October 16, 2025
Medical Device Evaluation Division
Pharmaceutical Safety Bureau
Ministry of Health, Labour and Welfare

Report on the Deliberation Results

Classification	Human Cellular/Tissue-based Products 2. Human Somatic Stem Cell-processed Products
Non-proprietary Name	Vandefitemcel
Brand Name	Akuugo Suspension for Intracranial Implantation
Applicant	SanBio Company Limited
Date of Application	June 12, 2025

Results of Deliberation

In its meeting held on October 16, 2025, the Committee on Regenerative Medicine Products and Biotechnology reached the following conclusion, and decided that this conclusion should be presented to the Pharmaceutical Affairs Council.

The partial change application may be approved with the approval conditions modified as follows.

Approval Conditions

1. ~~In view of the limited manufacturing experience with the product, the applicant is required to promptly collect information about the product's quality according to the plan, evaluate quality comparability between the product and the study product, and report the results. Based on these results, the applicant should file a necessary partial change application. The product must not be shipped before the approval of the partial change application.~~
2. The applicant is required to ensure that the product is used at medical institutions fully prepared for emergencies and by physicians with adequate knowledge and experience in the diagnosis and treatment of traumatic brain injuries and stereotactic brain surgery techniques who are also fully knowledgeable about the clinical study results and adverse events, etc. associated with the product.
3. During the period after the conditional and time-limited approval until the re-application for marketing authorization, the applicant is required to conduct a post-marketing approval condition assessment covering all patients treated with the product.

4. During the period after the conditional and time-limited approval until the re-application for marketing authorization, the applicant is required to collect information on biological characteristics that reflect the mechanism of action of the product, and take necessary measures such as improving the quality control strategy.

(Strikethrough denotes deletions.)

Duration of Approval

7 years

Review Report

October 8, 2025
Pharmaceuticals and Medical Devices Agency

The following are the results of the review of the following regenerative medical product submitted for marketing approval conducted by the Pharmaceuticals and Medical Devices Agency (PMDA).

Brand Name	Akuugo Suspension for Intracranial Implantation
Classification	Human Cellular/Tissue-based Products 2. Human Somatic Stem Cell-processed Products
Non-proprietary Name	Vandefitemcel
Applicant	SanBio Company Limited
Date of Application	June 12, 2025

Shape, Structure, Active Ingredients, Quantities, or Definition
The product consists of cells derived from human (allogeneic) bone marrow mesenchymal stem cells, into which the human Notch-1 intracellular domain gene has been transfected using a pN-2 plasmid vector.

Application Classification	(7) Other regenerative medical products
Reviewing Office	Office of Cellular and Tissue-based Products

Results of Review
As detailed in the attachment, one of the approval conditions “In view of the limited manufacturing experience with the product, the applicant is required to promptly collect information about the product’s quality according to the plan, evaluate quality comparability between the product and the study product, and report the results. Based on these results, the applicant should file a necessary partial change application. The product must not be shipped before the approval of the partial change application.” has been addressed by the applicant.

As a result of its review, PMDA has concluded that the product may be approved with the following approval conditions.

Indication or Performance
Improvement of chronic motor paralysis associated with traumatic brain injury

Dosage and Administration or Method of Use

Usually in adults, the cell suspension containing 5×10^6 viable cells (300 μL) of human (allogeneic) bone marrow-derived mesenchymal stem cells is transplanted to the surrounding area of the damaged tissue via stereotactic brain surgery using a dedicated delivery device set. The cell suspension is injected through a single small opening on the skull that leads to 3 transplantation routes reaching the area surrounding the injury. The dose of cell suspension is 100 μL per route, 20 μL each of which is transplanted at 5 points 5 to 6 mm apart, from the deepest point. The infusion rate should be approximately 10 μL/min. The following steps should be taken prior to the transplantation.

- Before starting the surgical procedure, attach the guide & stop in the dedicated delivery device set and the stylet-equipped inserter to the invasive cranial fixation device for neurosurgery.
- Thaw the cell suspension for intracerebral transplantation. After washing using the dedicated preparation solution, adjust the cell concentration using the dedicated solution so as to obtain cell suspension at the concentration of 1.67×10^6 cells/100 μL for transplantation. Cleanse the administration cannula-fixed microsyringe in the dedicated delivery device set using the dedicated preparation solution, and fill the microsyringe with the cell suspension.

Approval Conditions

~~1. In view of the limited manufacturing experience with the product, the applicant is required to promptly collect information about the product's quality according to the plan, evaluate quality comparability between the product and the study product, and report the results. Based on these results, the applicant should file a necessary partial change application. The product must not be shipped before the approval of the partial change application.~~

2. The applicant is required to ensure that the product is used at medical institutions fully prepared for emergencies and by physicians with adequate knowledge and experience in the diagnosis and treatment of traumatic brain injuries and stereotactic brain surgery techniques who are also fully knowledgeable about the clinical study results and adverse events, etc. associated with the product.
3. During the period after the conditional and time-limited approval until the re-application for marketing authorization, the applicant is required to conduct a post-marketing approval condition assessment covering all patients treated with the product.
4. During the period after the conditional and time-limited approval until the re-application for marketing authorization, the applicant is required to collect information on biological characteristics that reflect the mechanism of action of the product, and take necessary measures such as improving the quality control strategy.

(Strikethrough denotes deletions.)

Attachment

Review Report

October 6, 2025

The following is an outline of the data submitted by the applicant and content of the review conducted by the Pharmaceuticals and Medical Devices Agency (PMDA).

Product Submitted for Approval

Brand Name	Akuugo Suspension for Intracranial Implantation
Classification	Human Cellular/Tissue-based Products 2. Human Somatic Stem Cell-processed Products
Non-proprietary Name	Vandefitemcel
Applicant	SanBio Company Limited
Date of Application	June 12, 2025

Shape, Structure, Active Ingredients, Quantities, or Definition

The product consists of cells derived from human (allogeneic) bone marrow mesenchymal stem cells, into which the human Notch-1 intracellular domain gene has been transfected using a pN-2 plasmid vector.

Approval Conditions at the Time of Application

~~1. In view of the limited manufacturing experience with the product, the applicant is required to promptly collect information about the product's quality according to the plan, evaluate quality comparability between the product and the study product, and report the results. Based on these results, the applicant should file a necessary partial change application. The product must not be shipped before the approval of the partial change application.~~

2. The applicant is required to ensure that the product is used at medical institutions fully prepared for emergencies and by physicians with adequate knowledge and experience in the diagnosis and treatment of traumatic brain injuries and stereotactic brain surgery techniques who are also fully knowledgeable about the clinical study results and adverse events, etc. associated with the product.
3. During the period after the conditional and time-limited approval until the re-application for marketing authorization, the applicant is required to conduct a post-marketing approval condition assessment covering all patients treated with the product.
4. During the period after the conditional and time-limited approval until the re-application for marketing authorization, the applicant is required to collect information on biological characteristics that reflect the mechanism of action of the product, and take necessary measures, such as improving the quality control strategy.

(Strikethrough denotes deletions.)

List of Abbreviations

See Appendix.

1. Summary of the Data Submitted and Outline of the Review Conducted by PMDA

1.1 History of the implementation of comparability assessment

Akuugo is a combination product consisting of a primary component and secondary components. The primary component is a human (allogeneic)-derived intracranial transplant cell suspension (SB623) containing mesenchymal stem cells (MSCs) that is produced from bone marrow aspirate of human healthy adults, cultured for isolation and proliferation, and transfected with a plasmid vector encoding the intracellular domain of human Notch-1. The secondary components include a dedicated preparation solution used to prepare the transplant cell suspension and a dedicated delivery device set (comprising [1] microsyringe, [2] administration cannula, [3] inserter, [4] stylet, and [5] guide & stop). Akuugo is expected to promote the repair of neural cells through the proliferation and differentiation of endogenous neural stem cells, angiogenesis, and immunomodulation, etc. by secreting cytokines.

Comparability between the study product and the commercial product had yet to be proven adequately at the time of previous marketing approval of Akuugo. Due to the necessity for further assessment of comparability between the study product and the commercial product based on quality-related information collected promptly after additional production via the commercial manufacturing process, the above Approval Condition 1 was attached.

The comparability assessment was conducted in accordance with the said approval condition and demonstrated the comparability between the study product and the commercial product. On June 12, 2025, the applicant submitted a partial change application for the removal of the approval condition.

1.2 Summary of data submitted

The results of the comparability assessment conducted using 3 batches of the study product and 3 batches[1)] of the commercial product are shown in the table below.

[1)] Of the 3 batches manufactured after marketing approval, 1 batch ([redacted]) did not conform to the specification test ([redacted]). The cause of this was considered to be [redacted]. Comparability was assessed using data from the remaining 2 batches ([redacted], [redacted]) and 1 batch ([redacted]) manufactured during the review of the marketing application.

Table. Results of comparability assessment

Item		Control values/ specification limits/ acceptance criteria	Study product			Commercial product		
			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Specification test								
pN-2 plasmid copy number		[redacted] (copy per haploid genome)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Cell surface marker analysis	[redacted]	≥ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	≥ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	≥ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	≤ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	≤ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	≤ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Viability		≥ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Viable cell count		≥ [redacted] /vial	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		≥ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Intracellular FGF-2		≥ [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Sterility test		No growth detected	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Bacterial endotoxin		≤ [redacted] EU/mL	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Mycoplasma test		Not detectable	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Characterization								
[redacted]		[redacted] (h)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
In-process control tests								
[redacted]								
[redacted]		≥ [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]								
[redacted]		≥ [redacted]*1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]*2	[redacted]
[redacted]								
[redacted]		≥ [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]								
[redacted]		< [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		≥ [redacted] %	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		≥ [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Other endpoints (efficacy endpoints)								
[redacted]								
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]*3		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

*1 The acceptance criteria were established after the manufacture of the study product.
*2 [redacted]
*3 [redacted]

1.3 Outline of the review conducted by PMDA

The applicant's explanation:

The differences in quality attributes observed between the study product and the commercial product are unlikely to affect efficacy and safety for the following reasons:

- [redacted] tended to be high in the commercial product as compared to the study product but was within the specification, and [redacted] that is thought to be caused by [redacted] was comparable between the products.
- [redacted] tended to be high in the commercial product as compared to the study product, but [redacted] thought to be related to [redacted] was comparable between the study product and the commercial product.

PMDA concluded that the differences in quality attributes observed between the study product and the commercial product are unlikely to affect efficacy and safety, and that comparability between the study product and the commercial product has been confirmed.

2. Overall Evaluation

Based on the submitted data, PMDA concluded that the approval condition "In view of the limited manufacturing experience with the product, the applicant is required to promptly collect information about the product's quality according to the plan, evaluate quality comparability between the study product and the product, and report the results. Based on these results, the applicant should file a necessary partial change application. The product must not be shipped before the approval of the partial change application" has been fulfilled.

3. Other

At the time of marketing approval, [redacted] genomic integration of the Notch intracellular domain (NICD) gene and the neomycin resistance gene derived from the plasmid vector was evaluated.

The applicant's explanation:

Based on the following results, it is highly likely that the full-length transgene derived from the transfected plasmid vector is integrated into the genome of SB623:

- [redacted] was detected in the commercial product.
- [redacted] was detected in the commercial product.
- [redacted] of the commercial product was confirmed.

SB623 used in non-clinical studies and clinical studies presumably contains the transgene integrated into its genome, as with the commercial product. Based on the results of the non-clinical studies and clinical studies conducted, there are no particular safety concerns with the impact of genomic integration. In view of potential risks including tumorigenicity of SB623 attributed to genomic integration and

immunogenicity associated with neomycin resistance gene-derived protein, the applicant explained their intention to analyze cellular characteristics of the commercial product continuously and assess the safety of Akuugo through the post-marketing use-results survey in the future.

PMDA's view:
Although the data submitted indicate that the genome of SB623 contains the plasmid vector-derived transgene integrated, the non-clinical or clinical studies have so far revealed no safety concerns attributable to genomic integration. Therefore, additional evaluation is deemed unnecessary. The applicant's plan for the assessment, via the post-marketing use-results survey, on potential genomic integration-associated tumorigenicity and immunogenicity risks is acceptable.

Appendix

List of Abbreviations

Akuugo	Akuugo Suspension for Intracranial Implantation
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
CD	cluster of differentiation
FGF	fibroblast growth factor
[redacted]	[redacted]
[redacted]	[redacted]
MSC	mesenchymal stem cell
NICD	Notch intracellular domain
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
PMDA	Pharmaceuticals and Medical Devices Agency