

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207131Orig1s000

PHARMACOLOGY REVIEW(S)

**DIVISION OF ANTI-INFECTIVE PRODUCTS
PHARMACOLOGY/TOXICOLOGY REVIEW
NDA 207131**

Cefazolin Injection, USP in GALAXY™ Container (2 g/100 mL)

DATE: 3/16/15

TO: Fariba Izadi, Pharm.D.
Project Manager, DAIP
and
File, NDA 207131 (cefazolin injection in GALAXY plastic container)

FROM: Amy L. Ellis, Ph.D.
Pharmacologist, DAIP

THROUGH: Wendelyn Schmidt, Ph.D.
Supervisory Pharmacologist, DAIP

RE: Pharmacology/Toxicology Review of NDA 207131, Cefazolin Injection, USP in GALAXY Container (2 g/100 mL)

Celerity Pharmaceuticals, LLC (Rosemont, IL) submitted this NDA for a frozen, premixed, iso-osmotic, sterile, non-pyrogenic solution of cefazolin packaged in Baxter's GALAXY container (2 g (b) (4) 100 mL of diluent in each bag). Dextrose, USP is added to adjust the osmolality. The pH is adjusted with sodium bicarbonate (b) (4) to a range of 4.5 – 7.0. The proposed Cefazolin Injection, USP product is intended for intravenous use after thawing at room temperature or under refrigeration. Baxter Healthcare Corporation currently markets a 1g/50 ml cefazolin with the same excipients under ANDA 63002 (also a frozen premix in a GALAXY plastic container). Celerity has hired Baxter to manufacture and package their proposed 2 g/100 ml cefazolin product.

Each 100 ml of Cefazolin Injection contains:

Cefazolin	(b) (4)
Dextrose, anhydrous	(b) (4) g
Sodium Bicarbonate	(b) (4)
Water for Injection	(b) (4)

additional sodium bicarbonate could be added to adjust pH to 4.5-7.0

Celerity is requesting approval of the proposed product (b) (4) 2 g Cefazolin for Injection, USP and Dextrose Injection, USP marketed by B. Braun under NDA 50779. The B. Braun product is packaged in the Duplex® container (sterile dual chamber bag with solute in one chamber and diluent in the other). The diluent for B. Braun's product is 3% w/v dextrose and the volume is 50 ml per container. It is also iso-osmotic (about 290 mOsmol/kg) and pH was measured to be 5.0-

6.1. B. Braun's product does not contain sodium bicarbonate as an excipient and cefazolin sodium is used in its manufacture. Celerity considers Cefazolin Injection, USP in GALAXY Container (2 g/100 mL) to be bioequivalent to B. Braun's 2 g Cefazolin for Injection, USP and Dextrose Injection, USP in the Duplex Container (2 g/50 ml). Clinical studies were not conducted with Celerity's product and a request for waiver of in vivo bioavailability studies was submitted with the NDA.

NDA 207131 does not require a pharmacology/toxicology review. The sponsor did not conduct any additional nonclinical toxicology studies to support the current NDA. The Division agreed that nonclinical studies would not be necessary as long as there are no impurities or degradation products in Cefazolin Injection, USP in GALAXY Container (2 g/100 mL) that exceed ICH qualification threshold levels or the levels in comparable marketed products. There appear to be no impurities or degradation products in the current product that require qualification via nonclinical testing. The Chemistry Reviewer investigated impurity levels in other marketed cefazolin products and the proposed limits for the current product will not exceed them. Thus, the impurity limits proposed by the sponsor can be considered qualified for Cefazolin Injection, USP in GALAXY Container (2 g/100 mL). The sponsor has requested that the Agency rely on its findings of safety and effectiveness for the approved product 2 g Cefazolin for Injection, USP and Dextrose Injection, USP in the Duplex Container to support this NDA for the current product, Cefazolin Injection, USP in GALAXY Container (2 g/100 mL), as permitted under section 505(b)(2) of the FD&C Act. The cefazolin innovator product ANCEF, approved in 1973 under NDA 50461, is no longer being marketed, but there are a number of generic cefazolin products that are currently being marketed in the U.S.

There are several other approved products available as premixed solutions in GALAXY plastic containers. These include aztreonam, ceftriaxone, and nafcillin. Thus, there is ample precedent for the clinical use of premixed antimicrobials stored in the same type of container that would be used for the proposed cefazolin for injection.

The pharmacologist has no objection to the approval of 207131, Cefazolin Injection, USP in GALAXY Container (2 g/100 mL). The label for this product should, in general, be consistent with the label for Cefazolin for Injection, USP and Dextrose Injection, USP in the Duplex Container (NDA 50779). The label for Cefazolin for Injection, USP and Dextrose Injection, USP in the Duplex Container was written in PLR format. Although a few editorial changes to Sections 8.1 and 13 will be recommended, none are scientifically substantive.

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/s/

AMY L ELLIS
03/23/2015

WENDELYN J SCHMIDT
03/30/2015

**DIVISION OF ANTI-INFECTIVE PRODUCTS
PHARMACOLOGY/TOXICOLOGY REVIEW
MEMO TO FILE: PreNDA 207131**

DATE: 5/15/14

TO: Fariba Izadi, Pharm.D.
Project Manager, DAIP
and
File, NDA 207131 (cefazolin injection in Galaxy™ plastic container)

FROM: Amy L. Ellis, Ph.D.
Pharmacologist, DAIP

THROUGH: Wendelyn Schmidt, Ph.D.
Supervisory Pharmacologist, DAIP

RE: PreNDA Questions from Sponsor (Celerity Pharmaceuticals, LLC)

The sponsor, Celerity Pharmaceuticals, LLC (Rosemont, IL) is developing a premixed formulation of cefazolin for injection:

Cefazolin (b) (4)
Dextrose, anhydrous (b) (4)
Sodium Bicarbonate (b) (4)
Water for Injection (b) (4).
additional sodium bicarbonate could be added to adjust pH to 4.5-7.0

The formulation will be iso-osmotic, approximately (b) (4). The product will be frozen in Galaxy™ plastic containers and will be available in a 2 g/100 ml size. According to the sponsor, Baxter Healthcare Corporation currently markets a 1g/50 ml cefazolin with the same excipients under ANDA 063002 (also a frozen premix in a Galaxy™ plastic container). Celerity has hired Baxter to manufacture and package their proposed 2 g/100 ml cefazolin product.

There are several other approved products available as premixed solutions in Galaxy™ plastic containers. These include aztreonam, ceftriaxone, and nafcillin. Thus, there is ample precedent for the clinical use of premixed antimicrobials stored in the same type of container that would be used for the proposed cefazolin for injection.

Celerity also refers to a product marketed by B. Braun for 2 g cefazolin in the Duplex® container under NDA 050799. The diluent for B. Braun's product is 3% w/v dextrose and the volume is 50 ml per container. It is also iso-osmotic (about 290 mOsmol/kg) and pH was measured to be 5.0-6.1. B. Braun's product does not contain sodium bicarbonate as an excipient and cefazolin sodium is used in its manufacture.

There are a variety of injectable cefazolin products on the market in addition to the B. Braun product discussed above. The sponsor intends to use the Agency's findings of safety and effectiveness for the approved products to support an NDA for the current product, as permitted under section 505(b)(2) of the FD&C Act. [REDACTED] (b) (4)

The sponsor does not intend to conduct any additional nonclinical studies with cefazolin injection in the Galaxy container. This is acceptable providing that there are no unqualified impurities or degradants in the product.

The sponsor did not submit any nonclinical questions to the Division. The statement below should be sent as an additional comment:

TRANSMIT TO SPONSOR:

You should demonstrate that the impurity/degradation profile of cefazolin injection in the Galaxy container stored as directed in your proposed label does not differ significantly from that of other marketed cefazolin products OR show that any impurities or degradation products in your product do not exceed the thresholds for qualification discussed in the applicable ICH guidance documents. If there are no impurities or degradation products that exceed the levels in a marketed product or ICH qualification threshold levels, no nonclinical testing of cefazolin injection in the Galaxy container will be needed. If there are impurities or degradation products that must be qualified, limited nonclinical testing would be needed.

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/s/

AMY L ELLIS
05/21/2014

WENDELYN J SCHMIDT
05/22/2014