KAPRUVIA®
(difelikefalin) Injection

CKD-ASSOCIATED PRURITUS MORE THAN JUST AN 'ITCH'

CKD-associated pruritis (CKD-aP) has many consequences on patients' quality of life.

Routinely asking patients about 'itch' at their haemodialysis sessions is a good starting point to actively support your patients in getting the crucial diagnosis and treatment they need.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Vifor Pharma UK Ltd. (Tel 01276 853633). Email: medicalinfo_UK@viforpharma.com

KAPRUVIA® IS INDICATED FOR THE TREATMENT OF MODERATE-TO-SEVERE PRURITUS ASSOCIATED WITH CHRONIC KIDNEY DISEASE IN ADULT PATIENTS ON HAEMODIALYSIS.[1] KAPRUVIA® SHOULD BE RESTRICTED FOR IN-CENTRE HAEMODIALYSIS USE ONLY.[1]

Prescribing information can be found on the back page of this document.

VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

UK-DFK-2300101 | November 2023

CSL Vifor

HOW IS THE BURDEN OF CKD-aP AFFECTING YOUR PATIENTS ON HAEMODIALYSIS?

CKD-aP is defined as itching directly related to kidney disease and can vary in severity, be intermittent or persistent, and occur any time before, during or after dialysis.[2]

The burden your patients experience with itch can affect them both physically and emotionally. They may be struggling with symptoms of depression and poor sleep, which can lead to a reluctance in engaging in social activities.[3–6]

In the multinational DOPPS studies, patient data showed almost half of patients on haemodialysis in the UK may suffer from moderate-to-severe* CKD-aP.[3] The likelihood is that you will have treated a patient that was experiencing this condition.

48%

of UK patients (n=654/1,363) were moderately to severely† bothered by itch[3]

*In DOPPS, moderate-to-severe CKD-aP was based on self-reported degree to which patients were bothered by itchy skin in the past 4 weeks: moderately, very much, and extremely[3]

†Severity of itch was established from a single question of the KDQoL-36 questionnaire: In the past 4 weeks to what extent were you bothered by itchy skin?[3]

WITH SUCH A WIDESPREAD PREVALENCE AND POTENTIAL IMPACT ON PATIENTS' QUALITY OF LIFE, WHY IS CKD-aP NOT SPOKEN ABOUT MORE?

Despite the severe impact it has on so many patients, CKD-aP is under-recognised.

The documented prevalence of moderate-to-severe CKD-aP may not give us an accurate picture of how many patients are experiencing itch. One of the reasons is because 25% of all patients on haemodialysis who suffer with itchy skin do not report it to any healthcare professional.[7,8] This creates a gap in communication between healthcare specialists and their patients, potentially resulting in patients suffering in silence and not getting the help that they need.

Why do patients not speak about their itch?

PATIENTS UNAWARE OR RESIGNED

Some patients **do not understand** the link between CKD and itch; others are resigned to suffering from itch[9]

HIGH BURDEN, LOW PRIORITY

Itch is not **considered a priority symptom** in advanced CKD, so is often overlooked during consultations[9]

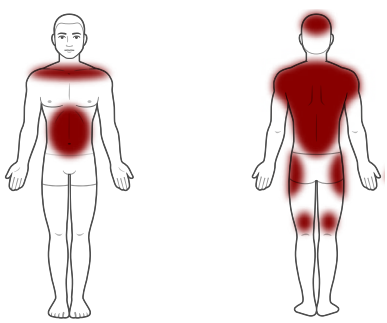
CONSULTATION TIME IS SHORT

With **limited consultation times**, patients and nephrologists may not get the chance to discuss itch[9]

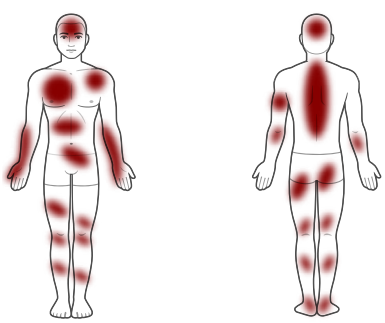
What questions could you ask to help make sure one of your patients isn't hiding their itch?

HOW TO IDENTIFY SIGNS THAT PATIENTS MAY BE EXPERIENCING CKD-aP

One method is to look out for any visible signs; **CKD-aP** is often bilaterally symmetrical, and can be **localised or generalised**[2,10]



GENERALISED



LOCALISED

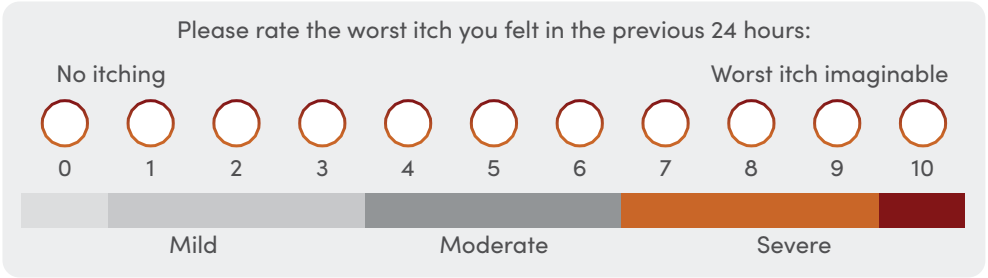
Due to its variability in presentation and high prevalence, HCPs could consider any itching in these patients to be related to CKD-aP, unless there is a clear alternative explanation[11]

Some patients may present with no visible signs of itch or scratching, which makes your conversations with them more important.

Start with one simple question to get the answers you need from your patients: 'How would you rate the worst itch you felt in the past 24 hours?'

WI-NRS assesses itch intensity[10,12]*

Using a simple numerical scale called the WI-NRS scale (Worst Itch-Numerical Rating Scale) can help to get the conversation started. This allows you to keep track of how your patients' treatments are working and help you to see if patients who began in the moderate-to-severe range of itch have had any improvements in their symptoms.



*WI-NRS is a validated 11-point scale ranging from 0–10 where 0 represents 'no itching' and 10 'worst itch imaginable'.[10,12]
The WI-NRS is based on a similar scale also validated for the measurement of pain.[12]

EVERY CONVERSATION COUNTS

What is the impact of CKD-aP on patients?

- Patients with moderate-to-severe CKD-aP have poor sleep, and significantly reduced physical and mental health-related quality of life[3–6]

Why is CKD-aP so under-recognised?

- 25% of all patients on haemodialysis who suffer from pruritus do not report it as they may not see the link between CKD and itch.[7,8]
- Pruritus may not be considered a priority symptom and is often not discussed during limited consultation times.[9]

How to support patients with CKD-aP?

- Routinely asking patients about itch at their haemodialysis sessions is a good place to begin actively supporting your patients, as some patients may present with no visible signs.

KAPRUVIA® is the only therapy licensed for the treatment of moderate-to-severe CKD-associated pruritus in adult patients receiving haemodialysis.[1,13] KAPRUVIA® should be restricted for in-centre haemodialysis use only.[1]

NICE RECOMMENDED TREATMENT

NICE recommends KAPRUVIA®, within its marketing authorisation, for treating moderate-to-severe CKD-associated pruritus in adults receiving in-centre haemodialysis[14]

References & abbreviations: AE, adverse events; **CKD-aP,** chronic kidney disease-associated pruritus; **DOPPS**, Dialysis Outcomes and Practice Patterns Study; **HCP**, healthcare professional; **KDQoL-36**, Kidney Disease Quality of Life; **NICE**, National Institute for Health and Care Excellence; **WI-NRS**, Worst Itch Numeric Rating Scale.

1. KAPRUVIA® Summary of Product Characteristics. **2.** Shirazian S, et al. *Int J Nephrol Renovascular Dis.* 2017;10:11–26. **3.** Sukul N, et al. *Kidney Medicine.* 2021;3(1):42–53. **4.** Pisoni RL, et al. *Nephrol Dial Transplant.* 2006;21:3495–3505 **5.** Silverberg J, et al. *Am J Clin Dermatol.* 2018;19(5):759–769. **6.** Ibrahim M, et al. *J Clin Diagn Res.* 2016;10(3):WC01–WC05. **7.** Rayner HC, et al. *Clin J Am Soc Nephrol.* 2017;12:2000–2007. (Supplementary Material). **8.** Rayner HC, et al. *Clin J Am Soc Nephrol.* 2017;12:2000–2007. **9.** Aresi G, et al. *J Pain Symptom Manage.* 2019;58(4):578–586. **10.** Mathur V, et al. *Clin J Am Soc Nephrol.* 2010;5:1410–1419. **11.** Verduzco HA & Shirazian S. *Kidney Int Rep.* 2020;5:1387–1402. **12.** Phan NC, et al. *Acta Derm Venereol.* 2012;92:502–7. **13.** Lipman ZM & Yosipovitch G. *Expert Opin. Pharmacother.* 2021;22(5):549–555. **14.** NICE (2023). Difelikefalin for treating pruritus in people having haemodialysis. Available at: https://www.nice.org.uk/guidance/TA890. Date accessed: November 2023.

PRESCRIBING INFORMATION

Kapruvia® ▼ (Difelikefalin)
Prescribing Information – United Kingdom
For full prescribing information refer to the Summary of Product Characteristics (SmPC)

Active ingredient: Difelikefalin
Presentation 50 microgram/mL solution for injection. Available as a 2mL vial (containing 1 mL of solution for injection)
Indication: Treatment of moderate-to-severe pruritus associated with chronic kidney disease in adult patients on haemodialysis
Dosage and Administration: Difelikefalin should be restricted for in-centre haemodialysis use only. Difelikefalin is administered 3 times per week by intravenous bolus injection into the venous line of the dialysis circuit at the end of the haemodialysis treatment during rinse-back or after rinse-back. The recommended dose of difelikefalin is 0.5 micrograms/kg dry body weight (i.e., the target postdialysis weight). The total dose volume (mL) required from the vial should be calculated as follows: 0.01 × dry body weight (kg), rounded to the nearest tenth (0.1 mL).
Difelikefalin is removed by the dialyzer membrane and must be administered after blood is no longer circulating through the dialyzer. When given after rinse-back, at least 10 mL of sodium chloride 9 mg/mL (0.9%) solution for injection rinse-back volume should be administered after injection of difelikefalin. If the dose is given during rinse-back, no additional sodium chloride 9 mg/mL (0.9%) solution for injection is needed to flush the line. Difelikefalin should not be diluted and should not be mixed with other medicinal products. For patients with a dry body weight equal to or above 195 kg the recommended dose is 100 micrograms (2 mL). Please refer to SmPC for a table detailing injection volumes of difelikefalin. If a regularly scheduled haemodialysis treatment is missed, difelikefalin should be administered at the next haemodialysis treatment at the same dose. If a 4th haemodialysis treatment is performed in a week, difelikefalin should be administered at the end of the haemodialysis per the recommended dose. No more than 4 doses per week should be administered even if the number of haemodialysis treatments in a week exceeds 4. Safety and efficacy of a 4th dose has not been fully established due to insufficient data. For haemodialysis treatments less than 1 hour, administration of difelikefalin should be withheld until the next haemodialysis session. No clinical interaction studies have been performed. Concurrent administration of medicinal products such as sedating antihistamines, opioid analgesics or other CNS depressants (e.g., clonidine, ondansetron, gabapentin, pregabalin, zolpidem, alprazolam, sertraline, trazodone) may increase the likelihood of dizziness and somnolence.
Contraindications: Hypersensitivity to active substance or to any of the excipients.
Special warnings and precautions: In the placebo-controlled clinical studies a numerically higher rate of adverse events of hyperkalaemia was reported for the difelikefalin treated patients compared to placebo. No causal relationship was established. Frequent monitoring of potassium levels is recommended. Difelikefalin has not been studied in patients with New York Heart Association class IV heart failure. In the pivotal clinical studies a small numerical imbalance of cardiac failure and atrial fibrillation events was observed in the difelikefalin treated patients compared to placebo, in particular among patients with a medical history of atrial fibrillation who discontinued or missed their atrial fibrillation treatment. No causal relationship was established. Difelikefalin is a peripherally acting kappa opioid receptor agonist with restricted access to the central nervous system (CNS). Patients with clinically important disruptions to the BBB (e.g., primary brain malignancies, CNS metastases or other inflammatory conditions, active multiple sclerosis, advanced Alzheimer's disease) may be at risk for difelikefalin entry into the CNS. Difelikefalin should be prescribed with caution in such patients taking into account their individual benefit-risk balance with observation for potential CNS effects. Dizziness and somnolence have occurred in patients taking difelikefalin and may subside over time with continued treatment. Concomitant use of sedating antihistamines, opioid analgesics or other CNS depressants may increase the likelihood of these adverse reactions and should be used with caution during treatment with difelikefalin.
Difelikefalin has minor influence on the ability to drive and use machines. Patients should be cautioned about driving or operating hazardous machinery until the effect of difelikefalin on the patient's ability to drive or operate machinery is known. This medicinal product contains less than 1 mmol sodium per vial.
Overdose: In the event of overdose, the appropriate medical attention based on patient's clinical status should be provided. Haemodialysis for 4 hours using a high-flux dialyzer effectively cleared approximately 70-80% of difelikefalin from plasma, and difelikefalin was not detectable in plasma at the end of the second of two dialysis cycles
Special populations: No dose adjustment is required for patients with mild or moderate hepatic impairment. Difelikefalin has not been studied in subjects with severe hepatic impairment and is therefore not recommended for use in this patient population. Dosing recommendations for elderly patients (≥ 65 years of age) are the same as for adult patients. The safety and efficacy of difelikefalin in children aged 0-17 years has not yet been established. There are no or limited amount of data from the use of difelikefalin in pregnant women. As a precautionary measure, it is preferable to avoid the use of difelikefalin during pregnancy. It is unknown whether difelikefalin is excreted in human breast milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from difelikefalin therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman. There are no data on the effect of difelikefalin on fertility in humans.
Undesirable effects: Common (≥1/100 to <1/10): Somnolence and paraesthesia. Please consult the SmPC in relation to other undesirable effects.
Legal category: POM
Price: Pack size of 12 x 2 ml vials (containing 1 mL of solution for injection) = £420.00
MA Number: PLGB 50784/0009, EU/1/22/1643/001, EU/1/22/1643/002
Date of Authorisation: 29/04/2022
MA Holder: Vifor Fresenius Medical Care Renal Pharma France, 100-101 Terrasse Boieldieu, Tour Franklin La Défense 8, 92042 Paris La Défense Cedex, France

Kapruvia® is a registered trademark

Document number: UK-DFK-2300107
Date of preparation: October 2023

This medicine is subject to additional monitoring.
Adverse events should be reported.
Reporting forms and information for United Kingdom can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Vifor Pharma Ltd.
Tel: +44 1276 853633.
E-mail: MedicalInfo_UK@viforpharma.com