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# Public summary of the evaluation of a proposed product-specific waiver

## Nintedanib for the treatment of systemic sclerosis

On 11 September 2015, the Paediatric Committee of the European Medicines Agency agreed a product-specific waiver* for nintedanib for the the treatment of systemic sclerosis (EMEA-001006-PIP02-15).

### What is nintedanib, and how is it expected to work?

Nintedanib is a medicine authorised in adults for the treatment of idiopathic pulmonary fibrosis (IPF). Nintedanib is currently being developed in adults for the treatment of systemic sclerosis (SSc) in patients with SSc-Interstitial Lung Disease (ILD).

Systemic sclerosis is a long lasting, debilitating disease in which for unknown reasons the immune system is overactivated, causing inflammation and excess production of various proteins, particularly collagen. The overproduction of collagen leads to the abnormal growth of connective tissue (the tissue that supports the skin and internal organs), causing the skin to become thick and hard. It can also damage tissues in the blood vessel walls of the internal organs, such as the heart, lungs and kidneys. This makes it more difficult for the blood to move through the vessels, causing tissue damage, circulation problems and high blood pressure. Systemic sclerosis may be life threatening because of its possible effects on the gut, heart, lungs and kidneys.

Nintedanib blocks the activity of some enzymes known as tyrosine kinases. These enzymes are present in certain receptors in cells in the lungs and other organs, where they activate several processes involved in the generation of fibrous tissue seen in systemic sclerosis. By blocking these enzymes, nintedanib is expected to reduce the formation of fibrous tissue, thereby helping to prevent the symptoms of systemic sclerosis from getting worse.

### What was the proposal from the applicant?

For children, the applicant proposed:

- not to do any study in children (from birth to less than 18 years of age), because the disease does not occur in children. Therefore, the applicant requested an exemption (waiver*) from the obligation to study the medicine in any children, in the condition treatment of systemic sclerosis.

## Is there a need to treat children affected by systemic sclerosis?

Taking into account the proposed indication in adults, and the characteristics of the medicine, the Paediatric Committee considered that this medicine could be of potential use for the treatment of systemic sclerosis in children (juvenile systemic sclerosis or jSSc), as the underlying disease process is not expected to be different between adults and children.

However, PDCO acknowledged that systemic sclerosis occurs only very rarely in children, and that therefore paediatric clinical studies in systemic sclerosis would likely not be feasible. In addition, in adults nintedanib is currently being developed to treat the lung disease occurring in systemic sclerosis, which is one of the main drivers of mortality in adults, but occurs only in a minority of the already rare children with systemic sclerosis.

PDCO also noted that it may not be safe to use nintedanib in children who are still growing, due to the expected effects of nintedanib on growing bone and teeth.

However, PDCO considers that the applicant should nevertheless explore ways to generate data in the rare cases of juvenile SSc e.g. post-marketing or by opening the adult study to adolescents.

## What did the Paediatric Committee conclude on the potential use of this medicine in children?

The Committee agreed with the request of the applicant to be exempt from performing studies in children from birth to less than 18 years of age, because the condition for which the medicinal product could potentially be used occurs so rarely in children that clinical studies are likely to be not feasible.

## What is the content of the Plan after evaluation?

The Paediatric Committee agreed a full product-specific waiver for children from birth to less than 18 years of age.

## What happens next?

The applicant has received the EMA Decision (P/0233/2015)* on this medicine. The Decision itself is necessary for the applicant to request a new indication, a new route of administration* or a new pharmaceutical form*, as this medicine is already authorised in the treatment of IPF and protected by a patent*.

## *Definitions

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| Applicant | The pharmaceutical company or person proposing the Paediatric Investigation Plan or requesting the Product-Specific Waiver |
| Children | All children, from birth to the day of the 18th birthday. |
| Paediatric investigation plan (PIP) | Set of studies and measures, usually including clinical studies in children, to evaluate the benefits and the risks of the use of a medicine in children, for a given disease or condition. A PIP may include "partial" waivers (for example, for younger children) and/or a deferral (see below). |
| Waiver | An exemption from conducting studies in children, for a given disease or condition. This can be granted for all children (product-specific waiver), or in specific subsets (partial waiver): for example, in boys or in children below a given age. |
| Deferral | The possibility to request marketing authorisation for the use of the medicine in adults, before completing one or more of the studies /measures included in a PIP. The Paediatric Committee may grant a deferral to avoid a delay in the availability of the medicine for adults. |
| Opinion | The result of the evaluation by the Paediatric Committee of the European Medicines Agency. The opinion may grant a product-specific waiver, or agree a PIP. |
| Decision | The legal act issued by the European Medicines Agency, which puts into effect the Opinion of the Paediatric Committee. |
| Pharmaceutical form | The physical aspect of the medicine (the form in which it is presented), for example: a tablet, capsule, powder, solution for injection, etc. A medicine can have more than one pharmaceutical form. |
| Placebo | A substance that has no therapeutic effect, used as a control in testing new drugs. |
| Active control | A medicine with therapeutic effect, used as a control in testing new drugs. |
| Historical control | A group of patients with the same disease, treated in the past and used in a comparison with the patients treated with the new drug. |
| Route of administration | How a medicine is given to the patient. For example: for oral use, for intramuscular use, for intravenous use, etc. The same medicine, or the same pharmaceutical form, may be given through more than one route of administration. |
| Patent | A form of protection of intellectual property rights. If a medicinal product is protected by a patent, the patent holder has the sole right to make, use, and sell the product, for a limited period. In certain circumstances, a patent for a medicinal product may be extended for a variable period by a Supplementary Protection Certificate. |
| Marketing Authorisation | When a Marketing Authorisation is granted, the pharmaceutical company may start selling the medicine in the relevant country (in the whole European Union, if the procedure was a centralised one). |