NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

The ARCHITECT and Alinity i Urine NGAL assay, NephroCheck Test and NGAL Test to help assess the risk of acute kidney injury for people who are being considered for admission to critical care

Final scope

September 2019

1 Introduction

The NephroCheck test is manufactured by Astute Medical. The medical technologies topic oversight group identified the NephroCheck test as potentially suitable for evaluation by the Diagnostics Assessment Programme on the basis of a briefing which was published as a NICE Medtech Innovation Briefing. Clinical experts contacted during scoping have also provided input and advice on the topic area for this scope.

The final scope was informed by discussions at the scoping workshop on 3 April 2019 and the assessment subgroup meeting on 15 April 2019. A change to this scope was made in September 2019 to reflect that the Abbott NGAL assay had become available for use on Alinity immunoassay analysers. A glossary of terms and a list of abbreviations are provided in appendices A and B.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE by companies and experts. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technologies

The NephroCheck Test and the NGAL assays may help to assess the risk of acute kidney injury in people who are at increased risk of developing the condition because they are extremely unwell in hospital. The tests can potentially detect kidney injury earlier than methods currently used for monitoring kidney function; serum creatinine and urine levels. Serum

creatinine levels are slow to rise following kidney injury. In addition, the use of intravenous fluids and diuretics can cause issues with the measuring urine levels to detect kidney injury.

The NephroCheck Test is indicated for use in people who are critically ill. At the scoping workshop and assessment subgroup meeting, clinical experts considered the different types of care for patients who are critically ill and determined who could benefit from use of the tests in the NHS. In the NHS, people who are critically ill and admitted to critical care units should already receive a range of interventions ('care bundles') designed to prevent acute kidney injury because they are extremely unwell. Therefore, the potential for the tests to improve outcomes in this population is limited in the NHS because the results of the tests are unlikely to change management decisions. Clinical experts highlighted that the tests could be useful for people who are critically ill and being considered for admission to critical care; that is, for whom a decision about admission has not already been made and where information from the test results could guide the use of acute kidney injury care bundles. The decision question for this assessment therefore focuses on this population.

Earlier identification of any stage of acute kidney injury could allow earlier adoption of measures such as acute kidney injury care bundles, that could prevent progression to more severe injury and reduce the risk of adverse outcomes for patients. This could include reducing the incidence of moderate to severe acute kidney injury, mortality, the length of time a person has to stay in hospital, the need for temporary renal replacement therapy and the risk of chronic kidney disease development or progression. Early identification of patients at low risk of developing acute kidney injury within the subsequent 24 hours could inform decisions about the 'step down' to a lower level of care within the hospital, reducing the use of critical or high dependency care beds.

2.2 Product properties

2.2.1 The NephroCheck Test

The NephroCheck Test (Astute Medical) measures the level of 2 biomarkers (tissue inhibitor of metalloproteinase 2 [TIMP-2] and insulin-like growth factor binding protein 7 [IGFBP-7]) in urine and uses the concentrations to help assess risk of moderate to severe acute kidney injury (defined as per KDIGO guidelines) in the subsequent 12 hours. The company state that the test result must be used in conjunction with clinical evaluation and results of other tests.

The concentrations of TIMP-2 and IGFBP-7 are used to calculate an AKIRisk score (the concentrations of each [ng/ml] multiplied together and divided by

1,000). A score of over 0.3 indicates a higher risk of developing moderate to severe AKI within 12 hours of assessment.

When used with the Astute 140 Meter the NephroCheck Test System consists of the following components:

- Astute140 Meter Kit (a benchtop analyser)
- Astute140 Electronic Quality Control device
- NephroCheck Test Kit (includes a single-use NephroCheck Test cartridge and reagents)
- NephroCheck Liquid Control kit
- NephroCheck Calibration Verification kit

A fresh or thawed urine sample (mixed with reagent) is added to a single-use test cartridge which is then inserted into an Astute140 Meter for incubation and result calculation. The company state sample preparation takes 3 to 5 minutes and that results are available in about 20 minutes. In the NHS, the Astute 140 Meter would be used in a laboratory and not at the point of care.

The test can also be run on the VITROS 3600 immunodiagnostic System and on the VITROS 5600 Integrated System clinical chemistry analysers. All systems generate a single numerical result (the AKIRisk score).

The company state that for surgical patients the NephroCheck test should be done 2 to 4 hours after surgery. Doing the test at a second time point within the first 24 hours may be considered.

The company state that the test is marketed in the UK for people aged over 21 years old.

2.2.2 Neutrophil gelatinase-associated lipocalin (NGAL) assays

2.2.2.1 ARCHITECT and Alinity i Urine NGAL assay

The ARCHITECT Urine NGAL assay (Abbott) is a chemiluminescent micro particle immunoassay for the quantitative determination of NGAL in human urine. It is intended to be used as a marker of kidney injury.

The company claims that the ARCHITECT Urine NGAL assay can be used as follows:

- Early detection of acute kidney injury
- Provides a measure of the severity of acute kidney injury
- Predicts the requirement for renal replacement therapy

- Helps differentiate acute kidney injury from chronic kidney disease and dehydration.

The company state that for diagnostic purposes, the test results should be used in conjunction with clinical assessment and the results of any other testing that has been done (including serum creatinine and urine output). In addition, if the NGAL results are inconsistent with clinical assessment and other test results the company recommend that additional testing can be done to confirm the NGAL result. The test could be used daily until a diagnosis is made or treatment for acute kidney injury is initiated

The company state that the expected range for the assay (for people without kidney injury) is less than or equal to 131.7 ng/ml, based on the 95th percentile from specimens from non-hospitalised donors, but results from individual laboratories may vary. The test has no age restrictions on use.

The assay is run on the ARCHITECT System (i1000SR, i2000, i2000SR, ci4100, ci8200 or ci16200) in a laboratory. The throughput of the system is up to 200 tests per hour, and the time to first result is 36 minutes.

In addition to the ARCHITECT Urine NGAL Reagent Kit, the following materials are also needed:

- ARCHITECT Urine NGAL Calibrators
- ARCHITECT Urine NGAL Controls or other control material
- ARCHITECT i pre-trigger solution
- ARCHITECT i trigger solution
- ARCHITECT i wash buffer
- ARCHITECT i reaction vessels
- ARCHITECT i sample cups
- ARCHITECT i septum
- ARCHITECT i replacement caps

During the assessment, the company informed NICE that their NGAL assay is also now available for use on Alinity immunoassay analysers, using the Alinity i Urine NGAL Reagent Kit. The company state that the Alinity and ARCHITECT NGAL assays use the same reagents, it is only the analysers they are run on that are different.

2.2.2.2 The NGAL Test

The NGAL Test (BioPorto Diagnostics) is a particle-enhanced turbidimetric immunoassay for the quantitative determination of NGAL in human urine, EDTA plasma and heparin plasma. The company state that NGAL

measurements are useful in the diagnosis of acute kidney injury which may lead to acute renal failure.

The company state that this is not a stand-alone test and clinicians should interpret the significance of any raised NGAL level in the light of a person's clinical features. It is intended to be used alongside monitoring of serum creatinine and urine output.

The company state that the test can be used as a single measurement, and potentially as a serial measurement to detect any further development of acute kidney injury during hospitalisation, or any improvement in the condition. The test can also be used in the intensive care unit as a test for predicting stage 2/3 acute kidney injury or as a negative predictive marker ruling out acute kidney injury.

The company advise that the NGAL concentration in an isolated sample of urine and/or EDTA plasma should exceed 250 ng/mL in order to indicate the presence of renal disorder, including acute kidney injury. The company state that this threshold has been chosen to minimise the risk of false positive results. In addition, this threshold can be used to predict acute kidney injury stage 2/3. The test has no age restrictions on use.

The assay can be run on various clinical chemistry analyser systems in a laboratory. The assay time is 10 minutes.

In addition to the NGAL Test Reagent Kit, the following materials are also needed:

- The NGAL Test Calibrator Kit
- The NGAL Test Control Kit
- 0.9% w/v aqueous sodium chloride solution as zero calibrator
- Analyzer-specific reagent containers

3 Target condition

3.1 Acute kidney injury

3.1.1 Causes of acute kidney injury

Acute kidney injury ranges from minor loss of kidney function to complete kidney failure. In current practice, reduced kidney function is identified, and staged (see below), by elevated serum creatinine levels and/or reduced urine output.

There are many causes of acute kidney injury (NHS Choices Acute Kidney Injury), including:

- **Pre-renal:** Reduced blood flow to the kidneys, caused by:
  - low blood volume (after bleeding, excessive vomiting or diarrhoea and severe dehydration),
  - reduced blood flow from the heart (potentially caused by sepsis or heart/liver failure)
  - damage to blood vessels which can be caused by inflammation or blockages within the kidneys
  - medications that affect blood flow to the kidneys

- **Intrinsic:** Damage to the kidney potentially caused by drugs, infections or contrast agents

- **Post-renal:** A blockage preventing drainage from the kidneys (potentially caused by an enlarged prostate, a tumour in the pelvis or kidney stones).

People often develop acute kidney injury after major surgery; vascular and cardiac surgery, in particular, may carry an increased risk of the condition (Park, 2017).

3.1.2 Staging acute kidney injury

Several tools are available for determining the stage of acute kidney injury. The NICE Clinical Knowledge Summary on acute kidney injury outlines a summarised staging system for acute kidney injury in adults based on the RIFLE, AKIN and KDIGO systems (see table 1). A person's acute kidney injury should be staged by the criterion which gives the highest stage. A classification of stage 1 or above is a diagnosis of acute kidney injury.

Table 1: Summarized staging system for acute kidney injury in adults (based on the RIFLE, AKIN, and KDIGO systems)

Stage	Criteria
1	Creatinine rise of 26 micromol or more within 48 hours OR Creatinine rise of 50–99% from baseline within 7 days* (1.50–1.99 x baseline) OR Urine output** < 0.5 mL/kg/h for more than 6 hours
2	100–199% creatinine rise from baseline within 7 days* (2.00–2.99 x baseline) OR Urine output** < 0.5 mL/kg/hour for more than 12 hours
3	200% or more creatinine rise from baseline within 7 days* (3.00 or more x baseline) OR Creatinine rise to 354 micromol/L or more with acute rise of 26 micromol/L or more within 48 hours or 50% or more rise within 7 days OR Urine output** < 0.3 mL/kg/hour for 24 hours or anuria for 12 hours

* The rise is known (based on previous blood tests) or presumed (based on history) to have occurred within 7 days.
** Measurement of urine output may not be practical in a primary care population, but can be considered in a person with a catheter.

People with acute kidney injury have a higher risk of mortality and spend longer in hospital (Bedford et al. 2014; Selby et al. 2012; Wang et al. 2012). In addition, acute kidney injury is associated with a higher risk of developing chronic kidney disease and end-stage renal disease. The risk of chronic kidney disease increases with severity of acute kidney injury. More severe acute kidney injury has also been associated with increased mortality, length of hospital stay and use of intensive care services, in addition to a reduced chance of renal recovery (Bedford et al. 2014; Selby et al. 2012). People with more severe acute kidney injury (and a greater loss of renal function) are more likely to need temporary renal replacement therapy.

3.2 Diagnostic and care pathway

The NICE clinical guideline on acute kidney injury recommends measuring serum creatinine and comparing with baseline for adults, children and young people with acute illness if risk factors for the condition are likely or present. Risk factors include hypovolemia and deteriorating early warning scores (using a paediatric version for children and young people). NHS England and NHS Improvement have endorsed the National Early Warning Score (NEWS) for use in acute and ambulance settings. An updated version of the score (NEWS2) was published in December 2017. The score should not be used in children (under 16 years) or pregnant women.

The NICE guideline further recommends monitoring serum creatinine regularly in all adults, children and young people with or at risk of acute kidney injury. The guideline development group did not wish to define 'regularly' because this would vary according to clinical need, but recognised that daily measurement was typical while in hospital.

An acute kidney injury algorithm to help with detection and diagnosis of the condition has been endorsed by NHS England. In some hospitals the algorithm has been integrated into Laboratory Information Management Systems (LIMS) to help identify potential cases of acute kidney injury from laboratory data in real time.

The KDIGO Clinical Practice Guideline for Acute Kidney Injury highlights the importance of screening patients who have had an exposure that may cause acute kidney injury (such as sepsis or trauma) and that high-risk patients should continue to be monitored until risk subsides. The guideline states that

intervals of checking serum creatinine is a matter of clinical judgement, but suggest as a general rule that high risk patients should have serum creatinine measured at least daily and more frequently after an exposure. Critically ill patients should also have urine output monitoring.

For adults who are at risk of acute kidney injury, the NICE acute kidney injury guideline also recommends that systems are in place to recognise and respond to oliguria (urine output less than 0.5 ml/kg/hour). For children and young people who are at risk of acute kidney injury, the guideline recommends:

- measure urine output
- record weight twice daily to determine fluid balance
- measure urea, creatinine and electrolytes
- think about measuring lactate, blood glucose and blood gases.

Further detail on these recommendations, and further recommendations on the ongoing assessment of the condition of patients in hospital, can be found in section 1.2 of the NICE clinical guideline on acute kidney injury.

The NICE guideline recommends diagnosing acute kidney injury in line with the RIFLE (or paediatric-modified RIFLE [pRIFLE]), AKIN or KDIGO definitions, by using any of the following criteria:

- a rise in serum creatinine of 26 micromol/litre or greater within 48 hours
- a 50% or greater rise in serum creatinine known or presumed to have occurred within the past 7 days
- a fall in urine output to less than 0.5 ml/kg/hour for more than 6 hours in adults and more than 8 hours in children and young people
- a 25% or greater fall in eGFR in children and young people within the past 7 days.

Prevention and treatment of acute kidney injury

There are no direct therapies for treating acute kidney injury. Care focuses on optimising haemodynamics and fluid status, avoiding nephrotoxic treatments, and carrying out investigations to identify and resolve the underlying cause as quickly as possible. Clinical experts commented that the goal of care is to prevent any further kidney injury and to try and stop progression of acute kidney injury; in particular, to try and prevent progression to a stage where renal replacement therapy is needed.

NICE has produced a summary of the evidence-base on the use of medicines in people with or at increased risk of acute kidney injury.

The NICE clinical guideline on acute kidney injury highlights the importance of identifying the cause, or causes, of acute kidney injury and has recommendations on the use of urinalysis and ultrasound for this purpose. The KDIGO Clinical Practice Guideline for Acute Kidney Injury also recommends prompt evaluation of people with acute kidney injury to determine the cause. Identifying possible reversible causes of the condition is highlighted as important to reduce severity of the condition.

The NICE clinical guideline on acute kidney injury has recommendations on managing acute kidney injury (section 1.5); covering removing urological obstruction, pharmacological management, renal replacement therapy and referral to nephrology services. The KDIGO Clinical Practice Guideline for Acute Kidney Injury recommends staging severity of acute kidney injury with serum creatinine and urine output, and to manage the condition according to stage and cause. General management principles for people at high risk of acute kidney injury (or with the condition) are to:

- discontinue nephrotoxic agents if possible,
- monitor volume status and perfusion pressure,
- consider functional haemodynamic monitoring,
- monitor serum creatinine and urine output,
- avoid hyperglycaemia,
- consider alternatives to radiocontrast procedures.

Further actions should only be considered at higher stages of acute kidney injury, such as renal replacement therapy and invasive diagnostic workup. Dosages of drugs may also need to be adapted because of reduced kidney function. The KDIGO guideline also has more detailed guidance on the prevention and treatment of acute kidney injury (section 3). This includes haemodynamic monitoring and support, glycemic control and nutritional support, the use of diuretics and vasodilator therapy.

Clinical experts commented that changes to care if a person had a positive NephroCheck or NGAL assay result would be likely to vary across the NHS, although in general, care is focussed on optimising fluid status and avoiding nephrotoxic treatments.

Additional guidelines in acute kidney injury include:

- The Royal College of Physicians' Acute care toolkit 12: Acute kidney injury and intravenous fluid therapy guidance on the management of acute kidney injury, including IV fluid therapy, and discharge planning.

- The International Club of Ascites consensus recommendations on the diagnosis and management of acute kidney injury in patients with cirrhosis (Angeli et al. 2015).
- The 'Think Kidneys' Recommended Minimum Requirements of a Care Bundle for Patients with AKI in Hospital - guidance on care bundles that can be used for acute kidney injury detected in hospital, including examples of established care bundles (appendix 8).

Place of tests in the care pathway

The tests can be used alongside serum creatinine and urine monitoring for assessing the risk of acute kidney injury in people who are being assessed for admission to critical care. This could result in earlier detection of kidney injury and earlier adoption of measures (discussed above) to try and prevent further injury and progression to higher stages of the condition. Patients may be tested more than once if there is no change in clinical condition and are still considered to be at risk of acute kidney injury.

Reference standard

Reference standards used to assess the ability of the tests to detect or predict acute kidney injury based on serum creatinine levels are likely to be imperfect because, for example, prerenal azotemia can cause low specificity and low sensitivity may occur because of renal reserve (KDIGO Clinical Practice Guideline for Acute Kidney Injury, appendix D). In addition, non-renal factors can influence levels, such as bodyweight and muscle metabolism.

3.3 Patient and carer issues and preferences

In addition to worse clinical outcomes, longer hospital stay may be needed if acute kidney injury progresses to higher stages, which can require temporary dialysis. This may not be available at a local hospital and could require a transfer to a hospital further from the patient's home. If a patient is admitted to intensive care, this can have a substantial emotional and financial impact on their carers.

Developing chronic kidney disease (or more rapid progression through the stages of the condition) as a result of an acute kidney injury will have longer term implications for patients. For example, medications may be required to prevent high blood pressure, and iron or an erythropoiesis-stimulating agent may be needed to treat anaemia. The use of medications to treat other conditions can be affected; for example, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) may be restricted. Modifications to a person's diet and fluid intake may also be needed. In more severe chronic kidney disease, long-term renal replacement therapy may be required. Any reduction

in the occurrence of chronic kidney disease or maintaining a greater level of kidney function would therefore be valued by patients.

Incorrectly identifying a person as being at high risk of acute kidney injury, when in fact they will not develop the condition, could mean that access to nephrotoxic treatments and scans (which may use contrast agents that are nephrotoxic) could be delayed and doses of medication are adjusted unnecessarily.

4 Comparator

No additional testing to identify people at high risk of developing acute kidney injury (other than standard serum creatinine and urine output monitoring).

5 Scope of the assessment

Table 1 Scope of the assessment

Decision question	Do the ARCHITECT and Alinity i Urine NGAL assay, NephroCheck Test and NGAL Test represent a cost-effective use of NHS resources when used to assess the risk of acute kidney injury in people who are critically ill who are being assessed for possible critical care admission?
Populations	People who are critically ill and considered at risk of developing acute kidney injury (that is, who are having their serum creatinine and urine output monitored), and who are being assessed for possible critical care admission. If data permits, subgroup analyses could be done for children and young people. If data permits, subgroup analyses could be done for people with a different underlying risk of acute kidney injury. These subgroups include: • chronic kidney disease • sepsis • hip fracture • major trauma • chronic liver disease • post major surgery. In addition, the tests may perform differently in people with urinary tract infections and other inflammatory conditions, if

	data permits results could be reported separately for this population.
Interventions	• ARCHITECT and Alinity i Urine NGAL (Abbott) • The NephroCheck test (Astute Medical) • The NGAL Test – using plasma (BioPorto Diagnostics) • The NGAL Test – using urine (BioPorto Diagnostics) Used alongside serum creatinine, urine output monitoring and clinical judgement
Comparator	Serum creatinine, urine output monitoring and clinical judgement only
Healthcare setting	Secondary/tertiary care
Outcomes	Intermediate measures for consideration may include: • Predictive accuracy / Diagnostic accuracy • Length of stay in critical/intensive care • Length of stay in hospital • Incidence of acute kidney injury (and severity/stage of condition) • Length of acute kidney injury episode • Incidence/duration of acute renal replacement therapy within 7 days • Incidence of chronic kidney disease-related renal replacement therapy post-acute kidney injury • Impact on steady state estimated glomerular filtration rate at 90 days • Impact of test result on clinical decision making • Incidence of hospital readmission post-discharge • Time to test result • Equivalence of biomarkers (for example, the NGAL assays)
	Clinical outcomes for consideration may include: • Mortality • Acute kidney injury-associated morbidity (such as chronic kidney disease/end stage renal disease)
	Patient-reported outcomes for consideration may include: • Health-related quality of life
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Costs related to use of the tests (including maintenance, controls, calibration, accreditation, staff time to run tests)

	• Costs related to assessment for people diagnosed with acute kidney injury (such as nephrology consultations, scans and renal biopsies) • Costs related to interventions used when acute kidney injury is predicted or diagnosed (such as optimising haemodynamics and fluid status) • Costs related to hospital stays (including critical/intensive care) • Costs related to renal replacement therapy during hospitalisation • Costs related to treating chronic kidney disease; including renal replacement therapy for end stage renal disease
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

6 Other issues for consideration

An NIHR funded report on the use of tests of acute kidney injury in critical care has been published (Hall et al. 2018), which included a systematic review and economic model. This includes an assessment of the NephroCheck test and NGAL.

If the tests have largely been assessed in adults, the assessment may need to consider whether the results are generalisable to children and young people.

Clinical experts advised that the tests should not be used for people who have received a kidney transplant, in the immediate post-transplant period. Other tests to monitor graft function would be used in this setting, and consequently, this population are excluded from the scope of this assessment.

There may be limited studies comparing test-guided implementation of preventive care with standard NHS practice and impact on clinical outcomes. A linked evidence approach may be needed for the economic model to link diagnostic accuracy to clinical outcomes. Recent studies have assessed the impact of adopting a 'KDIGO bundle' for people considered at high risk of AKI (based on their NephroCheck test score) when compared to standard care (Göcze et al. 2018; Meersch et al. 2017).

Clinical experts suggested that the tests may be used more than once per person. This would occur if a person had a negative test result, but there was no change in their clinical condition, and they were still considered to be at risk of acute kidney injury. A subset of this population was likely to have a second test; however the proportion is not known and this uncertainty may need to be investigated through sensitivity analyses in the economic model.

7 Potential equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

The presence of chronic kidney disease is a major risk factor for acute kidney injury. Therefore, populations with higher incidence of chronic kidney disease also have higher incidence of acute kidney injury. These include older people, people with diabetes and in certain ethnic groups, for example, people of south Asian family origin. Incidence is unlikely to be affected by the use of the technology but earlier detection and slowing of progression may be enabled.

The performance of the tests may be impacted by inflammation in people who have inflammatory conditions or an infection such as a urinary tract infection.

People with chronic kidney disease, diabetes or an inflammatory condition may be protected by the disability provision of the Equality Act 2010.

8 Potential implementation issues

Several key considerations for adoption of the test were highlighted during discussions with expert contributors.

Clinical experts highlighted uncertainty about what action to take if the test is positive. If used in critical care settings, people would already be having high intensity monitoring so they may be little benefit to any changes to care. A clinical expert also commented that people being tested for acute kidney injury would already have been assumed to be at risk and should already be on a preventative management plan.

Conversely, clinical experts also highlighted concern if any test produced for a lot of false positive test results and unnecessary over monitoring of patients with no change in patient outcome.

Clinical experts also highlighted that if an assay does not run on chemical analysers currently in a hospital's laboratory, there are likely to be issues with

space and cost if another company's analyser needs to be installed. In addition, external quality assurance and accreditation will be needed if a new biomarker is introduced to a laboratory.

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Appendix A Glossary of terms

Acute kidney injury
Acute kidney injury is a condition that affects the structure and function of the kidneys. It can be caused by many different conditions and is defined based on serum creatinine levels and urine output.

Chronic kidney disease
A long-term condition characterised by a loss of kidney function over time. It is normally asymptomatic.

Creatinine
Creatinine is the waste product of creatinine, which the muscles use to make energy. Creatinine is excreted in the urine via the kidneys. High levels in the blood might indicate that the kidneys are not working correctly.

End stage renal disease
End stage renal disease occurs when chronic kidney disease reaches an advanced state. The kidneys do not work well enough to support the body, therefore dialysis or a kidney transplant is needed.

Glomerular filtration rate
A measure of the flow rate of blood passing through the kidneys.

Nephrotoxic drugs
Drugs that can cause damage to the kidneys.

Prerenal azotemia
An increase in nitrogen waste products (including creatinine) caused by decreased blood flow to the kidneys.

Renal reserve
The ability of the kidney to increase glomerular filtration rate in response to stimuli or conditions.

Appendix B Abbreviations

AKIN
Acute Kidney Injury Network

CKD
Chronic kidney disease

GFR
Glomerular filtration rate

IGFBP7
Insulin-like growth factor-binding protein 7

KDIGO
Kidney Disease Improving Global Outcomes

RIFLE
Risk, Injury, and Failure; and Loss; and End-stage kidney disease

TIMP-2
Tissue inhibitor of metalloproteinases-2

Appendix C References

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