

Launch of Urine Free Metanephrines Testing via HRAM LC-MS Effective 29 July 2025

Dear Colleagues,

We are pleased to announce an important enhancement to our endocrine diagnostics service. As of 29 July 2025, our laboratory will transition from reporting **urine total (deconjugated) metanephrines** (currently performed via HPLC) to **urine free (unconjugated) metanephrines**, including **metanephrine, normetanephrine, and 3-methoxytyramine (3MT)**. These will be measured using **High-Resolution Accurate-Mass Liquid Chromatography–Mass Spectrometry (HRAM LC-MS)**.

The **Urine Free Metanephrines panel** will replace the current urine total metanephrines test. This panel includes **3-methoxytyramine (3MT)** at no additional cost.

This upgrade brings several clinically relevant advantages:

- **Improved sensitivity and specificity** for detecting catecholamine-secreting tumours (e.g., pheochromocytomas and paragangliomas), especially dopamine-secreting tumours that produce the 3MT metabolite
- **Measurement of free (unconjugated) metanephrines** better reflects real-time catecholamine secretion and tumour activity
- **Minimises analytical variability** related to diet, renal function, and urinary pH, compared to hydrolysed total metanephrines

Sample Requirements and Patient Preparation:

- 24-hour urine collection with boric acid preservative (sample bottles with pre-added **10 g boric acid preservative** will be supplied by your local PathCare lab)
- Urine collection start time/date and end time/date should be recorded on the request form
- Spot (random) urine collections may be accepted if 24-hour collection is not feasible, but interpretive caution is advised. Please indicate on the request form (e.g., "Random/Spot Sample")
- Avoid for 24 hours prior to and during collection: caffeine, nicotine, alcohol, banana, pineapple, tomato, avocado, eggplant, plums, beans, chocolate, vanilla, and nuts
- Medications that may interfere include: tricyclic antidepressants, SSRIs, MAOIs, levodopa, alpha-blockers, beta-blockers, venlafaxine, atypical antipsychotics, sympathomimetics, and midodrine. These should, where clinically appropriate, be withheld at least 48 hours before collection starts

Interpretation:

- **Reference intervals:** Age- and sex-specific, derived from LC-MS/MS-based studies
- **Diagnostic threshold:** Results $\geq 2\times$ upper reference limit (URL) are >99% specific for pheochromocytoma/paraganglioma and warrant imaging
- **Borderline elevations (1–2 \times URL):** Exclude common interferents and repeat testing with a 24-hour urine sample or confirm with plasma free metanephrines

Should you have any questions regarding this transition or require clinical guidance, please contact our chemical pathology team.