FOUNDATION REINVENTED

WITH DUAL ACTION in primary IgA nephropathy[1–3]

FILSPARI®▼ (sparsentan) is indicated for the treatment of adults with primary immunoglobulin A nephropathy (IgAN) with a urine protein excretion ≥1.0 g/day (or urine protein-to-creatinine ratio ≥0.75 g/g)[1]

Prescribing Information and Adverse Event reporting information can be found at the end of this document.

This medicine is subject to additional monitoring. Adverse events should be reported. Reporting forms and information for Great Britain (UK) can be found at https://yellowcard.mhra.gov.uk/ Adverse events should also be reported to Vifor Fresenius Medical Care Renal Pharma, care of Vifor Pharma Ltd. Tel: +44 1276 853633. E-mail: MedicalInfo_UK@viforpharma.com

CSL Vifor

UK-SPT-2500013 | July 2025

FILSPARI®▼ (sparsentan) tablets 200 mg/400 mg

Patients with IgAN (adult diagnosis) reached kidney failure at a mean of 49 years[4]

Retrospective cohort study: real-world evidence from the IgAN cohort of the UK National Registry of Rare Kidney Diseases (RaDaR) confirmed that patients with IgAN have a high risk of kidney failure[4]

RaDaR is a UK-based rare kidney disease registry with an IgAN cohort (N=2,439 patients: 2,299 adults and 140 children). This cohort was analysed in a study looking at long-term patient outcomes, with a focus on time from diagnosis to kidney failure or death. Patients eligible for enrolment had biopsy-proven IgAN, proteinuria >0.5 g/day or eGFR <60 mL/min/1.73 m^2 at any time in the history of their disease[4]

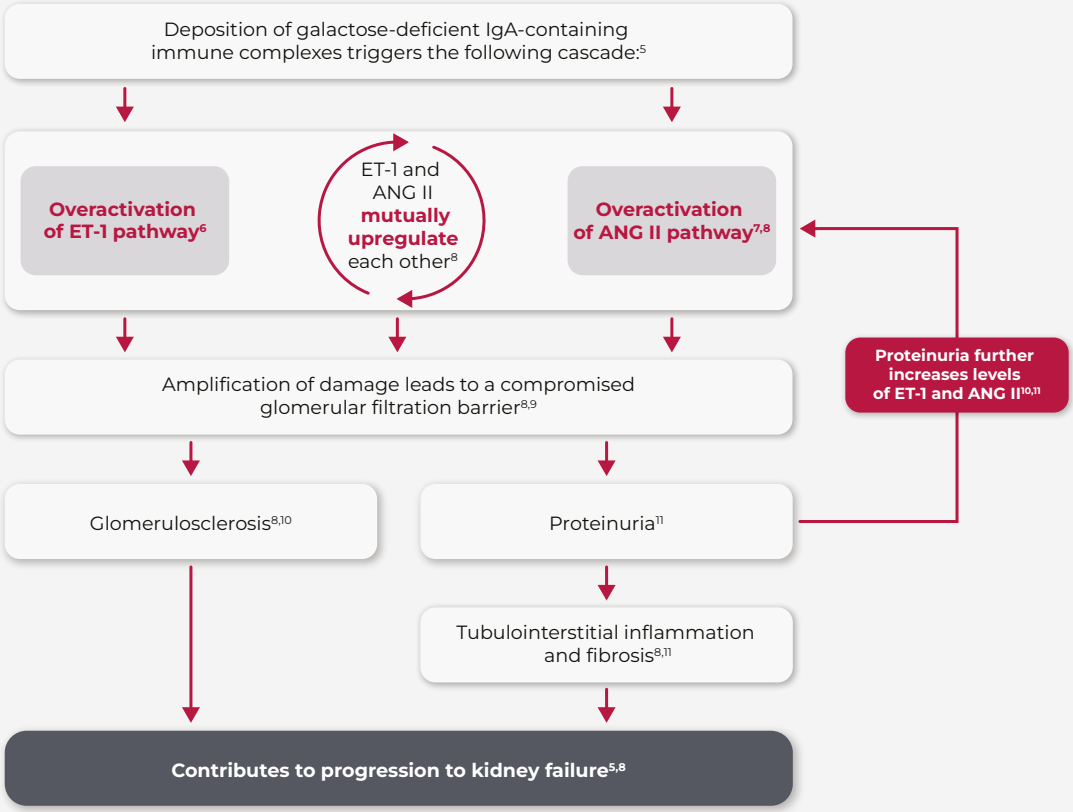
In the RaDaR cohort of adult patients with IgAN (n=2,299):[4]*

42 years	**5.8 years**	**50%**	**10–15 years**
Mean age at diagnosis	Median follow-up time	of patients reached kidney failure or died during the study period	after diagnosis, most patients progressed to kidney failure within this time frame

*UK-based study of biopsy-verified patients with IgAN (N=2,439 patients: 2,299 adults and 140 children).

Two critical pathways are involved in disease progression[5–8]

The mutual upregulation of ET-1 and ANG II is involved in the pathogenesis of IgAN[5–8]



Despite RASi treatment, just under half of patients with IgAN do not achieve adequate proteinuria reduction at 6 months[12†]

†In a prospective trial of first-line ACEi or ARB in patients with UP/C ≥1g/day, 43 out of 96 patients did not achieve UP/C <1g/day after 6 months.[12]

FILSPARI targets two critical pathways involved in IgAN disease progression in one molecule[1,13,14]

The first and only DEARA – dual endothelin angiotensin receptor antagonist[13,14]

FILSPARI
A dual endothelin angiotensin receptor antagonist **(DEARA)**

ET_A receptor
FILSPARI blocks ET-1 from binding to the ET_A receptor

AT_1 receptor
FILSPARI blocks ANG II from binding to the AT_1 receptor

ET-1, via ET_AR, and ANG II, via AT_1R, mediate processes that lead to IgAN progression through:[1]

Haemodynamic actions

Mesangial cell proliferation

Podocyte injury

Oxidative stress

Increased expression and activity of:

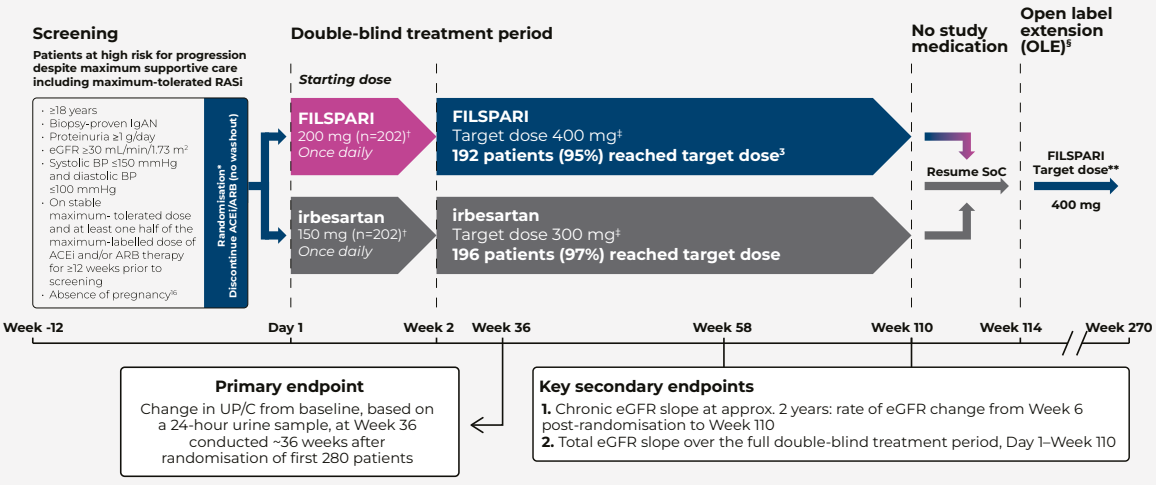
Pro-inflammatory mediators

Pro-fibrotic mediators

FILSPARI, a DEARA, is the first and only non-immunosuppressive IgAN therapy that targets both pathways[13,14]

FILSPARI is the only UK-licensed IgAN treatment evaluated head-to-head against irbesartan[3,14,15]

PROTECT is a randomised, double-blind (110 weeks), active-controlled, multicentre, global Phase 3 trial in patients with IgAN[1,15]



Adapted from Rovin B, *et al.* 2023[3]

*On Day 1, patients were randomised 1:1 to FILSPARI or irbesartan.[3]

†One patient in each arm did not receive the study drug and was excluded.[3]

‡Before the randomisation visit, participants discontinued prohibited concomitant medications, including RASi. The initial study drug dose for the first 2 weeks was half of the target dose (200 mg oral FILSPARI once daily; 150 mg oral irbesartan once daily). At the Week 2 visit, doses were titrated to the target dose (400 mg FILSPARI once daily; 300 mg irbesartan once daily) following evaluation of dose tolerability. Dose tolerance was defined as systolic BP higher than 100 mmHG, diastolic BP higher than 60 mmHg and no TEAEs. Participants with asymptomatic BP of 100/60 mmHg or less continued the initial dose. Dose titrations (down or back up) were permitted at any time at the investigator's discretion.[3]

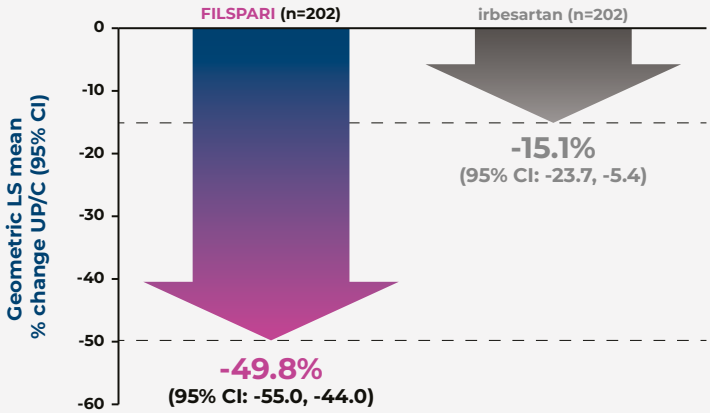
§Patients participating in the OLE period may be evaluated for eligibility to participate in the OLE sub-study. The OLE of PROTECT is currently ongoing.[17]

**Starting dose of FILSPARI for the OLE was 200 mg. Titration to 400 mg was based on tolerability after 2 weeks of treatment in the OLE.[16]

FILSPARI delivered significant and superior proteinuria reduction at Week 36 vs irbesartan[3,15]

Primary endpoint

% Change from baseline in UP/C at Week 36[15]



At Week 36:[15]

41%

relative reduction* of proteinuria with FILSPARI vs irbesartan **p<0.0001**

At Week 36:[15]

34.7%

absolute risk reduction

Baseline UP/C: FILSPARI: 1.3 g/g (0.8, 1.8) irbesartan: 1.2 g/g (0.9, 1.7)

Baseline UPE: FILSPARI: 1.8 g/day (1.2, 2.8) irbesartan: 1.8 g/day (1.3, 2.6)

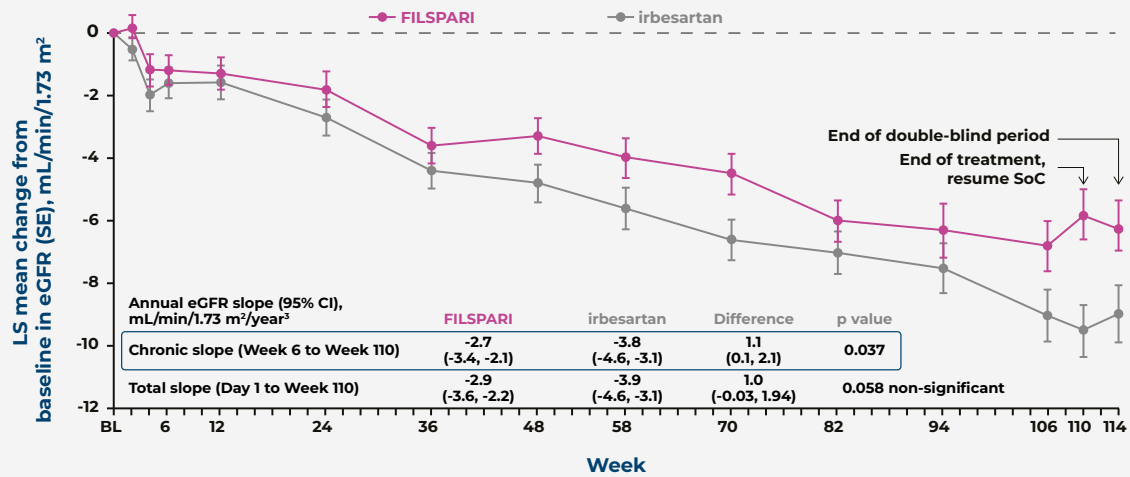
Adapted from Heerspink HJL, *et al.* 2023[15]

*Geometric LS mean ratio; 95% CI: 0.51, 0.69.[15]

FILSPARI significantly slowed the rate of eGFR decline vs irbesartan from Week 6 to Week 110[3†]

Key secondary endpoints

eGFR by visit to Week 114[3]



Annual eGFR slope (95% CI), mL/min/1.73 m²/year[3]	FILSPARI	irbesartan	Difference	p value
Chronic slope (Week 6 to Week 110)	-2.7 (-3.4, -2.1)	-3.8 (-4.6, -3.1)	1.1 (0.1, 2.1)	0.037
Total slope (Day 1 to Week 110)	-2.9 (-3.6, -2.2)	-3.9 (-4.6, -3.1)	1.0 (-0.03, 1.94)	0.058 non-significant

Baseline eGFR, mL/min/1.73 m² , mean (SD): **FILSPARI:** 56.8 (24.3) irbesartan: 57.1 (23.6)

Adapted from Rovin B, *et al.* 2023[3]

†Chronic slope.[3]

Absolute difference in change in eGFR from baseline to Week 110 was numerically better for FILSPARI vs irbesartan[3]

Other secondary endpoint

Under the hierarchical testing procedure, the study did not formally test the statistical hypotheses for 'other' prespecified secondary efficacy endpoints. No definite conclusions can be drawn from these data.

Absolute difference in change in eGFR from baseline to Week 110:

3.7
mL/min/1.73 m^2
(95% CI: 1.5, 6.0)

irbesartan

-9.5
mL/min/1.73 m^2
(95% CI: -11.2, -7.9)

FILSPARI

-5.8
mL/min/1.73 m^2
(95% CI: -7.4, -4.2)

Statistical hypotheses for other prespecified secondary efficacy endpoints were not formally tested under the hierarchical testing procedure because the p value for the eGFR total slope was more than 0.05[3]

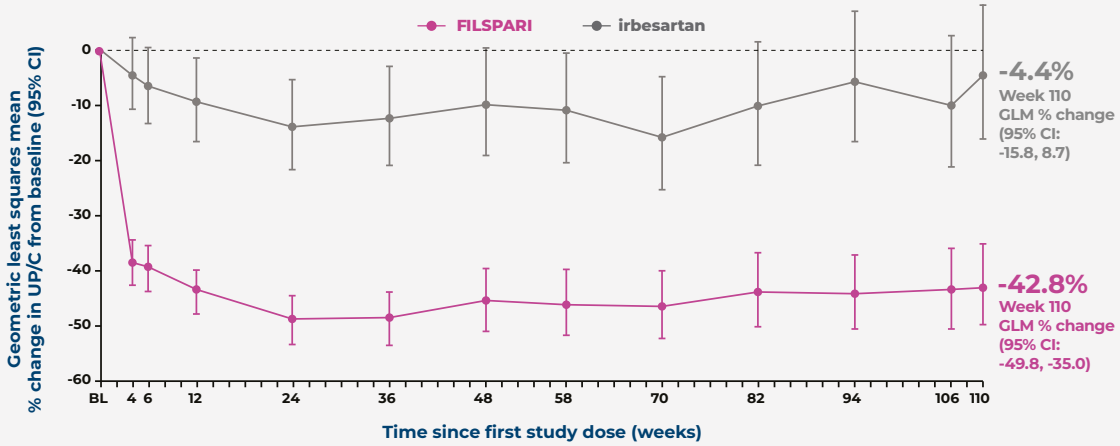
A numerical difference in proteinuria reduction for FILSPARI was observed through Week 110 vs irbesartan[3,15]

The reduction of proteinuria at Week 36 was sustained through Week 110 vs irbesartan[3]

Other secondary endpoint

Under the hierarchical testing procedure, the study did not formally test the statistical hypotheses for 'other' prespecified secondary efficacy endpoints. No definite conclusions can be drawn from these data.

% Change from baseline in UP/C to Week 110[3]

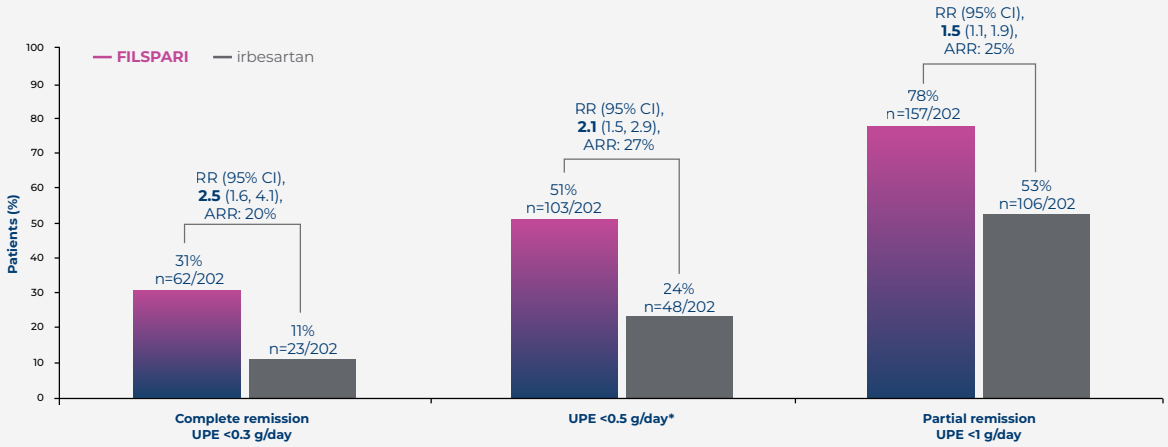


Adapted from Rovin B, *et al.* 2023[3]

Proportion of patients achieving complete (<0.3 g/day) or partial (1.0 g/day) proteinuria remission at any point up to Week 110[3,16]

Exploratory/post-hoc endpoints

Under the hierarchical testing procedure, the study did not formally test the statistical hypotheses for exploratory/post-hoc efficacy endpoints. No definite conclusions can be drawn from these data.



Adapted from Rovin B, *et al*. 2023 [Suppl Appendix][16]

*The proportion of patients achieving UPE <0.5 g/day was a post-hoc assessment[16]

Safety profile of FILSPARI

Safety outcomes

The most common adverse drug reactions observed during clinical trials[1]

Hypotension
10.8%

Hyperkalaemia
9.6%

Dizziness
7.8%

Peripheral oedema
5.4%

The most common serious adverse reaction reported was acute kidney injury (0.9%)[1]

One tablet, once daily. One molecule targeting two critical pathways involved in IgAN disease progression[1]

200 or 400 mg tablets

1x daily

With or without food
It is recommended to swallow the tablets whole with water to avoid bitter taste

Only initiate FILSPARI in verified absence of pregnancy and while on effective contraception

Posology[1]

Stop RASi if applicable	Initiate days 1–14	Maintain days 15+ dependent on tolerability
No washout[14]	**1 x 200 mg/day**	**1 x 400 mg/day**

Prior to starting treatment with FILSPARI, discontinue use of ARBs, ERAs or renin inhibitors. To reduce the risk of potential serious hepatotoxicity, serum aminotransferase levels and total bilirubin should be monitored prior to initiation of treatment and then continue monitoring every 3 months.

In women of childbearing potential, verify the absence of pregnancy prior to initiation/use of effective contraception[1]

Treatment with FILSPARI should be initiated at a dose of 200 mg once daily for 14 days and then increased to a maintenance dose of 400 mg once daily, dependent upon tolerability.

If patients experience tolerability issues (systolic BP ≤ 100 mmHg, diastolic BP ≤60 mmHg, worsening oedema, or hyperkalaemia), adjustment of concomitant medicinal products, followed by temporary down-titration or discontinuation of FILSPARI, is recommended[1]

Contraindications:[1]

- **Hypersensitivity to the active substance(s) or to any of the excipients**
- **Pregnancy**
- **Coadministration of ARBs, ERAs or renin inhibitors**

Despite RASi treatment, just under half of patients with IgAN do not achieve adequate proteinuria reduction at 6 months[12]*

FILSPARI: foundation reinvented with dual action[1–3]

FILSPARI: first and only DEARA[13,14]

Innovative non-immuno-suppressive dual MoA

- FILSPARI, a **DEARA, targets two critical pathways**, the endothelin and angiotensin pathways, **involved in IgAN disease progression** in one molecule[1]

Significantly slower rate of eGFR decline vs irbesartan†

- **Chronic slope for FILSPARI vs irbesartan was -2.7 vs -3.8 mL/min/1.73 m² per year,** respectively; difference, 1.1 mL/min/1.73 m² per year (95% CI: 0.1, 2.1; p=0.037)[3]

Significant and superior proteinuria reduction vs irbesartan

- **Significant and superior reduction from baseline in UP/C at Week 36 vs irbesartan (FILSPARI: -49.8%** [95% CI: -55.0, -44.0] **vs irbesartan: -15.1%** [95 CI: -23.7, -5.4])[3,15]
- Assessed in the only active controlled head-to-head trial in IgAN[3,14,15]

Convenient once-daily tablet[1]

- **One tablet, once daily**[1]

*In a prospective trial of first-line ACEi or ARB in patients with UP/C ≥1g/day, 43 out of 96 patients did not achieve UP/C <1g/day after 6 months.[12]

†Chronic slope. Key secondary endpoints included chronic eGFR slope (rate of eGFR change over Week 6 to Week 110) and total eGFR slope (Day 1–Week 110) over the full double-blind treatment period.[3]

References and Abbreviations

ACEi, angiotensin-converting enzyme inhibitor; **ANG II,** angiotensin II; **ARB,** angiotensin II receptor blocker; **ARR,** absolute risk reduction; **AT_1,** angiotensin II type 1; **AT_1R,** angiotensin II type 1 receptor; **BL,** baseline; **BP,** blood pressure; **CI,** confidence interval; **DEARA,** dual endothelin angiotensin receptor antagonist; **eGFR,** estimated glomerular filtration rate; **ERA,** endothelin receptor antagonist; **ET-1,** endothelin 1; **ET_A,** endothelin type A; **ET_AR,** endothelin type A receptor; **FDA,** US Food and Drug Administration; **FSGS,** focal segmental glomerularsclerosis; **GLM,** geometric least squares mean; **IgA,** immunoglobulin A; **IgAN,** immunoglobulin A nephropathy; **MoA,** mechanism of action; **OLE,** open-label extension; **RaDaR,** UK National Registry of Rare Kidney Diseases; **RASi,** renin-angiotensin system inhibitor; **RR,** relative risk; **SE,** standard error; **SoC,** standard of care; **TEAE,** treatment-emergent adverse event; **UK,** United Kingdom; **UP/C,** urine protein-to-creatinine ratio; **UPE,** urine protein excretion

1. FILSPARI. UK SmPC. **2.** Barratt J, et al. *Kidney Int Rep.* 2023;8(5):1043–56. **3.** Rovin B, et al. *Lancet.* 2023;402(10417):2077–90. **4.** Pitcher D, et al. *Clin J Am Soc Nephrol.* 2023;18(6):727–38. **5.** Lai KN, et al. *Nat Rev Dis Primers.* 2016;2:16001. **6.** Lehrke I, et al. *J Am Soc Nephrol.* 2001;12(11):2321–9. **7.** Chan LY, et al. *J Am Soc Nephrol.* 2005;16(8):2306–17. **8.** Komers R, Plotkin H. *Am J Physiol Regul Integr Comp Physiol.* 2016;310:R877–84. **9.** Kohan DE, et al. *Compr Physiol.* 2011;1:883–919. **10.** Raina R, et al. *Kidney Dis.* 2020;6:22–34. **11.** Sharma S, Smyth B. *Kidney Blood Press Res.* 2021;46:411–20. **12.** Bagchi S, et al. Kidney Int Rep. 2021;6:1661–8. **13.** Syed YY, et al. Drugs. 2023;83(6):563–8. **14.** Campbell KN, et al. *Int J Nephrol Renovasc Dis.* 2023;16:281–91. **15.** Heerspink HJL, et al. *Lancet.* 2023;401(10388):1584–94. **16.** Rovin B, et al. *Lancet.* 2023;402(10417):2077–90 [Suppl Appendix]. **17.** PROTECT ClinicalTrials.gov:http://clinicaltrials.gov/ct2/show/NCT03762850 (accessed May 2025).

CLICK THE LINKS BELOW TO VIEW THE FULL PRESCRIBING INFORMATION (PI) AND INFORMATION FOR REPORTING ADVERSE EVENTS

Filspari 200mg PI

Filspari 400mg PI

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