January 11, 2018
Sebia, Inc
Karen Anderson
Director of Technical and Regulatory
1705 Corporate Drive, Suite 400
Norcross, Georgia 30093

Re: K172195
Trade/Device Name: HYDRASHIFT 2/4 daratumumab, daratumumab Control
Regulation Number: 21 CFR 866.5510
Regulation Name: Immunoglobulins A, G, M, D, and E immunological test system
Regulatory Class: Class II
Product Codes: CFF, JJY
Dated: December 07, 2017
Received: December 12, 2017

Dear Karen Anderson:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR

Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kelly Oliner -S

For,
Lea Carrington
Director
Division of Immunology
and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K172195

Device Name
HYDRASHIFT 2/4 daratumumab
Daratbumumab Control

Indications for Use *(Describe)*

Assay:
The HYDRASHIFT 2/4 daratumumab test is intended for the qualitative detection of monoclonal proteins in human serum by immunofixation electrophoresis. The kits are to be used in conjunction with the HYDRAGEL IF kits and the semi-automated HYDRASYS 2 electrophoresis apparatus. The proteins, separated by electrophoresis on alkaline buffered agarose gels, are incubated with individual antisera that are specific against gamma (Ig G), alpha (Ig A) and mu (Ig M) heavy chains, and kappa (free and bound) and lambda (free and bound) light chains, respectively. After removing the non-reacted proteins, the immunoprecipitates are stained with acid violet. The electrophoregrams are evaluated visually for the presence of specific reactions with the suspect monoclonal proteins. The HYDRASHIFT 2/4 daratumumab kits remove the daratumumab Ig G, Kappa interference and enable the visual evaluation of the presence or absence of monoclonal proteins on the HYDRAGEL IF kits in patients who have received daratumumab therapy. For In Vitro Diagnostic Prescription Use Only.

Control:
The daratumumab Control is designed for qualitative quality control of the HYDRASHIFT daratumumab immunofixation procedure performed using the HYDRASYS 2 instrument. The daratumumab Control is designed for laboratory use. It should be used like a human serum. For In Vitro Diagnostic Prescription Use Only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510K SUMMARY (Summary of Safety and Effectiveness)

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Sebia, Inc.
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Date Prepared	January 4, 2018
Manufacturing	Sebia Parc Technologique Léonard de Vinci Rue Léonard de Vinci, CP 8010 LISSES, 91008 EVRY Cedex FRANCE Phone: (33) 1 69 89 80 80 Fax: (33) 1 69 89 78 78
Product Name	HYDRASHIFT 2/4 daratumumab Daratumumab CONTROL
Common Name	Hydrashift daratumumab Serum Immunofixation
Product Regulation No.	21CFR sec. 866.5510
Product Codes	CFF
Device classification and Panel Classification	Class II , Immunology
Establishment Registration No.	8023024

1. DEVICE DESCRIPTION

HYDRASYS 2 is a semi-automated multi-parameter system for start-to finish agarose gel electrophoresis: application of samples, migration, incubation, drying, staining, destaining and final-stage drying.

Abnormal bands in serum protein electrophoregrams, primarily those in the beta globulin and gamma globulin zones, are always suspected to be monoclonal proteins (M-proteins, paraproteins, monoclonal immunoglobulins) and therefore, an indication of performing an Immunofixation technique to type and confirm the monoclonal gammopathies.

Daratumumab is a human therapeutic Ig G Kappa monoclonal antibody and as such, during the clinical monitoring of patients treated with daratumumab, this antibody simulates a band detected by serum protein electrophoresis and immunofixation in the gamma region. It can simulate an endogenous Ig G Kappa paraprotein.

Daratumumab CONTROL is a qualitative quality control for the assay.

Reagents:
REAGENTS AND MATERIALS SUPPLIED IN THE HYDRASHIFT 2/4 daratumumab KITS

ITEMS	PN 4639 (20 TESTS)	PN 4640 (40 TESTS)
Anti-daratumumab antiserum (ready to use)	1 vial, 0.4 mL	1 vial, 0.85 mL
Sample diluent (ready to use)	1 vial, 2,2 mL	1 vial, 2,2 mL
Green applicators (ready to use)	1 pack of 10 (15 teeth)	2 packs of 10 (15 teeth)

REAGENTS REQUIRED BUT NOT SUPPLIED

	SEBIA PRODUCT NUMBER
HYDRAGEL 2 or 4 IF Acid violet - Dynamic mask	4302, 4304 or 4381*
Antisera and Fixative for immunofixation IF - Dynamic mask	4315
or	
HYDRAGEL 2 or 4 IF Acid violet - Standard mask	4802, 4804 or 4881*
Antisera and Fixative for immunofixation IF - Standard mask	4815
and	
Daratumumab CONTROL	4765
DESTAINING SOLUTION	4540
HYDRASYS WASH SOLUTION	4541

HYDRAGEL IF SAMPLE DILUENT	4588
FLUIDIL	4587
DTT DILUENT (IF / IT)	4589
BETA-MERCAPTOETHANOL (BME or 2MERCAPTOETHANOL)	Not supplied by SEBIA

2. INDICATIONS FOR USE

The HYDRASHIFT 2/4 daratumumab test is intended for the qualitative detection of monoclonal proteins in human serum by immunofixation electrophoresis. The kits are to be used in conjunction with the HYDRAGEL IF kits and the semi-automated HYDRASYS 2 electrophoresis apparatus. The proteins, separated by electrophoresis on alkaline buffered agarose gels, are incubated with individual antisera that are specific against gamma (Ig G), alpha (Ig A) and mu (Ig M) heavy chains, and kappa (free and bound) and lambda (free and bound) light chains, respectively. After removing the non-reacted proteins, the immunoprecipitates are stained with acid violet. The electrophoregrams are evaluated visually for the presence of specific reactions with the suspect monoclonal proteins. The HYDRASHIFT 2/4 daratumumab kits remove the daratumumab Ig G, Kappa interference and enable the visual evaluation of the presence or absence of monoclonal proteins on the HYDRAGEL IF kits in patients who have received daratumumab therapy. For *In Vitro* Diagnostic Prescription Use Only.

The daratumumab Control is designed for the qualitative quality control of the HYDRASHIFT daratumumab immunofixation procedure performed using the HYDRASYS 2 instrument. The daratumumab Control is designed for laboratory use. It should be used like a human serum sample. For *In Vitro* Diagnostic Prescription Use Only.

3. TECHNOLOGICAL CHARACTERISTICS

The HYDRASHIFT daratumumab immunofixation procedure performed on HYDRAGEL IF 2/4 gel is based on the creation of a daratumumab / anti-daratumumab antibody complex and shifting it outside the gammaglobulins zone. With the HYDRASHIFT daratumumab procedure, the daratumumab / anti-daratumumab antibody complex is visualized in alpha-1 zone on Ig G and Kappa immunofixation tracks and then the interference is removed from the gamma zone.

4. SUBSTANTIAL EQUIVALENCE INFORMATION:

Predicate Device Name	Predicate Device 510(k) number	Product Code	Regulation No.
HYDRAGEL IF	K960669	CFF	866.5510

Similarities between the candidate device (HYDRASHIFT 2/4 daratumumab) and the predicate device (HYDRAGEL IF) (Table A).

Similarities		
Table A	HYDRASHIFT 2/4 daratumumab **Candidate Device**	HYDRAGEL IF **Predicate Device (K960669)**
Intended use	The HYDRASHIFT 2/4 daratumumab test is intended for the qualitative detection of monoclonal proteins in human serum by immunofixation electrophoresis. The kits are to be used in conjunction with the HYDRAGEL IF kits and the semi-automated HYDRASYS 2 electrophoresis apparatus. The proteins, separated by electrophoresis on alkaline buffered agarose gels, are incubated with individual antisera that are specific against gamma (Ig G), alpha (Ig A) and mu (Ig M) heavy chains, and kappa (free and bound) and lambda (free and bound) light chains, respectively. After removing the non-reacted proteins, the immunoprecipitates are stained with acid violet. The electrophoregrams are evaluated visually for the presence of specific reactions with the suspect monoclonal proteins. The HYDRASHIFT 2/4 daratumumab kits remove the daratumumab Ig G, Kappa interference and enable the visual evaluation of the presence or absence of monoclonal proteins on the HYDRAGEL IF kits in patients who have received daratumumab therapy. For *In Vitro* Diagnostic Prescription Use Only.	The HYDRAGEL 1 IF, 2 IF, 4 IF and 9 IF kits are designed for detection of monoclonal proteins in human serum and urine by immunofixation electrophoresis. The kits are used in conjunction with the semi-automated HYDRASYS electrophoresis apparatus. The proteins, separated by electrophoresis on alkaline buffered agarose gels, are incubated with individual antisera that are specific against gamma (Ig G), alpha (Ig A) and mu (Ig M) heavy chains, and kappa (free and bound) and lambda (free and bound) light chains, respectively. After removing the non-reacted proteins, the immunoprecipitates are stained either with acid violet or amidoblack. The electrophoregrams are evaluated visually for the presence of specific reactions with the suspect monoclonal proteins.
Assay Principle	Agarose Gel Electrophoresis	Agarose Gel Electrophoresis
Program	Same	Uses IF Program on Hydrasys 2
Reagents Gel kit Antisera kit Accessory	 Same Same HYDRASHIFT 2/4 daratumumab	 HYDRAGEL IF Antisera and Fixative for immunofixation IF NA

Table B. Differences between the predicate device (HYDRAGEL IF) and the candidate device (HYDRASHIFT 2/4 daratumumab) in (Table B).

Differences		
Table B	HYDRASHIFT 2/4 daratumumab **Candidate Device**	HYDRAGEL IF **Predicate Device** K960669**)**
Specimen Type	Human Serum	Human Serum, Human Urine
Reagents	Using anti-daratumumab antibody	No anti-daratumumab antibody
Daratumumab band	Removed from gamma zone into alpha zone	Remains in Gamma zone

5. Performance Data:

a) Repeatability

Ten (10) different serum samples, including 1 normal serum sample and 9 serum samples with monoclonal components, were run using the HYDRASHIFT 2/4 daratumumab procedure used in conjunction with each of the following kits: - HYDRAGEL 4 IF Acid violet Standard mask, - HYDRAGEL 4 IF Acid violet Dynamic mask.
Each sample was run 4 times within the same gel.
For each tested sample, all repeats gave 100 % of concordant results within gel.

Sample No.	Type	Within gel	Total analyses per gel
Sample No. 1	Normal	100% concordant result	4
Sample No. 2	Ig G, L + Ig A, K + Ig M, L	100% concordant result	4
Sample No. 3	Ig G, K	100% concordant result	4
Sample No. 4	Ig G, L	100% concordant result	4
Sample No. 5	Ig A, K	100% concordant result	4
Sample No. 6	Ig A, L	100% concordant result	4
Sample No. 7	2 Ig M, K	100% concordant result	4
Sample No. 8	Ig M, L	100% concordant result	4
Sample No. 9	Kappa free	100% concordant result	4
Sample No. 10	Lambda free	100% concordant result	4

b) Reproducibility between gels, between lots and between instruments

Ten (10) different serum samples, including 1 normal serum sample and 9 serum samples with monoclonal components, were run using the HYDRASHIFT 2/4 daratumumab procedure used in conjunction with each of the following kits : - HYDRAGEL 4 IF Acid violet Standard mask, - HYDRAGEL 4 IF Acid violet Dynamic mask.

This study was performed with 3 HYDRASYS 2 instruments and with 3 lots of HYDRASHIFT 2/4 daratumumab kit.
The normal sample was analyzed on 9 runs including one analysis per gel on 3 gels over 3 working days.
The samples with monoclonal components were analyzed on 9 runs with one analysis per gel, over 3 working days.
All samples gave 100 % of concordant results between gels on the 3 HYDRASYS 2 instruments and with 3 lots of HYDRASHIFT 2/4 daratumumab kit.

Sample No.	Type	Instrument No. 1 / Lot No. 1			Instrument No. 2 / Lot No. 2			Instrument No. 3 / Lot No. 3			Total analyses per sample
		Day No. 1	Day No. 2	Day No. 3	Day No. 1	Day No. 2	Day No. 3	Day No. 1	Day No. 2	Day No. 3	
1	Normal	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	27
2	Ig G, L + Ig A, K + Ig M, L	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
3	Ig G, K	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
4	Ig G, L	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
5	Ig A, K	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
6	Ig A, L	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
7	Ig M, K	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
8	Ig M, L	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
9	Kappa free	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9
10	Lambda free	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	100 % concordant result	9

c) External comparative studies

The results presented below have been obtained from 2 external studies performed in the USA. The external study No. 1 was performed on 198 samples and the external study No. 2 was performed on 172 samples. The first 172 samples have been analyzed on both sites.

External study No. 1

Comparative study No. 1 was performed on 198 serum samples analyzed with:

- HYDRAGEL 4 IF Acid Violet Dynamic Mask kit,
- HYDRASHIFT 2/4 daratumumab used in conjunction with HYDRAGEL 4 IF Acid Violet Dynamic Mask kit.

With the HYDRAGEL 4 IF Acid Violet Dynamic Mask procedure, the daratumumab was visualized on G track and on Kappa track for 113 samples. For those samples, the HYDRASHIFT 2/4 daratumumab used in conjunction with HYDRAGEL 4 IF Acid Violet Dynamic Mask kit allows the shifting of the daratumumab.

For the other 85 samples, the characterization (normal or abnormal with monoclonal components) was the same between both procedures.

This study demonstrated 100 % concordant result:

- For 42 normal serum samples: 100 % concordant result.
- For the 156 pathological serum samples: 100 % concordant result.

External study No. 2

Comparative study No. 2 was performed on 172 serum samples analyzed with:

- HYDRAGEL 4 IF Acid Violet Standard Mask kit,
- HYDRASHIFT 2/4 daratumumab used in conjunction with HYDRAGEL 4 IF Acid Violet Standard Mask kit.

With the HYDRAGEL 4 IF Acid Violet Standard Mask procedure, the daratumumab was visualized on G track and on Kappa track for 98 samples. For those samples, the HYDRASHIFT 2/4 daratumumab used in conjunction with HYDRAGEL 4 IF Acid Violet Standard Mask kit allows the shifting of the daratumumab.

For the other 74 samples, the characterization (normal or abnormal with monoclonal components) was the same between both procedures.

This study demonstrated 100 % concordant result:

- For 38 normal serum samples: 100 % concordant result.
- For the 134 pathological serum samples: 100 % concordant result.

d) Sensitivity

Six (6) serum samples, including 2 normal serum samples and 4 serum samples with different monoclonal components, added with daratumumab at different concentrations (final concentrations in sample between 0.1 and 3.0 g/L) were analyzed with the HYDRASHIFT 2/4 daratumumab procedure used in conjunction with each of the following kits: - HYDRAGEL 4 IF Acid Violet Standard Mask, - HYDRAGEL 4 IF Acid Violet Dynamic Mask.

The detection limit of daratumumab and/or daratumumab /anti-daratumumab antibody complex visualized is 0.3 g/L.

e) Controls

It is recommended to run an assayed control serum (such as daratumumab CONTROL, SEBIA PN 4765) after each change of lot of a reagent.

f) Interferences

The common interfering factors with the HYDRASHIFT 2/4 daratumumab procedure (bilirubin, triglycerides, hemoglobin and rheumatoid factor) were evaluated in studies based on the Clinical Laboratory Standards Institute (CLSI - USA) EP7-A2 guideline “Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition”. Additional inferference studies included: Human Anti-Mouse Antibody (HAMA, Pomalidomide, Lenalidomide, Dexamethasone, Bortezomib).

The results are summarized below

No interference with the HYDRASHIFT 2/4 daratumumab procedure was detected due to the serum sample’s concentration of the following interfering factors tested at levels equal to the concentrations listed below :

Interfering factor	Concentration	Interfering factor/ Drug	Concentration
Bilirubin	20 mg/dL (342 µM)	Pomalidomide,	1 mg/L
Triglycerides	3,00 g/dL (34,5 mM)	Lenalidomide	4 mg/L
Hemoglobin	2 g/L (0,2 g/dL)	Dexamethasone	1 mg/L
Rheumatoid factor	2000 UI/mL	Bortezomib	2 mg/L
Human Anti-Mouse Antibody (HAMA)	Titer : 640		

g) Results

Interpretation, Interference and Limitations and Troubleshooting: See the instructions for use of the HYDRAGEL IF Standard mask or Dynamic mask kits.

A band on G and K immunofixation tracks outside the gammaglobulins zone and in alpha-1 zone corresponds to the daratumumab / anti-daratumumab antibody complex. *NOTE: Sometimes, the daratumumab complex is more faint in K track than in G track.*

The HYDRASHIFT 2/4 daratumumab immunofixation removes the daratumumab Ig G, Kappa interference and enables the visual evaluation of the presence or absence of monoclonal proteins on the HYDRAGEL IF kits, a negative test demonstrates the absence of monoclonal proteins in patients who have received daratumumab therapy.

The absence of any monoclonal protein on HYDRASHIFT 2/4 daratumumab immunofixation assay in either Alpha 2, Beta or Gamma zones is interpreted as a negative assay for monoclonal protein.

The presence of a monoclonal protein (or biclonal) on HYDRASHIFT 2/4 daratumumab immunofixation assay in either Alpha 2, Beta or Gamma zones is interpreted as a positive assay for monoclonal protein.

Some samples may give a faint band close to the application point due to a non-specific precipitation of proteins. This band may be visible on the G track and more particularly on the K track and cannot be confused with a monoclonal component

6. IMWG Response Criteria

The current standard of practice for monitoring responses and relapses in multiple myeloma involve serum protein electrophoresis (SPEP) and Immunofixation (IF) (to determine complete response). International guidelines such as the National Comprehensive Cancer Network Clinical Practice Guidelines for Multiple Myeloma (NCCN) use reductions of monoclonal protein by SPEP and normalization of IFE to stratify response.

NCCN Guidelines Version 3.2017
*The Lancet Oncology 17 Kumar S, Paiva B, Anderson K, et al. International Myeloma Working Group consensus criteria for response and minimal response disease assessment in multiple myeloma, e328-46

*New criteria (2016) - International Myeloma Working Group	
Stringent complete response	Complete response as defined below plus normal FLC ratio** and absence of clonal cells in bone marrow biopsy by immunohistochemistry (κ/λ ratio ≤4:1 or ≥1:2 for κ and λ patients, respectively, after counting ≥100 plasma cells)††
Complete response	Negative immunofixation on the serum and urine and disappearance of any soft tissue plasmacytomas and <5% plasma cells in bone marrow aspirates
Very good partial response	Serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥90% reduction in serum M-protein plus urine M-protein level <100 mg per 24 h
Partial response	≥50% reduction of serum M-protein plus reduction in 24-h urinary M-protein by ≥90% or to <200 mg per 24 h; If the serum and urine M-protein are unmeasurable, a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria; If serum and urine M-protein are unmeasurable, and serumfree light assay is also unmeasurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma-cell percentage was ≥30%. In addition to these criteria, if present at baseline, a ≥50% reduction in the size (sum of the products of the maximal perpendicular diameters [SPD] of measured lesions)§§ of soft tissue plasmacytomas is also required
Minimal response	≥25% but ≤49% reduction of serum M-protein and reduction in 24-h urine M-protein by 50%–89%. In addition to the above listed criteria, if present at baseline, a ≥50% reduction in SPD§§ of soft tissue plasmacytomas is also required

Stable disease	Not recommended for use as an indicator of response; stability of disease is best described by providing the time-to-progression estimates. Not meeting criteria for complete response, very good partial response, partial response, minimal response, or progressive disease
Progressive disease	Any one or more of the following criteria: Increase of 25% from lowest confirmed response value in one or more of the following criteria:
	Serum M-protein (absolute increase must be ≥0.5 g/dL); Serum M-protein increase ≥1 g/dL, if the lowest M component was ≥5 g/dL; Urine M-protein (absolute increase must be ≥200 mg/24 h); In patients without measurable serum and urine M-protein levels, the difference between involved and uninvolved FLC levels (absolute increase must be >10 mg/dL); In patients without measurable serum and urine M-protein levels and without measurable involved FLC levels, bone marrow plasma-cell percentage irrespective of baseline status (absolute increase must be ≥10%); Appearance of a new lesion(s), ≥50% increase from nadir in SPD§§ of >1 lesion, or ≥50% increase in the longest diameter of a previous lesion >1 cm in short axis; ≥50% increase in circulating plasma cells (minimum of 200 cells per µL) if this is the only measure of disease
Clinical relapse	Clinical relapse requires one or more of the following criteria: Direct indicators of increasing disease and/or end organ dysfunction (calcium elevation, renal failure, anemia, lytic bone lesions [CRAB features]) related to the underlying clonal plasma-cell proliferative disorder. It is not used in calculation of time to progression or progression-free survival but is listed as something that can be reported optionally or for use in clinical practice; Development of new soft tissue plasmacytomas or bone lesions (osteoporotic fractures do not constitute progression); Definite increase in the size of existing plasmacytomas or bone lesions. A definite increase is defined as a 50% (and ≥1 cm) increase as measured serially by the SPD§§ of the measurable lesion; Hypercalcemia (>11 mg/dL); Decrease in hemoglobin of ≥2 g/dL not related to therapy or other non-myeloma-related conditions; Rise in serum creatinine by 2 mg/dL or more from the start of the therapy and attributable to myeloma; Hyperviscosity related to serum paraprotein

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7. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.