CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125319Orig1s085, 086, 087

PRODUCT QUALITY REVIEW(S)

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Biotechnology Products

Memorandum of Review

Date: 9/16/2016

To: File for STN: 125319/85, 86, 87

From: Chikako Torigoe, CDER/OBP/DBRRII

Chikako Torigoe -A Digitally signed by Chikako Torigoe -A DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300430897, cn=Chikako Torigoe -A Date: 2016.09.21 12:20:08 -04'00'

Through: Rashmi Rawat, Team Leader, CDER/OBP/DBRRII

Rashmi Rawat -S Digitally signed by Rashmi Rawat -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Rashmi Rawat -S, 0.9.2342.19200300.100.1.1=0014337532 Date: 2016.09.21 12:38:40 -04'00'

Juhong Liu, Acting Review Chief, CDER/OBP/DBRRII

Juhong Liu -S Digitally signed by Juhong Liu -S DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Juhong Liu -S, 0.9.2342.19200300.100.1.1=0010401517 Date: 2016.09.21 12:04:12 -04'00'

Subject: Addition of new indications: Tumor necrosis factor receptor associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome/mevalonate kinase deficiency (HIDS/MKD), familial Mediterranean fever (FMF)

Applicant: Novartis

Product: Canakinumab (Ilaris), human IgG1(κ) against IL-1β

Indications: Cryopyrin-associated periodic syndromes, systemic juvenile idiopathic arthritis

Supplement Receipt Date: SUPPL-85: 3/23/2016, SUPPL-86: 3/28/2016, SUPPL-87: 3/29/2016
PDUFA Goal Date: 9/23/2016

Link: \\Cdsesub1\evsprod\BLA125319\125319.enx

Recommendation: From product quality perspective, the liquid in vial dosage form is comparable to the currently approved powder for solution dosage form.

Review Summary
These three supplements propose the addition of new indications for canakinumab. These indications are TRAPS, HIDS/MKD and FMF. For the clinical studies of these indications, a new presentation of canakinumab drug product, 150 mg/mL solution for injection in vial, was used. The product quality information and the results of comparability assessments of this new drug product presentation with the currently-approved canakinumab powder for solution for injection were submitted in the

supplement 85 and in the CMC supplement 88. The CMC supplement 88 contains the manufacturing, comparability and labeling information on the new liquid in vial drug product presentation. The review of the comparability study of product quality of liquid in vial dosage form to powder for solution concluded that both dosage forms are comparable. However, the supplement 88 was issued a complete response on 7/29/2016 due to microbiological issues.
The review of the product quality information and the results of comparability assessment of the two drug product dosage forms, liquid in vial and the currently-approved powder for solution for injection is on file for the supplement 88. The review of the proposed label that includes the information on the new drug product presentation was performed by Jibril Abdus-Samad in OBP and is on file for the supplement 88.

Environmental Assessment
The sponsor requested a categorical exclusion from the environmental assessment requirement pursuant to 21 CFR 25.15 (d) based on the exclusion allowed by 21 CFR 25.31 (b and c) and the request is acceptable.

Conclusion: From the product quality perspective, canakinumab liquid in vial dosage form is comparable to the currently approved powder for solution for injection dosage form.

BLA-125319-SUPPL-85 » Manufacturing Facility Inspection

Overall Manufacturing Inspection Recommendation

Task Summary | Task Details | Documents | Approvals | Updates | Application Life Cycle

Inspection Management Form

As of Sep 2, 2016 10:03 am G

Inspection Management Form

BLA-125319-SUPPL-85

NOVARTIS PHARMA STEIN AG | 3002653483 | SVL SMALL VOLUME PARENTERAL, LYOPHILIZED | Approve Facility

NOVARTIS PHARMA STEIN AG | 3002653483 | SVS STERILE-FILLED SMALL VOLUME PARENTERAL DRUGS | Approve Facility

NOVARTIS PHARMA AG | 3002807772 | CTL CONTROL TESTING LABORATORY | Approve Facility

(b) (4)

NOVARTIS PHARMA SAS CENTRE DE BIOTECHNOLOGIE | 3004864869 | BTP BIOLOGICAL THERAPEUTIC PRODUCTS | Approve Facility

(b) (4)

Overall Manufacturing Inspection Recommendation

- (•) Approve
- ( ) Withhold

Cancel

Submission Manufacturing Facilities

Facility Status	Completion Date	Project Name	FEI	DUNS	Global ID	Facility Name
Approve Facility	4/25/2016	BLA-125319-SUPPL-85	3002653483	488152505	25063	NOVARTIS PHARMA STEIN AG
Approve Facility	(b) (4)	BLA-125319-SUPPL-85	(b) (4)			b) (4)
Cancelled		BLA-125319-SUPPL-85				
Approve Facility		BLA-125319-SUPPL-85				b) (4)
Approve Facility	4/8/2016	BLA-125319-SUPPL-85	3004864869	263159719	73202	NOVARTIS PHARMA SAS CENTRE DE BIOTECI
Cancelled	(b) (4)	BLA-125319-SUPPL-85	(b) (4)			
Approve Facility	4/8/2016	BLA-125319-SUPPL-85	3002807772	482347168	33740	NOVARTIS PHARMA AG
Approve Facility	4/8/2016	BLA-125319-SUPPL-85	3002653483	488152505	25063	NOVARTIS PHARMA STEIN AG

BLA-125319-SUPPL-86 » Manufacturing Facility Inspection

Overall Manufacturing Inspection Recommendation

Task Summary | Task Details | Documents | Approvals | Updates | Application Life Cycle

Inspection Management Form

As of Sep 2, 2016 10:05 am G

Inspection Management Form

BLA-125319-SUPPL-86

NOVARTIS PHARMA STEIN AG | 3002653483 | SVL SMALL VOLUME PARENTERAL, LYOPHILIZED | Approve Facility

NOVARTIS PHARMA STEIN AG | 3002653483 | SVS STERILE-FILLED SMALL VOLUME PARENTERAL DRUGS | Approve Facility

NOVARTIS PHARMA AG | 3002807772 | CTL CONTROL TESTING LABORATORY | Approve Facility

(b) (4)

NOVARTIS PHARMA SAS CENTRE DE BIOTECHNOLOGIE | 3004864869 | TRP THERAPEUTIC RECOMBINANT PRODUCTS | Approve Facility

(b) (4)

Overall Manufacturing Inspection Recommendation

- Approve
- Withhold

Cancel

Submission Manufacturing Facilities

Facility Status	Completion Date	Project Name	FEI	DUNS	Global ID	Facility Name
Approve Facility	4/25/2016	BLA-125319-SUPPL-86	3004864869	263159719	73202	NOVARTIS PHARMA SAS CENTRE DE BIOTECH
Approve Facility	4/25/2016	BLA-125319-SUPPL-86	3002653483	488152505	25063	NOVARTIS PHARMA STEIN AG
Approve Facility	4/25/2016	BLA-125319-SUPPL-86	3002653483	488152505	25063	NOVARTIS PHARMA STEIN AG
Approve Facility	(b) (4)	BLA-125319-SUPPL-86	(b) (4)			(b) (4)
Approve Facility		BLA-125319-SUPPL-86				(b) (4)
Approve Facility	4/25/2016	BLA-125319-SUPPL-86	3002807772	482347168	33740	NOVARTIS PHARMA AG

Facilities Pending Profile Entry

BLA-125319-SUPPL-87 » Manufacturing Facility Inspection

Overall Manufacturing Inspection Recommendation

Task Summary | Task Details | Documents | Approvals | Updates | Application Life Cycle

Inspection Management Form

As of Sep 2, 2016 10:06 am G

Inspection Management Form

BLA-125319-SUPPL-87

(b) (4)

NOVARTIS PHARMACEUTICALS CORPORATION | 2416082 | SVL SMALL VOLUME PARENTERAL, LYOPHILIZED |

NOVARTIS PHARMA STEIN AG | 3002653483 | SVL SMALL VOLUME PARENTERAL, LYOPHILIZED | Approve Facility

NOVARTIS PHARMA STEIN AG | 3002653483 | SVS STERILE-FILLED SMALL VOLUME PARENTERAL DRUGS | Approve Facility

NOVARTIS PHARMA AG | 3002807772 | CTL CONTROL TESTING LABORATORY | Approve Facility

(b) (4)

NOVARTIS PHARMA SAS CENTRE DE BIOTECHNOLOGIE | 3004864869 | TRP THERAPEUTIC RECOMBINANT PRODUCTS | Approve Facility

(b) (4)

Overall Manufacturing Inspection Recommendation

- Approve
- Withhold

Cancel

Submission Manufacturing Facilities

Facility Status	Completion Date	Project Name	FEI	DUNS	Global ID	Facility Name
No Further Evaluation	4/25/2016	BLA-125319-SUPPL-87	2416082	808931344	83948	NOVARTIS PHARMACEUTICALS CORPOF
Approve Facility	4/25/2016	BLA-125319-SUPPL-87	3002653483	488152505	25063	NOVARTIS PHARMA STEIN AG
Approve Facility	4/25/2016	BLA-125319-SUPPL-87	3002653483	488152505	25063	NOVARTIS PHARMA STEIN AG
Approve Facility	4/25/2016	BLA-125319-SUPPL-87	3004864869	263159719	73202	NOVARTIS PHARMA SAS CENTRE DE BIC
Approve Facility	4/25/2016	BLA-125319-SUPPL-87	3002807772	482347168	33740	NOVARTIS PHARMA AG
Approve Facility	(b) (4)	BLA-125319-SUPPL-87	(b) (4)			
Approve Facility		BLA-125319-SUPPL-87				
No Further Evaluation		BLA-125319-SUPPL-87				