Docusign Envelope ID: 9CF6E927-E3C0-8D8B-8213-BB057B7E4B24

Ref Num: RA/071/26/st

Roche (Malaysia) Sdn. Bhd.
Level 21, The Pinnacle,
Persiaran Lagoon, Bandar Sunway,
47500 Subang Jaya, Selangor Darul Ehsan,
Malaysia.

13 October 2026

Direct Healthcare Professional Communication:

CELLCEPT Capsule 250mg [MAL06030803ACRZ]
CELLCEPT Tablet 500mg [MAL06030804ACRZ]

CellCept® (Mycophenolate mofetil): Update to post-treatment contraception period for women of childbearing potential (extension from 6 weeks to 6 months)

Dear Healthcare Professional,

Please cascade this Direct Healthcare Professional Communication (DHPC) to personnel (e.g. transplant surgeons, nephrologists, rheumatologists, gynaecologists, pharmacists and nurses) who are part of the patient management team for CellCept.

Roche (Malaysia) Sdn. Bhd. would like to inform you of the following:

Summary

- Mycophenolate mofetil (CellCept) is a potent human teratogen, associated with a high risk of spontaneous abortions and congenital malformations when used during pregnancy.
- Updated recommendation: Women of childbearing potential must use effective contraception during treatment and for **6 months** after discontinuation of CellCept (previously 6 weeks).
- This update is a proactive measure to align with international regulatory recommendations for genotoxic medicinal products.
- Healthcare professionals should ensure patients are fully informed of the risks and adhere to updated contraception requirements.

The communication of this information has been agreed with the National Centre for Adverse Drug Reaction Monitoring, National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health Malaysia.

Docusign Envelope ID: 9CF6E927-E3C0-8D8B-8213-BB057B7E4B24

Indications approved in Malaysia

- CellCept capsules and tablets are indicated for the prophylaxis of acute organ rejection in patients receiving allogeneic renal transplants.
- CellCept capsules and tablets are indicated for the prophylaxis of acute organ rejection in patients receiving allogeneic cardiac transplants.
- CellCept capsules and tablets are indicated for the prophylaxis of acute organ rejection in patients receiving allogeneic hepatic transplants.
- CellCept should be used concomitantly with cyclosporine and corticosteroids.
- CellCept is indicated for induction and maintenance treatment of lupus nephritis. CellCept should be used concomitantly with corticosteroids.

Further information on the safety concern

CellCept is contraindicated:

- during pregnancy due to its mutagenic and teratogenic potential
- in women of childbearing potential not using highly effective contraceptive methods
- in women who are breastfeeding

The following malformations were most frequently reported post-marketing, in children of patients exposed to mycophenolate mofetil in combination with other immunosuppressants during pregnancy:

- Facial malformations such as cleft lip, cleft palate, micrognathia and hypertelorism of the orbits;
- Abnormalities of the ear (e.g. abnormally formed or absent external/middle ear) and eye (e.g. coloboma, microphthalmos);
- Malformations of the fingers (e.g. polydactyly, syndactyly, brachydactyly);
- Cardiac abnormalities such as atrial and ventricular septal defects;
- Oesophageal malformations (e.g. oesophageal atresia);
- Nervous system malformations (such as spina bifida).

Rationale for the updated recommendation:

Based on a comprehensive review of current regulatory guidance and scientific best practices, the recommended duration of post-treatment contraception for women of childbearing potential has been **extended from 6 weeks to 6 months.** The 6-month duration was determined in accordance with updated European Medicines Agency Safety Working Party (EMA SWP) / Non-clinical Working Party (NcWP) recommendations for medicinal products with genotoxic potential. The recommendation takes into account both drug elimination and the maturation cycle of human oocytes, providing a conservative and harmonised approach to minimising the potential risk of embryo-fetal exposure from oocytes affected during treatment. This change is driven by proactive alignment with updated international regulatory recommendations for genotoxic medicinal products, guidance from the EMA SWP and United States Food and Drug Administration (US FDA), as well as emerging scientific consensus, supporting more conservative contraception durations to ensure an adequate safety margin, considering drug elimination and the human reproductive cycle. This update aims to ensure continued protection against potential embryo-fetal exposure and to harmonise CellCept prescribing information with current global standards.

Docusign Envelope ID: 9CF6E927-E3C0-8D8B-8213-BB057B7E4B24

Women of childbearing potential:

- Before the start of treatment, must be made aware of the increased risk of pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention, and planning.
- Should use two reliable forms of contraception simultaneously, at least one of which must be highly effective,
    - before starting treatment,
    - during treatment,
    - and for **6 months after discontinuation**

  unless abstinence is the chosen method of contraception.

Healthcare professionals should ensure that patients are fully informed of the teratogenic risks associated with mycophenolate and the updated contraception requirements.

This update is reflected in the product information and will reflect in associated risk minimisation materials.

Status for product information

The Malaysian Package Insert has already been updated to reflect the revised post-treatment contraception period for women of childbearing potential (under section 2.5.1 Females and Males of Reproductive Potential - Contraception).

Call for adverse event reporting

To make a report, kindly contact the National Centre for Adverse Drug Reaction Monitoring, National Pharmaceutical Regulatory Agency (NPRA):

1. Visit www.npra.com.my
2. Select “Reporting ADR” under Health Professionals
    a. Choose Online Reporting; or
    b. Download the manual form and submit the completed form via email to fv@npra.gov.my
    Alternatively, post to:
    Pharmacovigilance Section
    National Pharmaceutical Regulatory Agency (NPRA)
    Lot 36, Jalan Profesor Diraja Ungku Aziz (Jalan Universiti)
    46200 Petaling Jaya
    Selangor, Malaysia

Docusign Envelope ID: 9CF6E927-E3C0-8D8B-8213-BB057B7E4B24

Company contact point

Adverse drug reactions should be reported to **Roche (Malaysia) Sdn. Bhd, Casey Lim Kai Xin (Patient Safety Lead) at +603 7628 5600,** or email to my.drugsafety@roche.com.

Product complaints should be reported to **Roche (Malaysia) Sdn. Bhd** via the **Roche Medinfo Website** at https://medinfo.roche.com/my/en.html or via Roche Malaysia Hotline at **+6012-243 0605 (via WhatsApp only).**

For further medical information on **CellCept**, please contact **Roche (Malaysia) Sdn. Bhd** via email: my.medinfo@roche.com.

Yours sincerely,

Signed by:
Otan Akin
8ED90AC340A4420...

13-Oct-2026

Dr. Otan Akin
Medical, Innovation and Regulatory Chapter Lead
Roche (Malaysia) Sdn. Bhd.

References

- *European Medicines Agency (EMA), Committee for Medicinal Products for Human Use (CHMP), 2023. NcWP/SWP recommendations on the duration of contraception following the end of treatment with a genotoxic drug, EMA/CHMP/SWP/74077/2020 rev. 1. Amsterdam: European Medicines Agency.*
- *U.S. Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER), 2019. Oncology pharmaceuticals: Reproductive toxicity testing and labeling recommendations: Guidance for industry. Silver Spring, MD: U.S. Department of Health and Human Services.*
- *Bowman, C. J., et al. (2023). Science-Based Approach to Harmonize Contraception Recommendations in Clinical Trials and Pharmaceutical Labels. Clinical Pharmacology & Therapeutics, 113(2), pp. 226–245.*