NEWS RELEASE

NIPPON SHINYAKU CO., LTD.

March 19, 2025

Launch of Uptravi® Tablets for Pediatric 0.05 mg for the Treatment of Pulmonary Arterial Hypertension in Japan

Kyoto, Japan, March 19, 2025 - Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters, Kyoto; President, Toru Nakai) announced today that it has launched Uptravi® tablets for pediatric 0.05 mg (hereinafter "this drug") for the treatment of pulmonary arterial hypertension (PAH) in Japan.

PAH is a disease with a poor prognosis characterized by abnormally high blood pressure in the pulmonary artery. It is classified into idiopathic PAH, heritable PAH and PAH associated with various diseases such as connective tissue disease and congenital heart disease. Because the disease pathology of PAH is similar between pediatric and adult patients, combination therapy of prostacyclin pathway drug, endothelin receptor antagonist and phosphodiesterase-5 inhibitor, is also recommended for pediatric PAH patients. However, treatment options for pediatric PAH are limited in Japan. Particularly, in the case of prostacyclin pathway drug, only an injectable formulation requiring continuous intravenous infusion is available. Therefore, there has been an unmet need for oral formulations of prostacyclin pathway drug.

Uptravi® is an oral prostacyclin receptor (IP receptor) agonist with high selectivity for the IP receptor among prostacyclin pathway drugs. Uptravi® is believed to reduce pulmonary arterial pressure by binding to the IP receptors on vascular smooth muscle cells and increasing cAMP production, thereby leading to vasodilation and inhibition of vascular smooth muscle proliferation.

The optimal dose of this drug for each patient is determined by dose titration. This drug allows for finer dosing for pediatric patients, but some patients may need to take a larger number of tablets at one time. To support patents and healthcare professionals who take and dispense this drug, we developed a new pill case especially for this drug. (the figure on the right; Download image click here). With the dedicated filler for the case, healthcare professionals can dispense the correct number of tablets simply by filling the case. Then, patients can take the correct number of tablets by dispensing them in a single row from the case each time they take this drug.

Nippon Shinyaku focuses on rare and intractable diseases as a key area and continues to make further efforts to develop new treatments and provide product information. With the launch of Uptravi® tablets for pediatric 0.05mg, we hope to contribute even more to pediatric patients suffering from PAH, their families, and healthcare providers.

Summary of Uptravi® tablets for pediatric 0.05 mg

<table>
<tr><td>Brand name</td><td>Uptravi® tablets for pediatric 0.05 mg</td></tr>
<tr><td>Generic name</td><td>Selexipag</td></tr>
<tr><td>Date of approval</td><td>December 27, 2024</td></tr>
<tr><td>Date of NHI reimbursement price listing</td><td>March 19, 2025</td></tr>
<tr><td>Date of launch</td><td>March 19, 2025</td></tr>
<tr><td>Number of approval</td><td>30600AMX00313000</td></tr>
<tr><td>Dosage Forms and Strengths</td><td>A round film-coated tablet containing 0.05 mg of selexipag per tablet</td></tr>
<tr><td>Indication</td><td>Pulmonary arterial hypertension</td></tr>
<tr><td>Dosage and administration</td><td>For pediatric patients aged two years or older, the starting dose in the table below are usually administered orally twice daily after meals. While confirming the tolerability, the maintenance dose is determined by increasing the dosage to the maximum tolerated dose according to the table below at intervals of 7 days or more. It is not allowed to exceed the maximum dose in the table below. In any dose, and oral administration is performed twice daily after meals at each dose.
<table>
<tr><th>Body weight (kg)</th><th>Starting dose (per dose)</th><th>Increasing dose (per dose)</th><th>Maximum dose (per dose)</th></tr>
<tr><td>≥9kg to <25kg</td><td>0.1mg</td><td>0.1mg</td><td>0.8mg</td></tr>
<tr><td>≥25 to <50 kg</td><td>0.15mg</td><td>0.15mg</td><td>1.2mg</td></tr>
<tr><td>≥50 kg</td><td>0.2mg</td><td>0.2mg</td><td>1.6mg</td></tr>
</table></td></tr>
<tr><td>Precautions concerning dosage and administrations (excerpt of items)</td><td>This drug should not be used in combination with 0.2mg and 0.4mg tablets.
When administering selexipag to children weighing less than 50 kg, pediatric 0.05mg tablets should be used until the maintenance dose is reached. If the maintenance dose can be adjusted using 0.2mg and 0.4mg tablets, switching to these tablets is permissible.</td></tr>
<tr><td>NHI reimbursement price</td><td>JPY 443. 50/tablet</td></tr>
<tr><td>Packaging unit</td><td>500 tablets (supplied in bottles in bulk with desiccant)</td></tr>
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About Nippon Shinyaku

Based on Nippon Shinyaku's business philosophy, "Helping people lead healthier, happier lives," we aim to be an organization trusted by the community through creating unique medicines that will bring hope to patients and families suffering from illness. Please visit our website (https://www.nippon-shinyaku.co.jp/english/) for products or detailed information.

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