

January 18, 2024  
Nobelpharma Co., Ltd.

**mTOR inhibitor “RAPRLIMUS®” Approved for  
Additional Indication for Tablets 1 mg and  
Additional Formulation of Granule 0.2%**

Nobelpharma Co., Ltd. (Headquarters: Chuo-ku, Tokyo, Managing Director & CEO: Jin Shiomura) announced today that an additional indication for the company’s product RAPALIMUS® Tablets 1 mg and an additional formulation of granules 0.2% have been approved.

We are deeply grateful for all of the efforts of the principal investigator, Dr. Michio Ozeki, Department of Pediatrics, Gifu University and many other physicians participated in the investigator initiated studies and the specified clinical researches, the cooperation from the patients entered in the clinical trials, as well as the assistance from Japan Agency for Medical Research and Development (AMED) and National Institutes of Biomedical Innovation, Health and Nutrition, owing to which the additional indication of “intractable vascular tumors and vascular malformations” and the additional formulation for the same indication were approved.

(RAPALIMUS granules 0.2% is under preparation for launch.)

	Indications
RAPALIMUA tablets 1 mg	<ul style="list-style-type: none"> <li>○ lymphangiomyomatosis</li> <li>○ The Following intractable <u>vascular tumors and intractable vascular malformations:</u> <ul style="list-style-type: none"> <li>- Lymphatic malformation,</li> <li>- Generalized lymphatic anomaly,</li> <li>- Gorham-Stout disease,</li> <li>- Lymphangiectasia</li> <li>- Hemangioendothelioma, tufted angioma</li> <li>- Venous malformation, blue rubber bleb nevus syndrome</li> <li>- Complex-combined vascular malformation, Klippel-Trenaunay-Weber syndrome</li> </ul> </li> </ul>
<u>RAPALIMUS granules 0.2%</u>	<ul style="list-style-type: none"> <li>○The Following intractable <u>vascular tumors and intractable vascular malformations:</u> <ul style="list-style-type: none"> <li>- Lymphatic malformation,</li> <li>- Generalized lymphatic anomaly,</li> <li>- Gorham-Stout disease,</li> <li>- Lymphangiectasia</li> </ul> </li> </ul>

	<ul style="list-style-type: none"> <li>- Hemangioendothelioma, tufted angioma</li> <li>- Venous malformation, blue rubber bleb nevus syndrome</li> <li>- Complex-combined vascular malformation, Klippel-Trenaunay-Weber syndrome</li> </ul>
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\* Newly approved additional indications and newly approved formulation are underlined.

○ “Vascular Tumors and Vascular Malformation (Vascular Anomalies)”

“Vasculature” includes “blood vessels” and “lymphatic vessels.”

“Vascular tumors” mainly means angioma that is made of quickly dividing cells of blood vessel walls, while the size of which tends to change in size within a short period as the tumor cells grow and involute. On the other hand, “vascular malformation” differs from tumors and does not change much in size but does not disappear either. In a longer term, it is said to enlarge as the patients grow and may become worse driven by certain events, including age of puberty, pregnancy, infection and trauma.<sup>1)</sup>

○ Refractory Vascular Anomalies

Stubborn cases are called “refractory” and the treatment may become lengthy depending on the sites, size and symptoms. The symptoms of each case vary from continuing pain and hemorrhagic tendency to breathing trouble due to lesion sites. Some may interfere with certain aspects of life and cause aesthetic problems.<sup>1)</sup>

○ Treatment

The therapeutic approaches for vascular anomalies include surgical, laser, and intravascular treatments. As a course of medication for symptoms, pain relief (such as acetaminophen) and hemostat (such as tranexamic acid) have been used. For the disorder itself, various molecular targeted drugs is recently becoming high-profile, while steroids and anticancer drugs were used to be prescribed.<sup>1)</sup>

○ Number of Refractory Vascular Anomalies

It is estimated approximately 6,000 – 8,000 people in Japan have intractable vascular tumor or intractable vascular malformation (including arteriovenous malformation and Sturge-Weber syndrome which are not the indications of this product).

We hope the RAPALIMUS tablets become one of the treatment options and can be of any help for refractory vascular anomaly patients.

We have also created the web site for lymphatic disorder in Nobelpharma corporate site.

<https://www.nobelpharma.co.jp/general/lymphangioma/>

<sup>1)</sup> Site for Information of Drug Therapy Working Group for Intractable Vascular Anomalies

<https://cure-vas.jp/>

We are determined to continue contributing to society by providing critical but neglected pharmaceuticals and medical devices.

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