

## HEALTH TECHNOLOGY BRIEFING AUGUST 2020

### Dapagliflozin for chronic kidney disease

<b>NIHRIO ID</b>	26894	<b>NICE ID</b>	10148
<b>Developer/Company</b>	AstraZeneca UK Ltd	<b>UKPS ID</b>	Not available

<b>Licensing and market availability plans</b>	Currently in phase III trials.
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### SUMMARY

Dapagliflozin is in clinical development for the treatment of chronic kidney disease (CKD). CKD is a long-term condition where the kidneys do not work as well as they should. CKD is often caused by other conditions that put a strain on the kidneys, the most common being high blood pressure and diabetes. Most people with CKD have no symptoms because the body can tolerate even a large reduction in kidney function. However, if kidney function continues to deteriorate, kidney failure may occur. Symptoms can include weight loss, insomnia and shortness of breath. There are currently no treatments available to specifically treat CKD. Current strategies involve treatment of contributing conditions and complications that arise from CKD.

Dapagliflozin blocks the action of a protein in the kidneys called sodium-glucose cotransporter 2 (SGLT2). As blood is filtered by the kidneys, SGLT2 stops glucose in the bloodstream from being passed out into the urine. By blocking the action of SGLT2, dapagliflozin causes the kidney to pass out more glucose in the urine, thereby reducing the levels of glucose in the blood. SGLT2 inhibitors have exhibited beneficial effects on kidney function in those with diabetes and more recently has shown improvements in kidney function and all-cause mortality in those with CKD without a diabetes. If licensed, dapagliflozin may provide a treatment option specifically for people with CKD.

## PROPOSED INDICATION

Prevention of the progression of chronic kidney disease or cardiovascular/renal death.<sup>1</sup>

## TECHNOLOGY

### DESCRIPTION

Dapagliflozin (Forxiga) is a highly potent (K<sub>i</sub>: 0.55 nM), selective and reversible inhibitor of sodium-glucose co-transporter 2 (SGLT2). The SGLT2 is selectively expressed in the kidney with no expression detected in more than 70 other tissues including liver, skeletal muscle, adipose tissue, breast, bladder and brain. SGLT2 is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Despite the presence of hyperglycaemia in type 2 diabetes, reabsorption of filtered glucose continues. Dapagliflozin improves both fasting and post-prandial plasma glucose levels by reducing renal glucose reabsorption leading to urinary glucose excretion. This glucose excretion (glucuretic effect) is observed after the first dose, is continuous over the 24-hour dosing interval and is sustained for the duration of treatment. The amount of glucose removed by the kidney through this mechanism is dependent upon the blood glucose concentration and glomerular filtration rate (GFR). Dapagliflozin does not impair normal endogenous glucose production in response to hypoglycaemia. Dapagliflozin acts independently of insulin secretion and insulin action. Improvement in homeostasis model assessment for beta cell function (HOMA beta-cell) has been observed in clinical studies with dapagliflozin. Dapagliflozin does not inhibit other glucose transporters important for glucose transport into peripheral tissues and is > 1,400 times more selective for SGLT2 versus SGLT1, the major transporter in the gut responsible for glucose absorption.<sup>2</sup>

Dapagliflozin is currently in development for the treatment of chronic kidney disease (CKD). In the phase III clinical trial (NCT03036150; Dapa-CKD), patients receive 10mg dapagliflozin tablets once daily, per oral use for up to approximately 45 months (the trial is event-driven).<sup>1,3</sup>

### INNOVATION AND/OR ADVANTAGES

Four large cardiovascular outcome trials have demonstrated that the benefit of SGLT2 inhibitors extends beyond glycaemic control.<sup>4</sup> These trials recruited patients with type 2 diabetes and either established cardiovascular disease or cardiovascular risk factors. In all three of these trials, the preservation of renal function has been reported. However, the proportion of participants with CKD was low and the number of patients reaching end-stage renal disease (ESRD) small, highlighting the need for dedicated outcome trials to define the efficacy and safety of SGLT2 inhibitors in patients with established CKD. The first trial of SGLT2 inhibition to include patients with type 2 diabetes and CKD reported that canagliflozin 100 mg/day reduced the risk of a composite renal endpoint (comprised of doubling of serum creatinine, ESRD or death due to renal or cardiovascular disease) by 30% compared with placebo.<sup>3</sup>

In the cardiovascular and renal outcome trials described above, the renoprotective benefits of the SGLT2 inhibitors did not appear to be completely explained by the modest reductions in (haemoglobin A1C) HbA1c, which are attenuated in patients with a low estimated glomerular filtration rate (eGFR). Other mechanisms of benefit, including activation of tubuloglomerular feedback and reduction in intrarenal hypoxia, have been proposed to explain the beneficial effects of SGLT2 inhibitors on renal function; these may be relevant to patients with CKD who do not have diabetes.<sup>3</sup>

## DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Dapagliflozin is indicated for the following indications in the EU/UK:<sup>2</sup>

### Type 2 diabetes mellitus – 5mg and 10mg doses

Dapagliflozin is indicated in adults for the treatment of insufficiently controlled type 2 diabetes mellitus (T2DM) as an adjunct to diet and exercise

- As a monotherapy when metformin is considered inappropriate due to intolerance;
- In addition to other medicinal products for the treatment of T2DM.

### Type 1 diabetes mellitus – 5mg dose only<sup>5</sup>

Dapagliflozin is indicated in adults for the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin in patients with BMI  $\geq 27$  kg/m<sup>2</sup>, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy.

Very common ( $\geq 1/10$ ) and common ( $\geq 1/100$  to  $< 1/10$ ) adverse reactions may include: hypoglycaemia (when used with SU or insulin), genital infections, urinary tract infection, diabetic ketoacidosis (when used in Type 1 diabetes), dizziness, rash, back pain, dysuria, and polyuria (among potential others).<sup>2,5</sup>

Dapagliflozin is currently in phase II and phase III clinical development for COVID-19, CKD, weight loss, diabetes mellitus (type I and II), prediabetes, heart failure with preserved or reduced ejection fraction, polycystic ovary syndrome, nonalcoholic steatohepatitis and asymptomatic hyperuricemia.<sup>6</sup>

## PATIENT GROUP

### DISEASE BACKGROUND

Chronic kidney disease (CKD) is characterised by persisting renal damage and/or loss of renal function.<sup>7</sup> Kidney disease is most often caused by other conditions that put a strain on the kidneys. Hypertension and diabetes are the most common causes of kidney disease. The evidence indicates that high blood pressure causes just over a quarter of all cases of kidney failure. Diabetes has been established as the cause of around 40% of all cases. Other conditions that less commonly cause CKD include glomerulonephritis (inflammation of the kidney), pyelonephritis (infection in the kidney) and polycystic kidney disease, among others.<sup>8</sup>

Most people with CKD have no symptoms because the body can tolerate even a large reduction in kidney function. A change in kidney function is usually discovered through a routine blood or urine test. If the kidneys continue to lose function and there is progression towards kidney failure (established renal failure or ERF), this will usually be tracked by blood tests and monitoring. If kidney failure does occur, the symptoms may include weight loss, swollen ankles, feet or hands (due to water retention), shortness of breath, and insomnia among others.<sup>9</sup>

CKD is classified into stages by using eGFR of the kidneys and urinary albumin-to-creatinine ratio (uACR). With the eGFR measurement, a higher stage indicates more severe kidney damage:<sup>10</sup>

- stage 1 (G1) – a normal eGFR above 90ml/min, but other tests have detected signs of kidney damage
- stage 2 (G2) – a slightly reduced eGFR of 60 to 89ml/min, with other signs of kidney damage
- stage 3a (G3a) – an eGFR of 45 to 59ml/min
- stage 3b (G3b) – an eGFR of 30 to 44ml/min

- stage 4 (G4) – an eGFR of 15 to 29ml/min
- stage 5 (G5) – an eGFR below 15ml/min, meaning the kidneys have lost almost all of their function

uACR measurements are also placed into categories, where a higher stage indicates more severe kidney damage:<sup>11</sup>

- A1 – normal to mildly increased uACR of <30 mg/g
- A2 – moderately increased uACR of 30-300mg/g
- A3 – severely increased (including nephrotic syndrome) uACR of >300mg/g

The relationship between both reduced eGFR and increased albuminuria and poor clinical outcomes is well established. A meta-analysis of general population cohorts demonstrated that the relative risk of CV and all-cause mortality as well as ESRD increases with declining eGFR and that greater albuminuria increases the relative risk of these outcomes at all levels of eGFR.<sup>12</sup> uACR testing allows earlier diagnosis (of CKD stages 1 & 2) than eGFR alone and provides a good indicator of prognosis. NICE CKD guidelines recommend that uACR testing should be used alongside eGFR to diagnose CKD, however in reality uACR testing rates are very low in UK clinical practice, particularly in non-diabetic patients.<sup>13</sup>

CKD is common and mainly associated with ageing. The older people get, the more likely they are to have some degree of kidney disease. It is estimated that about one in five men and one in four women between the ages of 65 and 74 years has some degree of CKD. CKD is more common in people of south Asian origin (those from India, Bangladesh, Sri Lanka and Pakistan) and black people than the general population. The reasons for this include higher rates of diabetes in south Asian people and higher rates of high blood pressure in African or Caribbean people.<sup>14</sup>

Living with CKD may affect a person's ability to work, which can cause financial issues. For people on dialysis, sexual difficulties are also common. Loss of sex drive in both men and women and impotence in men are commonly reported problems. Late stage CKD can also make pregnancy more difficult. In women, menstruation may be affected and in men, a reduction in sperm count can occur. Overall, CKD may put a strain on the affected individual, their friends and their family.<sup>15</sup>

## CLINICAL NEED AND BURDEN OF DISEASE

In England in 2014, it was estimated that 2.6 million people aged 16 years and older in England have CKD stage 3-5. This is equal to 6.1% of the population of this age group. CKD stage 3-5 prevalence is higher in women than in men, at 7.4% versus 4.7%. There is a clear association between increasing age and higher CKD prevalence; with 1.9% of people aged 64 and under having CKD stage 3-5, 13.5% of people aged 65-74 and 32.7% of people aged 75 and over.<sup>16</sup>

Applying these figures to the latest population estimate of England in Mid-2019 equates to around 2,773,687 (2.7 million) people with stage 3-5 CKD.<sup>17</sup>

Regarding future prevalence of CKD in England, Between 2011 and 2036 the prevalence of CKD stage 3-5 among people aged 16 years and over is expected to increase to 4.2 million or 8.3%.<sup>16</sup>

It is estimated that there are 40,000–45,000 premature deaths each year in people with CKD. A large proportion of deaths in people with CKD are due to cardiovascular events such as strokes and heart attacks.<sup>18</sup> In England in 2018, there were 2,005 deaths that were directly attributable to chronic renal failure (another term for CKD).<sup>19</sup> It is possible, that official data substantially underestimate the contribution of CKD to premature mortality. In view of the

prevalence of comorbidities in people with CKD, and the high risk of cardiovascular events in this population, it is likely that CKD is under-recorded on death certificates.<sup>18</sup>

## PATIENT TREATMENT PATHWAY

### TREATMENT PATHWAY

The current NICE pathway for the management of CKD recommends offering people with CKD education and information tailored to the severity and cause of CKD, the associated complications and the risk of progression.<sup>20</sup> People with CKD are offered lifestyle and diet advice to encourage people with CKD to exercise, achieve a healthy weight and to stop smoking.<sup>21</sup> This supports self-management of the condition, enabling people to make informed choices.<sup>22</sup>

### CURRENT TREATMENT OPTIONS

In many patients with CKD, current strategies are focussed on treatment of the problems that cause the condition and the complications that can happen as a result of it.<sup>23</sup>

For blood pressure control and antihypertensive treatment, it is recommended that a low-cost renin-angiotensin system antagonist is offered to people with CKD and:<sup>24</sup>

- diabetes and an uACR of 3 mg/mmol or more (ACR category A2 or A3)
- hypertension and an ACR of 30 mg/mmol or more (ACR category A3)

CKD is directly treated using the same approach (low-cost renin-angiotensin system antagonists) in certain subgroups of patients who do not have additional underlying diabetes, hypertension or other cardiovascular disease, but who have significant proteinuria/albuminuria (ACR of 70 mg/mmol or more).

For the prevention and treatment of cardiovascular disease:

- Antiplatelet drugs (e.g. apixaban) may be offered to people with CKD for the secondary prevention of cardiovascular disease.<sup>25</sup>
- Atorvastatin may be offered to people with CKD for the primary or secondary prevention of cardiovascular disease.<sup>26</sup>

### PLACE OF TECHNOLOGY

If licensed, dapagliflozin will provide a treatment option for patients with CKD.

## CLINICAL TRIAL INFORMATION

<b>Trial</b>	<b>Dapa-CKD; <a href="#">NCT03036150</a>; EudraCT <a href="#">2016-003896-24</a>; A Study to Evaluate the Effect of Dapagliflozin on Renal Outcomes and Cardiovascular Mortality in Patients With Chronic Kidney Disease</b> <b>Phase III - Active, not recruiting</b> <b>Location(s):</b> United states, Canada, Europe (incl UK), other countries. <b>Primary completion date:</b> June 2020
<b>Trial design</b>	Randomised, placebo-controlled, parallel assignment, quadruple-blinded.

<b>Population</b>	<ul style="list-style-type: none"> <li>• n= 4304 (estimated),</li> <li>• eGFR <math>\geq 25</math> and <math>\leq 75</math> mL/min/1.73m<sup>2</sup> (CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration Formula) at visit 1</li> <li>• evidence of increased albuminuria 3 months or more before visit 1 and UACR <math>\geq 200</math> and <math>\leq 5000</math> mg/g at visit 1</li> <li>• stable, and for the patient maximum tolerated labelled daily dose, treatment with ACE-I or ARB for at least 4 weeks before visit 1, if not medically contraindicated</li> <li>• aged <math>\geq 18</math> years at the time of consent</li> </ul>
<b>Intervention(s)</b>	Dapagliflozin (tablet) 10mg or 5mg.
<b>Comparator(s)</b>	Matched placebo.
<b>Outcome(s)</b>	<p>Primary Outcome(s):</p> <ul style="list-style-type: none"> <li>• Time to the first occurrence of any of the components of the composite: <math>\geq 50\%</math> sustained decline in eGFR or reaching end stage renal disease (ESRD) or cardiovascular death or renal death. [Time frame: from randomization (day 0) up to approximately 4 years].</li> </ul> <p>See trial record for full list of other outcomes.</p>
<b>Results (efficacy)</b>	-
<b>Results (safety)</b>	-

## ESTIMATED COST

Dapagliflozin is already marketed in the UK for the treatment of T2DM (type 2 diabetes mellitus); a pack of 28 x 5mg tablets or a pack of 28 x 10mg tablets costs £36.59.<sup>27</sup>

## RELEVANT GUIDANCE

### NICE GUIDANCE

- NICE guideline in development. Chronic kidney disease: assessment and management (update) (GID-NG10118). Expected date of publication: June 2021.
- NICE guideline. Chronic kidney disease: managing anaemia (NG8). June 2015.
- NICE clinical guideline. Chronic kidney disease in adults: assessment and management (CG182). January 2015.
- NICE clinical guideline. Chronic kidney disease (stage 4 or 5): management of hyperphosphataemia (CG157). March 2013.
- NICE quality standard. Chronic kidney disease in adults (QS5). July 2017.

### NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS Standard Contract: For Adult Kidney Transplant Service (A07/S/a). 2013.<sup>28</sup>

### OTHER GUIDANCE

- Kidney Disease Improving Global Outcomes (KDIGO). KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). 2017.<sup>29</sup>
- Kidney Disease Improving Global Outcomes (KDIGO). KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. 2013.<sup>30</sup>
- Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of chronic kidney disease: A national clinical guideline (SIGN 103). June 2008.<sup>31</sup>

## ADDITIONAL INFORMATION

AstraZeneca UK Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

## REFERENCES

- 1 Clinicaltrials.gov. A Study to Evaluate the Effect of Dapagliflozin on Renal Outcomes and Cardiovascular Mortality in Patients With Chronic Kidney Disease (Dapa-CKD). *Trial ID: NCT03036150*. 2017; Status: Active, not recruiting Available from: <https://clinicaltrials.gov/ct2/show/NCT03036150>.
- 2 electronic Medicines Compendium (eMC). *Forxiga 10 mg film-coated tablets*. 2020. Available from: [https://www.medicines.org.uk/emc/product/7607/smpc#PHARMACOLOGICAL\\_PROPS](https://www.medicines.org.uk/emc/product/7607/smpc#PHARMACOLOGICAL_PROPS) [Accessed 05 July 2020].
- 3 Heerspink HJL, Stefansson BV, Chertow GM, Correa-Rotter R, Greene T, Hou F-F, et al. Rationale and protocol of the Dapagliflozin And Prevention of Adverse outcomes in Chronic Kidney Disease (DAPA-CKD) randomized controlled trial. *Nephrology Dialysis Transplantation*. 2020;35(2):274-82. Available from: <https://doi.org/10.1093/ndt/gfz290>.
- 4 Cannon PC. Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes Trial - VERTIS CV. *American Diabetes Association Virtual Scientific Sessions*. 2020. Available from: <https://www.acc.org/latest-in-cardiology/clinical-trials/2020/06/16/11/24/vertis>.
- 5 electronic Medicines Compendium. *Forxiga 5 mg film-coated tablets*. 2020. Available from: <https://www.medicines.org.uk/emc/product/2865/smpc> [Accessed 27 July 2020].
- 6 ClinicalTrials.gov. *Recruiting, Not yet recruiting, Active, not recruiting, Completed, Enrolling by invitation Studies | Dapagliflozin | Phase 2, 3*. 2020. Available from: [https://clinicaltrials.gov/ct2/results?cond=&term=&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age\\_v=&gndr=&intr=Dapagliflozin+&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd\\_s=&strd\\_e=&prcd\\_s=&prcd\\_e=&sfpd\\_s=&sfpd\\_e=&rfpd\\_s=&rfpd\\_e=&lupd\\_s=&lupd\\_e=&sort=](https://clinicaltrials.gov/ct2/results?cond=&term=&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=Dapagliflozin+&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=) [Accessed 06 July 2020].
- 7 Delles C, Vanholder R. Chronic kidney disease. *Clinical Science*. 2017;131(3):225-6. Available from: <https://doi.org/10.1042/cs20160624>.
- 8 NHS Inform. *Causes of chronic kidney disease*. 2020. Available from: <https://www.nhsinform.scot/illnesses-and-conditions/kidneys-bladder-and-prostate/chronic-kidney-disease#causes-of-chronic-kidney-disease> [Accessed 13 August 2020].
- 9 NHS Inform. *Symptoms of chronic kidney disease*. 2020. Available from: <https://www.nhsinform.scot/illnesses-and-conditions/kidneys-bladder-and-prostate/chronic-kidney-disease#symptoms-of-chronic-kidney-disease> [Accessed 06 July 2020].
- 10 National Health Service (NHS). *Test results and stages of CKD*. 2019. Available from: <https://www.nhs.uk/conditions/kidney-disease/diagnosis/> [Accessed 06 July 2020].
- 11 Levin A SP, Bilous RW, Coresh J, De Francisco A.L.M, De Jong PE, Griffith KE, Hemmelgarn BR, Iseki K, Lamb EJ, Levey AS, Riella MC, Shlipak MG, Wang H, White CT, Christopher GW., Kidney disease: Improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice

- guideline for the evaluation and management of chronic kidney disease. *Kidney International Supplements*. 2013;3(1):1-150. Available from: <https://doi.org/10.1038/kisup.2012.73>.
- 12 Levey AS dJP, Coresh J, Nahas ME, Astor BC, Matsushita K, Gansevoort RT, Kasiske BL, Eckardt K., The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. 2011. Available from: <https://doi.org/10.1038/ki.2010.483>.
- 13 National Institute for Health and Care Excellence. *Chronic kidney disease in adults: assessment and management. Clinical guideline [CG182]*. 2014 (updated 2015). Available from: <https://www.nice.org.uk/guidance/cg182> [Accessed 31 July 2020].
- 14 NHS inform. *Chronic Kidney Disease: Who is affected?* 2020. Available from: <https://www.nhsinform.scot/illnesses-and-conditions/kidneys-bladder-and-prostate/chronic-kidney-disease> [Accessed 06 July 2020].
- 15 NHS inform. *Living with chronic kidney disease*. 2020. Available from: <https://www.nhsinform.scot/illnesses-and-conditions/kidneys-bladder-and-prostate/chronic-kidney-disease#living-with-chronic-kidney-disease> [Accessed 06 July 2020].
- 16 Public Health England. *Chronic kidney disease prevalence model*. 2014. Available from: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/612303/ChronicKidneyDiseaseCKDprevalencemodelbriefing.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/612303/ChronicKidneyDiseaseCKDprevalencemodelbriefing.pdf) [Accessed 06 July 2020].
- 17 Office for National Statistics. *Estimates of the population for the UK, England and Wales, Scotland and Northern Ireland: Mid 2019*. Available from: <https://www.ons.gov.uk/file?uri=/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland/mid20182019laboundaries/ukmidyearestimates20182019ladcodes.xls>
- 18 Kerr M. *Chronic Kidney Disease in England: The Human and Financial Cost*. 2012. Available from: <https://www.england.nhs.uk/improvement-hub/wp-content/uploads/sites/44/2017/11/Chronic-Kidney-Disease-in-England-The-Human-and-Financial-Cost.pdf> [Accessed 09 July 2020].
- 19 NHS Digital. *Mortality from chronic renal failure: directly standardised rate, all ages, annual trend, MFP*. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/compendium-mortality/current/mortality-from-chronic-renal-failure/mortality-from-chronic-renal-failure-directly-standardised-rate-all-ages-annual-trend-mfp>
- 20 National Institute for Health and Care Excellence (NICE). *Management of chronic kidney disease: Information and Education*. 2020. Available from: <https://pathways.nice.org.uk/pathways/chronic-kidney-disease#path=view%3A/pathways/chronic-kidney-disease/management-of-chronic-kidney-disease.xml&content=view-node%3Anodes-information-and-education> [Accessed 09 July 2020].
- 21 National Institute for Health and Care Excellence (NICE). *Management of chronic kidney disease: Lifestyle and diet advice*. 2020. Available from: <https://pathways.nice.org.uk/pathways/chronic-kidney-disease#path=view%3A/pathways/chronic-kidney-disease/management-of-chronic-kidney-disease.xml&content=view-node%3Anodes-lifestyle-and-diet-advice> [Accessed 09 July 2020].
- 22 National Institute for Health and Care Excellence (NICE). *Management of chronic kidney disease: Self-management*. 2020. Available from: <https://pathways.nice.org.uk/pathways/chronic-kidney-disease#path=view%3A/pathways/chronic-kidney-disease/management-of-chronic-kidney-disease.xml&content=view-node%3Anodes-self-management> [Accessed 09 July 2020].
- 23 National Health Service (NHS). *Treatment - Chronic kidney disease*. 2019. Available from: <https://www.nhs.uk/conditions/kidney-disease/treatment/> [Accessed 09 July 2020].
- 24 National Institute for health and Care Excellence (NICE). *Management of chronic kidney disease: Blood pressure control and antihypertensive treatment*. 2020. Available from: <https://pathways.nice.org.uk/pathways/chronic-kidney-disease#path=view%3A/pathways/chronic-kidney-disease/management-of-chronic-kidney-disease.xml&content=view-node%3Anodes-blood-pressure-control-and-antihypertensive-treatment> [Accessed 13 August 2020].
- 25 National Institute for Health and Care Excellence (NICE). *Management of chronic kidney disease: Preventing and treating cardiovascular disease*. 2020. Available from: <https://pathways.nice.org.uk/pathways/chronic-kidney-disease#path=view%3A/pathways/chronic-kidney-disease/management-of-chronic-kidney-disease.xml&content=view-node%3Anodes-preventing-and-treating-cardiovascular-disease> [Accessed 13 August 2020].
- 26 National Institute for health and Care Excellence (NICE). *Lipid modification therapy for preventing cardiovascular disease: Primary prevention*. 2019. Available from:



- <https://pathways.nice.org.uk/pathways/cardiovascular-disease-prevention/lipid-modification-therapy-for-preventing-cardiovascular-disease#content=view-node%3Anodes-primary-prevention> [Accessed 09 July 2020].
- 27 Medicines Complete. *Medicinal forms: Forxiga 5mg tablets (AstraZeneca UK Ltd), Forxiga 10mg tablets (AstraZeneca UK Ltd)*. 2019. Available from: <https://www.medicinescomplete.com/#/content/bnf/245194163> [Accessed 27 July 2020].
- 28 National Health Service (NHS). *NHS Standard Contract: For Adult Kidney Transplant Service (A07/S/a)*. 2013. Available from: <https://www.england.nhs.uk/wp-content/uploads/2018/08/Renal-transplantation-adult.pdf> [Accessed 27 July 2020].
- 29 Kidney Disease Improving Global Outcomes (KDIGO). *KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD)*. *Official Journal of the International Society of Nephrology*. 2017;7(1):1-59. Available from: <https://doi.org/https://kdigo.org/wp-content/uploads/2017/02/2017-KDIGO-CKD-MBD-GL-Update.pdf>.
- 30 Kidney Disease Improving Global Outcomes (KDIGO). *KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease*. *Kidney International Supplements*. 2013;3(1):1-150. Available from: <https://www.sciencedirect.com/journal/kidney-international-supplements/vol/3/issue/1>.
- 31 Scottish Intercollegiate Guidelines Network (SIGN). *Diagnosis and management of chronic kidney disease: A national clinical guideline. (SIGN 103)*. Available from: [http://www.seqc.es/download/gpc/62/3729/1043258133/1073968/cms/sign-diagnosis-and-management-of-chronic-kidney-disease\\_guideline.pdf/](http://www.seqc.es/download/gpc/62/3729/1043258133/1073968/cms/sign-diagnosis-and-management-of-chronic-kidney-disease_guideline.pdf/) [Accessed 10 July 2020].

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