injection is indicated for use in combination with cyclophosphamide as a conditioning regimen prior to allogeneic hematopoietic progenitor cell transplantation for chronic myelogenous leukemia.

The Dosing and Administration will be the same as noted in the attached link to the labeling of Busulfex Injection from DailyMed.

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=03dc50f9-c7bd-4c0c-8bbb-c1216ec90c95

Product Name: Busulfan Injection 5mg/mL

Proposed composition:

Qualitative composition of Busulfan Injection

Sr. No.	Ingredient	Pharmaceutical Function
1	Busulfan	API
2	Polyethylene Glycol 400	Co-Solvent
3	Acetone[#]	Co-Solvent

[#] does not remain in Final Formulation except in traces. It will be removed during processing.

Quantitative Composition of Busulfan Injection

Sr. No.	Ingredient	Specification	Quantity per mL	mg/mL	%
1	Busulfan[*]	USP	5.00 mg	5.00	0.50%
2	Polyethylene Glycol 400	NF	1.00 mL	1130.00	100.00% v/v
3	Acetone[#]	NF	--	--	--

*The quantity of Busulfan is on dried basis of actual Assay and Loss on drying. The actual quantity will vary depending on potency calculation.
[@]Considering 1.13 g/mL density; the amount of PEG 400 in 1 mL is 1130.00 mg. This is corresponding to 100.00% v/v.
[#] does not remain in Final Formulation except in traces. It will be removed during processing.

For the reason mentioned above, the Commissioner should approve this petition no later than 90 days after this petition is submitted and authorize the submission of an ANDA for Busulfan Injection, USP 5 mg/mL strength.

C. Environmental Impact

The actions requested herein are subject to categorical exclusion under 21 CFR §25.31(a).

D. **Economic Impact**

An economic impact statement will be submitted upon request should the Commissioner determine such assessment is necessary in evaluating this petition.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the petition.

Please direct any questions or comments regarding this submission to my attention via phone at (202) 672-5430, e-mail at drosen@foley.com or facsimile at (202) 672-5399.

Respectfully submitted,

David L. Rosen, BS Pharm, JD

Attachment