

*This document is an English-translated version of an attachment of a notification for Revision of PRECAUTIONS issued by the Ministry of Health, Labour and Welfare.*

*This English version is intended to be a reference material to provide convenience for users.*

*In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.*

# Revision of PRECAUTIONS

## Tacrolimus hydrate (oral and injectable dosage forms)

March 17, 2026

### **Therapeutic category**

Agents affecting metabolism, n.e.c. (not elsewhere classified)

### **Non-proprietary name**

Tacrolimus hydrate (oral and injectable dosage forms)

### **Safety measure**

PRECAUTIONS should be revised.

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Revised language is underlined.

Current	Revision
<p>9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS</p> <p>9.5 Pregnant Women</p> <p>Pregnant women or women who may be pregnant should be administered this drug only if the potential therapeutic benefits are considered to outweigh the potential risks. Teratogenic effects and fetal toxicity have been reported in animal studies in rabbits. Placental transfer in humans has been reported. Premature birth and effects on infants (low birth weight, congenital anomalies, hyperkalaemia, renal impairment) have been reported in women who received this drug during pregnancy.</p>	<p>9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS</p> <p>9.5 Pregnant Women</p> <p><u>Taking into account the following reports</u>, pregnant women or women who may be pregnant should be administered this drug only if the potential therapeutic benefits are considered to outweigh the potential risks.</p> <p><u>&lt; Common to all indications &gt;</u></p> <p>Teratogenic effects and fetal toxicity have been reported in animal studies in rabbits.</p> <p>Placental transfer in humans has been reported.</p> <p>Premature birth and effects on infants (low birth weight, congenital anomalies, hyperkalaemia, renal impairment) have been reported in women who received this drug during pregnancy.</p> <p><u>&lt; Liver and kidney transplant &gt;</u></p> <p><u>In an overseas cohort study on 2,905 cases of pregnancy in liver and kidney transplant recipients which were available from the database of Transplant Pregnancy Registry International, the following results were reported from prospectively-reported cases.</u></p> <p><u>• Major malformations were observed in 6/297 livebirths (2.0%) in the tacrolimus group and in 1/53 livebirths (1.9%)<sup>Note 2)</sup> in the non-tacrolimus-containing regimen group<sup>Note 1)</sup>.</u></p>

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• Minor malformations were observed in 12/297 livebirths (4.0%) in the tacrolimus group and not observed in the non-tacrolimus-containing regimen group <sup>Note 2)</sup>.

• Spontaneous abortions were observed in 33/335 cases (9.9%) in the tacrolimus group and in 3/56 cases (5.4%) in the non-tacrolimus-containing regimen group <sup>Note 2)</sup>.

• Pre-eclampsia was observed in 84/226 cases (37.2%) in the tacrolimus group and in 7/37 cases (18.9%) in the non-tacrolimus-containing regimen group among kidney transplant recipients.

• Early pre-term birth was observed in 156/352 livebirths (44.3%) in the tacrolimus group and in 25/59 livebirths (42.4%) in the non-tacrolimus-containing regimen group.

• A normal birth weight for gestational age was reported in 289/352 livebirths (82.1%) in the tacrolimus group and in 40/59 livebirths (67.8%) in the non-tacrolimus-containing regimen group.

Note 1) Patients who received treatment with regimens containing one or more of the following: azathioprine, cyclosporine, everolimus, mycophenolic acid, prednisone, and sirolimus.

Note 2) The analysis results obtained after excluding patients who had mycophenolic acid exposure during the period from 6 weeks prior to pregnancy through childbirth

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[References] A Non-interventional Post-authorization Safety Study (NI-PASS) of Outcomes Associated with the Use of Tacrolimus Around Conception, or During Pregnancy or Lactation Using Data from the Transplant Pregnancy Registry International (TPRI) :  
[https://catalogues.ema.europa.eu/system/files/2025-09/Tacrolimus\\_F506-PV-0001\\_CSR%20draft%20v2.0%2022Nov2024-Disclosure-Redacted.pdf](https://catalogues.ema.europa.eu/system/files/2025-09/Tacrolimus_F506-PV-0001_CSR%20draft%20v2.0%2022Nov2024-Disclosure-Redacted.pdf)