CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20849

CHEMISTRY REVIEW(S)

ORIGINAL AUG 13 1998

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-849 **DATE REVIEWED:** August 13th , 1998

REVIEW #: 2 **REVIEWER:** David Lewis, Ph.D.

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	07-31-98		
Amendment	08-06-98		

NAME & ADDRESS OF APPLICANT: Baxter Healthcare Corporation
Route 120 & Wilson Road
Round lake, Illinois 60073

DRUG PRODUCT NAME
Proprietary: ProSol™-sulfite-free (Amino Acid) Injection in PL 146® Plastic Containers.

Established:
Code Name/#:
Chem.Type/Ther.Class:

APPEARS THIS WAY ON ORIGINAL

PHARMACOL. CATEGORY/INDICATION: Amino Acid Injection/An adjunct for offsetting nitrogen loss or in the treatment of negative nitrogen balance in patients.

DOSAGE FORM: Injection
STRENGTHS: 20%
ROUTE OF ADMINISTRATION: Intravenous
Rx/OTC: X **Rx** _____ **OTC**

APPEARS THIS WAY ON ORIGINAL

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

REMARKS: This is a review of the amendment dated 07-31-98, which concerns Baxter's responses to a draft letter containing eleven (11) deficiencies/ requests for information, which was sent to the firm *via* TeleFAX Baxter Healthcare sent responses to the requests for information via TeleFAX communication: FAX Nº 1, dated July 31st, 1998; FAX Nº 2, dated August 4th, 1998, and FAX Nº 3, dated August 6th, 1998. The FAX transmission dated August 6th, 1998 includes the information communicated in the two previous FAX transmissions

Literature references were included as supporting material for two of the information requests

A hard copy of the final FAX transmission is being prepared by Baxter, and will be sent shortly to DMEDP as an official amendment to NDA 20-849.

As a result of the information received in response to the deficiency letter/request for information, all of the questions regarding the submission have been answered in a satisfactory fashion. The submission is approvable, regarding chemistry, manufacturing and controls, pending completion of the site inspection (EER) report. The trade name ***20% ProSol™ sulfite-free (Amino Acid) Injection in PL 146® Plastic Containers*** was submitted to the labeling & Nomenclature Committee (LNC) for trade name review; no objections were voiced. The proposed trade name is also acceptable to this reviewer, and may be considered acceptable for use with this drug product.

CONCLUSIONS & RECOMMENDATIONS: Adequate information has been provided. The application is now approvable, regarding chemistry, manufacturing and controls information pending a satisfactory inspection report from the office of compliance (OC).

APPEARS THIS WAY
ON ORIGINAL

cc:
Org. NDA 20-849
HFD-510/ Division File
HFD-820/Chemist/D Lewis/DGWu
HFD-510/S. McCort

/S/ 8-13-98
David B. Lewis, Ph.D.
Review Chemist

R/D Init by: /S/ 8/13/98
Filename: NDA 20-849 Review # 2

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-849 **DATE REVIEWED:** July 14th, 1998

REVIEW #: 1 **REVIEWER:** David B. Lewis

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	08/27/97	08-28-97	09/08/97
CORRESPONDENCE	11/11/97		
AMENDMENT	12/09/98		
AMENDMENT	12/19/98.		

APPEARS THIS WAY ON ORIGINAL

NAME & ADDRESS OF APPLICANT: Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

DRUG PRODUCT NAME
Proprietary: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

APPEARS THIS WAY ON ORIGINAL

Established:
Code Name/#:
Chem.Type/Ther. Class: 3S

PHARMACOL. CATEGORY/INDICATION: Amino Acid Injection/An adjunct for offsetting nitrogen loss or in the treatment of negative nitrogen balance in patients.

DOSAGE FORM: Injection

STRENGTHS: 20% amino acid(s) solution in 500 mL, 1000 mL, and 2000 mL polyvinyl chloride (PVC) plastic bags.

ROUTE OF ADMINISTRATION: Intravenous

Rx/OTC: X Rx _____ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

SUPPORTING DOCUMENTS:

CONSULTS: Microbiology

PATENT INFORMATION: Included in Vol. 1.1, p. 17

DEBARMENT CERTIFICATION: A signed debarment certificate dated 8-25-97 is included in Vol. 1.1, p. 11.

REMARKS: In NDA 20-849, the sponsor (Baxter Healthcare Corp.) proposes to market a new product, 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® PVC plastic containers. The drug product is a sterile, nonpyrogenic, hypertonic solution of essential and nonessential amino acids in a Pharmacy Bulk Package, and is intended to be diluted (admixed with other parenteral nutritional drug products) before use, and not administered directly to patients. This drug product, because of its higher concentration (i.e., 20%) can thus, supply an amino acid dose equivalent to lower concentration products, but in a smaller volume, therefore reducing fluid intake. *The formulation of the drug product contains only drug substances already approved in other Baxter Amino Acid Products (NDA 20-147 and 20-678; marketed under the trade names of Travasol®*

NDA 20-147, and 20-678 are referenced in the application, along with the DMF's pertaining to Chemistry, manufacturing and controls information on the drug substances (i.e., essential and non-essential amino acids).

The PL 146® plastic container has been previously reviewed,

The deficiencies regarding this application lie mainly in the presented stability data, and in the stability protocol. The stability profile of 20% ProSol™ differs from that which was seen in previously approved Baxter Parenteral (Amino Acid) Injections in PL 146® plastic containers. Several issues regarding the provided stability data, and the proposed stability protocol (specifications, methods, frequency of testing) need to be cleared up prior to approval from the standpoint of chemistry, manufacturing and controls information. Other deficiencies are relatively minor, and are of an informative nature. The microbiology review has been completed, and the application is recommended for approval for microbiology issues concerning sterility assurance (see micro. Review # 1, dated 3-18-98; N. Sweeney, Ph.D., reviewer). cGMP inspection has been completed for all facilities, and, as of 7-14-98, acceptable status was issued with two inspection still scheduled.

The correspondence dated 11-11-97 provides for two samples of empty containers supplied to D. Lewis by Dr. Itani of Baxter Healthcare. The amendments dated 12-09-97 and 12-19-97 provide for a duplicate patent certificate and additional information regarding container-related extractables. An environmental assessment is not necessary because amino acids are considered naturally occurring (drug) substances which are exempted under 21 CFR 25.31(c).

CONCLUSIONS & RECOMMENDATIONS: The application is approvable, pending a satisfactory response to the deficiencies/information request, *and a satisfactory EES report*. See list of deficiencies & request for further information to be communicated to the sponsor. The communication may be send via teleFAX since the inspection has not been completed as of 7-14-98.

cc:
Org. NDA 20-849
HFD-510/ Division File
HFD-820/Chemist/D Lewis/DGWu
HFD-510/S. McCort

/S/

David B. Lewis, Ph.D.
Review Chemist

R/D Init by: /S/ 7/15/98
Filename: NDA 20-849 Review