This Dosing and Administration Guide has been developed by Otsuka Pharmaceuticals (UK) Ltd and is intended for UK-registered healthcare professionals only.

A link to Prescribing information and adverse event reporting details can be found at the end of the document.

Otsuka

LUPKYNIS®▼ (voclosporin)

Dosing and Administration Guide

LUPKYNIS® is indicated in combination with mycophenolate mofetil for the treatment of adult patients with active class III, IV or V (including mixed class III/V and IV/V) lupus nephritis.[1]

LUPKYNIS® is the **first oral calcineurin inhibitor** licensed for the treatment of **active lupus nephritis**.[1-4] Please refer to the Summary of Product Characteristics (SmPC) for full prescribing information.

POSOLOGY AND METHOD OF ADMINISTRATION

LUPKYNIS® treatment should be initiated and supervised by a qualified physician experienced in the diagnosis and treatment of lupus nephritis.[1]

Twice daily, taken orally[1]

The recommended dose is 23.7 mg **(three 7.9 mg soft capsules), twice daily***

*Doses may vary, please refer to the SmPC.

Taken with or without food[1]

Take a missed dose within 4 hours[1]

Beyond the 4-hour time frame, the next regular dose should be taken at the usual scheduled time. **The next dose should not be doubled**

12-hour schedule[1]

Administer consistently as close to a 12-hour schedule as possible, with a **minimum of 8 hours between each dose**

Swallow whole[1]

Avoid grapefruit[1]

It is recommended not to take LUPKYNIS® with grapefruit or grapefruit juice

Physicians should evaluate the efficacy of treatment at a time point of at least 24 weeks and make an appropriate risk-benefit analysis for continuation of therapy.[1]

DOSE ADJUSTMENTS BASED ON EGFR

Careful monitoring of renal function is advised. It is recommended to establish a baseline eGFR before starting treatment with LUPKYNIS®, and assess every two weeks for the first month, and every four weeks thereafter.[1]

Recommended starting doses based on eGFR[1]

Baseline eGFR	
30 to <45 mL/min/1.73 m²	• Limited data are available • Use LUPKYNIS® only if the benefits outweigh the risk • Starting dose of 23.7 mg twice daily
<30 mL/min/1.73 m²	• LUPKYNIS® has not been studied in this patient group • Not recommended, unless the benefits outweigh the risk • Starting dose of 15.8 mg twice daily

For patients already taking LUPKYNIS®, regular monitoring of eGFR levels is recommended, with dose adjustments required for those patients with confirmed eGFR reduction below 60 mL/min/1.73 m².[1] In the first four weeks of treatment with LUPKYNIS®, haemodynamic reductions in eGFR have been observed, which can be managed by dose adjustments.[1]

Recommended dose adjustments for patients receiving LUPKYNIS®[1]

eGFR (2 consecutive assessments within 48 hours)			
≥60 mL/min/1.73 m²		No dose adjustments necessary	
<60 mL/min/1.73 m²		**≤20% reduction** from baseline	• Maintain current dose and monitor
		>20% and <30% reduction from baseline	• Reduce dose of LUPKYNIS® by 7.9 mg (one capsule) BID • Reassess eGFR within two weeks; if eGFR decrease has not recovered, reduce further by 7.9mg (one capsule) BID
		≥30% reduction from baseline	• Stop LUPKYNIS® • Restart treatment upon eGFR recovery at 7.9 mg (one capsule) BID and increase as tolerated based on renal function

Patients requiring a reduction in dose should be reassessed for eGFR recovery within two weeks. For patients that had a decrease in dose due to eGFR reduction, consider increasing the dose by 7.9 mg twice a day for each eGFR measurement that is ≥80% of baseline; the starting dose should not be exceeded.

DOSING RECOMMENDATIONS IN SOME SPECIAL POPULATIONS

Co-administration with CYP3A4 inhibitors[1]

When co-administering LUPKYNIS® with moderate cytochrome P450 (CYP)3A4 inhibitors (e.g., verapamil, fluconazole, diltiazem), daily dose must be reduced to 15.8 mg in the morning and 7.9 mg in the evening. Note that co-administration with strong CYP3A4 inhibitors is contraindicated.

Hepatic impairment[1]

In patients with mild and moderate hepatic impairment (Child-Pugh Class A and B, respectively), the recommended starting dose is 15.8 mg twice daily. The effect of LUPKYNIS® in patients with severe hepatic impairment (Child-Pugh Class C) has not been assessed and LUPKYNIS® is not recommended in this patient population.

Elderly[1]

Data are limited in lupus nephritis patients >65 years, and there are no data in patients aged >75 years. LUPKYNIS® is not recommended in patients >75 years of age.

Paediatric population[1]

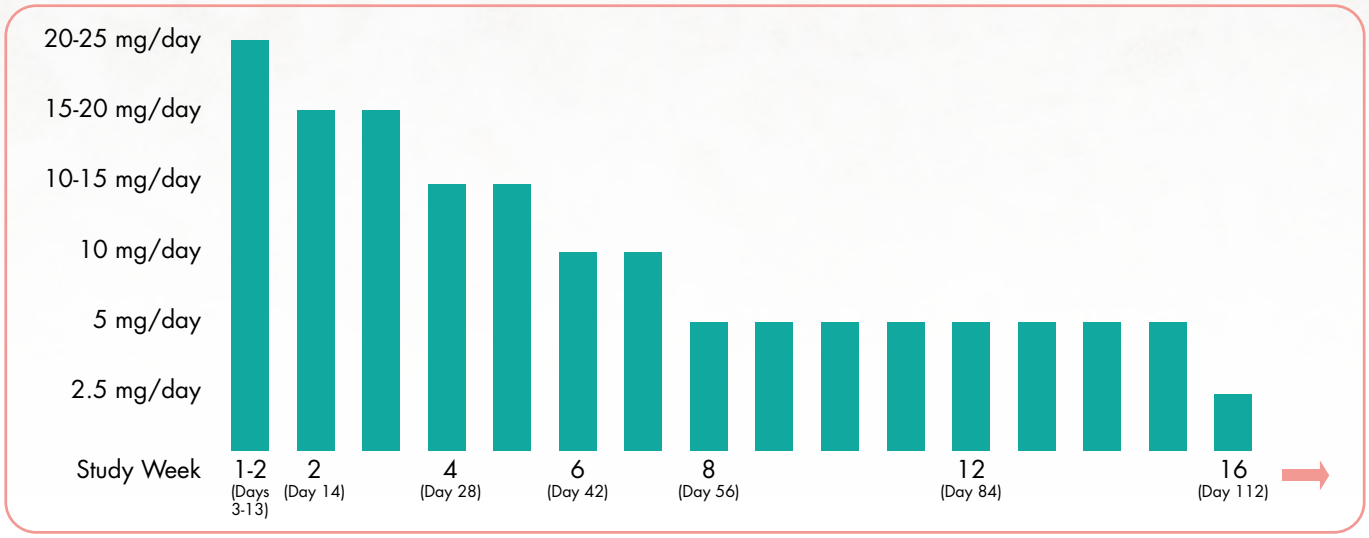
The safety and efficacy of LUPKYNIS® in children and adolescents aged 5 to 18 years have not yet been established. No data are available. There is no relevant use of LUPKYNIS® in children below the age of 5 years in lupus nephritis.

STEROID TAPERING REGIMEN

- In AURORA 1, the LUPKYNIS® phase 3, double-blind, randomised, placebo-controlled clinical trial,* all patients received a target dose of MMF of 1 g twice daily (total 2 g/day)[2]
- All patients were administered IV methylprednisolone once daily on days 1 and 2 (0.5 g/day for patients that weighed ≥45 kg and 0.25 g/day for patients that weighed <45 kg)[2]
- All patients then began a rapid taper of oral prednisone on Day 3 commencing at 20-25 mg per day[2]
- The dose decreased over time to 2.5 mg per day at Week 16 according to a protocol predefined schedule and adjusted at investigator discretion[2]

*Comparing LUPKYNIS® + MMF + corticosteroids vs. placebo + MMF + corticosteroids in adults with class III, IV, or V (alone or in combination with class III or IV) lupus nephritis.

Oral prednisone taper



Adapted from Supplementary material: Rovin BH, *et al. Lancet* 2021;29;**397**(10289):2070-2080.

PHARMACOKINETICS AND PHARMACODYNAMICS

LUPKYNIS® has been shown to have a predictable pharmacokinetic and pharmacodynamic profile[4]

Based on trial experience from AURORA 1, TDM was not conducted in LUPKYNIS®-treated patients[5]

Please refer to the LUPKYNIS® SmPC for additional important safety information including special warning and precautions about the patient specific dosing.[1]

References

1. Lupkynis® UK SmPC.
2. Rovin BH, *et al. Lancet* 2021;29;**397**(10289):2070-2080.
3. Anders HJ, *et al. Nat Rev Dis Primers* 2020;**6**(1):7.
4. Anglade E *et al. Clin Ophthalmol* 2008;**2**:693-702.
5. van Gelder T *et al.* Presented at the American Society of Nephrology Kidney Week 2020 virtual meeting (abstract number PO1918).

LUPKYNIS® Prescribing Information (UK)

eGFR: estimated glomerular filtration rate; IV: intravenous; TDM: therapeutic drug monitors

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