

**NIHR Innovation Observatory
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Axitinib for patients at high risk of recurrence of renal cell carcinoma – adjuvant

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LAY SUMMARY

Renal cell carcinoma (RCC) is the most common type of kidney cancer. RCC affects the lining of tiny tubes within the kidney which filter waste from the blood, making urine. Symptoms include blood in urine, feeling of lump or mass in the kidney area, weight loss, raised temperature and sweating, back pain on one side (below the ribs), tiredness, loss of appetite and a general feeling of poor health. The main treatment for RCC is surgery to remove the cancer by partly or totally removing the kidney. Some patients are at high risk of their cancer returning after surgery, especially those who have large tumours which may not be possible to totally remove.

Axitinib is a tablet taken twice per day which works by interfering with the growth of the blood vessels which supply blood to the cancer cells. In other types of cancer, Axitinib has been seen to slow down the growth and stop cancers from spreading to other parts of the body. Axitinib is already available to treat RCC which has already advanced or spread, however if axitinib is licenced for use after surgery to prevent the growth and spread of further tumours (as an adjuvant therapy), this may prevent the progression and spread of RCC to other sites of the body.

This briefing reflects the evidence available at the time of writing. A version of the briefing was sent to the company for a factual accuracy check. The company was available to provide comment. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information.

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TARGET GROUP

Patients at high risk of recurrence of renal cell carcinoma – adjuvant

DESCRIPTION

Axitinib (Inlyta) is a potent and selective tyrosine kinase inhibitor of vascular endothelial growth factor receptors (VEGFR)-1, VEGFR-2 and VEGFR-3. These receptors are implicated in pathologic angiogenesis, tumour growth, and metastatic progression of cancer. Axitinib has been shown to inhibit VEGF-mediated endothelial cell proliferation and survival. Axitinib inhibited the phosphorylation of VEGFR-2 and produced tumour growth delay, regression, and inhibition of metastases in many experimental models of cancer.¹

In the phase III clinical trial, NCT01599754, axitinib is administered orally at 5mg twice daily for three years.²

Axitinib is indicated for the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine (aldesleukin or interferon alfa).^{1, 3}

Very common side effects of axitinib (affecting more than 1 in 10 people) are hypothyroidism, decreased appetite, headache, dysgeusia, hypertension, haemorrhage, dyspnoea, cough, dysphonia, diarrhoea, vomiting, nausea, abdominal pain, constipation, stomatitis, dyspepsia, palmar-plantar erythrodysesthesia, rash, dry skin, arthralgia, pain in extremity, proteinuria, fatigue, asthenia, mucosal inflammation and decreased weight.¹

Axitinib is currently in phase II trials for:⁴

- Prostate cancer
- Osteosarcoma
- Ewing Sarcoma
- Non-small cell lung cancer
- Salivary gland cancer
- Soft tissue sarcoma
- Rhabdomyosarcoma
- Neuroendocrine tumours
- Leiomyosarcoma
- Angiosarcoma
- Chondrosarcoma
- Peripheral Nerve Sheath Tumour (Neurofibrosarcoma)
- Recurrent Glioblastoma Multiforme
- Synovial sarcoma

INNOVATION and/or ADVANTAGES

If licensed, axitinib will offer a treatment option for patients with RCC who are at high risk of recurrence after surgery for which there is currently no licenced treatment option in the UK. If axitinib is successfully suppressing secondary tumour formation in patients undergoing surgery for RCC, this could potentially improve survival and reduce the need for further treatments for recurring RCC.

DEVELOPER

Pfizer Ltd

REGULATORY INFORMATION/ MARKETING PLANS

Axitinib was designated orphan drug in the EU for the treatment of renal cell carcinoma on 23 February 2011.⁵

PATIENT GROUP

BACKGROUND

Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults. RCC starts in the lining of the tubules (the smallest tubes of the nephrons of the kidneys) which filter blood and make urine. There are several types of RCC depending on the type of cell in which the cancer originates, including; clear cell RCC (75% of RCCs), papillary (10% of RCCs) and chromophobe (5% of RCCs). The remaining types of RCC comprise of rare carcinomas of the collecting ducts and renal medullary carcinoma.⁶ RCCs are usually initially treated using surgery to remove the tumour and are monitored following surgery to see if the cancer recurs. Several factors can put patients at high risk of RCC returning after surgery including; having a tumour larger than 5cms across, changes to the tumour cells (sarcomatoid dedifferentiation), remaining tumour cells at the edge of the tissue that the surgeon removed during surgery (called a positive margin), having raised blood levels of lactate dehydrogenase.⁷

Several factors increase a person's risk of developing RCC, such as age, genetics, and exposure to risk factors (including some potentially avoidable lifestyle factors). It is estimated that 42% of RCCs in the UK are linked to lifestyle factors including smoking and obesity. Ionising radiation, certain occupational exposures, and certain medicines also cause RCC. Certain medical conditions and inadequate physical activity may relate to higher RCC risk.⁸

Symptoms of RCC include haematuria (occurring in approximately 50% people diagnosed with kidney cancer when they first go to the doctor), lumps or masses around the kidney, weight loss, high temperature, pain in the back on one side (below the ribs) that won't go away, tiredness, loss of appetite and general feeling of poor health.⁹ Signs of RCC are difficult to detect in the early stages of disease and about half of patients are diagnosed when the cancer has spread around the kidney or to other sites in the body.⁵ Living with RCC requires many daily adjustments including lifestyle changes such as stopping smoking (where relevant), keeping to a healthy weight, avoiding high protein diets (as these can stress the kidney), eating healthily, drinking plenty of water, avoiding products high in salts and avoiding some medications and supplements which may damage the kidney (e.g. painkillers like aspirin and ibuprofen). Living with RCC may also impact emotions and relationships, causing anxiety, fear and depression for the patient and relatives and friends.¹⁰

CLINICAL NEED and BURDEN OF DISEASE

RCC is the most common type of kidney cancer in adults, making up 80% of kidney cancer cases in the UK.⁶

Kidney cancer is the 7th most common cancer in the UK, accounting for 3% of all new cancer cases. There are 12,600 new kidney cancer cases in the UK every year, equating to 34 cases every day. In

England in 2016, there were a total of 4,608 newly diagnosed cases of kidney cancer (IDC-10 code C64).¹¹ The incidence rate of kidney cancer cases in England in 2015 was 19.2 per 100,000. Incidence rates for kidney cancer are projected to rise by 26% in the UK from 21 cases per 100,000 in 2014 to 32 cases per 100,000 people by 2035.¹² 56% of patients diagnosed with kidney cancer in England during 2013-2014 had surgery to remove the primary tumour (not including biopsies and palliative surgery) as part of their primary cancer treatment. The proportion of patients receiving surgery to remove the primary tumour is influenced by the stage of cancer at diagnosis with 70%, 78%, 88% and 27% patients receiving surgery with stage 1, stage 2, stage 3 and stage 4 kidney cancer respectively.¹³ However, up to 40% patients with localized regional RCC will experience relapse after surgery, resulting in metastasis.¹⁴

In England, the one and five year age-standardised net survival rate for kidney cancer in adults diagnosed between 2011 and 2015 is of 76.5% and 60.8% respectively.¹⁵ Kidney cancer survival is highest in those aged 50 years and younger, with approximately 75% people diagnosed with kidney cancer in the UK aged 15-49 years old expected to survive for five years or more compared to approximately 38% in those aged over 80 years old. Kidney cancer survival has improved over the last 40 years in the UK, increasing from 23% (in 1971-1972) survival to 50% survival (in 2010-2011) over 10 years.¹⁶

Kidney cancer accounts for 3% of all cancer deaths in the UK, with 51% of kidney cancer deaths occurring in people aged over 75 years old.¹⁷ In England and Wales in 2016 there were a total of 3,577 registered deaths due to malignant neoplasm of kidney (IDC-10 code C64).¹⁸

In 2016-2017 in the UK there were 15,740 hospital admissions with a primary diagnosis of malignant neoplasm of kidney (ICD-10 code C64), 19,056 finished consultant episodes and 56,957 bed days for malignant neoplasm of the kidney, except renal pelvis.¹⁹

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal guidance in development. Renal cell carcinoma - sunitinib (ID1076). Expected date of issue to be confirmed
- NICE technology appraisal guidance in development. Cabozantinib for untreated locally advanced or metastatic renal cell carcinoma (ID1208). Expected October 2018.
- NICE technology appraisal guidance in development. Nivolumab with ipilimumab for untreated metastatic renal cell carcinoma (ID1182). Expected October 2018.
- NICE technology appraisal guidance. Tivozanib for treating renal cell carcinoma (TA512). March 2018.
- NICE technology appraisal guidance. Lenvatinib with everolimus for previously treated advanced renal cell carcinoma (TA498). January 2018.
- NICE technology appraisal guidance. Nivolumab for previously treated advanced renal cell carcinoma (TA417). November 2016. Last updated November 2017.
- NICE technology appraisal guidance. Cabozantinib for previously treated advanced renal cell carcinoma (TA463). August 2017.
- NICE technology appraisal guidance. Everolimus for advanced renal cell carcinoma after previous treatment (TA432). February 2017.

- NICE technology appraisal guidance. Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment (TA333). February 2015.
- NICE technology appraisal. Pazopanib for the first-line treatment of advanced renal cell carcinoma (TA215). August 2013.
- NICE technology appraisal. Bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma (TA178). August 2009.
- NICE technology appraisal. Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma (TA169). March 2009.
- NICE interventional procedure guidance. Irreversible electroporation for treating renal cancer (IPG443). February 2013.
- NICE interventional procedure guidance. Laparoscopic cryotherapy for renal cancer (IPG405). August 2011.
- NICE interventional procedure guidance. Percutaneous cryotherapy for renal cancer (IPG402). July 2011.
- NICE interventional procedure guidance. Percutaneous radiofrequency ablation for renal cancer (IPG353). July 2010.
- NICE interventional procedure guidance. Laparoscopic partial nephrectomy (IPG151). January 2006.
- NICE interventional procedure guidance. Laparoscopic nephrectomy (including nephroureterectomy) (IPG136). August 2005

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Cancer: Specialised Kidney, Bladder and Prostate Cancer Services (Adult). B14/S/a
- NHS England. 2013/14 NHS Standard Contract for Ex-Vivo Partial Nephrectomy Services (Adult). A06/S(HSS)b
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.
- NHS England. Clinical Commissioning Policy: Robotic assisted surgery for early kidney cancers that are unsuitable for conventional laparoscopic surgery. NHS England: 16060/P. August 2016.
- NHS England. Clinical Commissioning Policy: The use of Stereotactic ablative radiotherapy (SABR) as a treatment option for patients with renal cancer. NHS England: 16023/P. July 2016.

OTHER GUIDANCE

- NICE Pathways. Renal Cancer (CSG2).²⁰
- National Comprehensive Cancer Network. Kidney Cancer, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology. 2017.²¹
- European Society for Medical Oncology (ESMO). Renal Cell Carcinoma: ESMO Clinical Practice Guidelines. September 2016.²²
- European Association of Urology. Guidelines on Renal Cell Carcinoma. March 2015.²³

CURRENT TREATMENT OPTIONS

Treatment of kidney cancer depends on many factors including the patient's general health and fitness, the size and location of the cancer in the kidney, whether the cancer has spread to surrounding lymph nodes or elsewhere in the body.²⁴

The main treatment for kidney cancer which has not yet spread (stage 1, 2 and 3) is surgery.²⁴ Surgery can involve removing part of the kidney (partial nephrectomy) or removing the whole kidney (radical nephrectomy).²⁵ Stage 1 and 2 kidney cancer can often be cured by surgery, stage 3 (locally advanced) kidney cancers can also be cured by surgery if it is possible to remove all of the cancer. If a cancer is smaller than 3 centimetres (cm), the patient may not receive treatment at first but be monitored. If it is not possible to have surgery, patients may be offered cryotherapy, radio wave treatment, radiotherapy or arterial embolization (surgery to block blood supply to the cancer).²⁴

Initial treatment for advanced kidney cancer which has metastasised (stage 4) include biological drugs which have been shown to stop or slow the growth of the cancer for months to years. Surgery may also be performed if the patient is well enough to remove the affected kidney and secondary cancers. Other treatments (in addition to or in place of surgery) for metastasised kidney cancer include cryotherapy, radio wave treatment, radiotherapy, arterial embolization, hormone therapy and chemotherapy (although this is not generally used to treat RCC).²⁴

Kidney cancer will return in up to 40% of people who have had surgery, and in this case further treatment will be needed.¹⁴ In these cases, biological therapies may be recommended to reduce the chance of the cancer coming back again or treat metastasis.²⁴ First line biological therapies recommended by NICE include sunitinib and pazopanib. Second line biologic therapies for advanced and metastatic kidney cancer recommended by NICE include:²⁶

- lenvatinib with everolimus – for treatment of advanced RCC in adults who have had one previous VEGF targeted therapy
- cabozantinib – for treatment of advanced RCC in adults who have had 1 previous VEGF targeted therapy
- everolimus – for treatment of advanced RCC that has progressed during or after treatment VEGF targeted therapy
- nivolumab – for treatment of previously treated advanced RCC in adults
- axitinib – for treatment of advanced RCC after failure of treatment with a first-line tyrosine kinase inhibitor or a cytokine

EFFICACY and SAFETY

Trial	ATLAS, NCT01599754, ; 2013-003905-24; EudraCT-2013-003905-24; axitinib vs placebo; phase III
Sponsor	SFJ Pharma Ltd and Pfizer
Status	Ongoing
Source of Information	Trial registry ²
Location	2 EU countries (not including UK), USA and 6 countries in Asia.
Design	Randomised, double blind, placebo-controlled

Participants	n=700 (planned); aged 18 years and older; histologically confirmed preponderant, defined as >50%, clear cell RCC, following surgery to remove primary tumour, no evidence of macroscopic residual disease or metastatic disease, have not received any previous systemic (includes chemotherapeutic, hormonal, or immunotherapeutic) treatment for RCC, have not received any previous anti angiogenic treatment.
Schedule	Participants are randomly assigned in a 1:1 ratio to one of 2 treatment arms: <ul style="list-style-type: none"> - Experimental arm – one 5mg oral axitinib taken twice daily - Placebo arm – placebo tablet taken twice daily
Follow-up	Active treatment for 3 years. Follow up of outcome measures for 5 years.
Primary Outcomes	<ul style="list-style-type: none"> • Disease Free Survival (DFS) - improvement in disease free survival (DFS) in patients at high risk of recurrent RCC randomly assigned to adjuvant axitinib (Arm A) vs. Placebo (Arm B) after nephrectomy. [Time Frame: 5 years]
Secondary Outcomes	<ul style="list-style-type: none"> • Overall Survival (OS) - OS defined as the time from the date of randomization to the date of death due to any cause. [Time Frame: 5 years] • Safety - Assessment of adverse events will include: type, incidence, severity (graded by the National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE], Version 4.0), timing, seriousness, and relatedness; and laboratory abnormalities. [Time Frame: 5 years]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Estimated primary completion date September 2018 Estimated study completion date May 2019

ESTIMATED COST and IMPACT

COST

Axitinib is already marketed in the UK for the treatment of advanced renal cell carcinoma following failure of previous treatment with sunitinib or a cytokine (aldesleukin or interferon alfa); a pack of 56 x 1mg tablets costs £703 (hospital only), a pack of 56 x 3mg tablets costs £2,110 (hospital only), a pack of 56 x 5mg tablets costs £3,517 (hospital only) and a pack of 56 x 7mg tablets costs £4,924 (hospital only).²⁷

IMPACT – SPECULATIVE

IMPACT ON PATIENTS AND CARERS

- | | |
|--|---|
| <input checked="" type="checkbox"/> Reduced mortality/increased length of survival | <input type="checkbox"/> Reduced symptoms or disability |
| <input checked="" type="checkbox"/> Other: <i>potential reduced risk in RCC recurrence</i> | <input type="checkbox"/> No impact identified |

IMPACT ON HEALTH and SOCIAL CARE SERVICES

- Increased use of existing services Decreased use of existing services
- Re-organisation of existing services Need for new services
- Other: *potentially reduced use of services in the future due to reduced risk of RCC recurrence* None identified

IMPACT ON COSTS and OTHER RESOURCE USE

- Increased drug treatment costs Reduced drug treatment costs
- Other increase in costs Other reduction in costs: *potentially reduced need for future interventions*
- Other None identified

OTHER ISSUES

- Clinical uncertainty or other research question identified None identified

REFERENCES

¹ electronic Medicines Compendium. *Inlyta 5 mg film-coated tablets*. Available from: https://www.medicines.org.uk/emc/product/4325#UNDESIRABLE_EFFECTS [Accessed 13 March 2018]

² ClinicalTrials.gov. *Adjuvant Axitinib Therapy of Renal Cell Cancer in High Risk Patients (ATLAS)*. Available from: <https://clinicaltrials.gov/ct2/show/NCT01599754> [Accessed 13 March 2018]

³ National Institute for Health and Care Excellence. *BNF: axitinib*. Available from: <https://bnf.nice.org.uk/drug/axitinib.html#indicationsAndDoses> [Accessed 13 March 2018]

⁴ GlobalData. *Axitinib*. Available from: <https://pharma.globaldata.com/ProductsView.aspx?ProductType=0,1&ProductID=788> [Accessed 13 March 2018]. Login required.

⁵ European Medicines Agency. *EU/3/10/844*. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/orphans/2011/03/human_orphan_000888.jsp&mid=WC0b01ac058001d12b [Accessed 13 March 2018]

⁶ Cancer Research UK. *Kidney cancer – Types and grades*. Available from: <http://www.cancerresearchuk.org/about-cancer/kidney-cancer/stages-types-grades/types-grades> [Accessed 13 March 2018]

- ⁷ Cancer Research UK. *Kidney cancer – Follow up*. Available from: <http://www.cancerresearchuk.org/about-cancer/kidney-cancer/treatment/follow-up> [Accessed 13 March 2018]. Last Updated 03 February 2016.
- ⁸ Cancer Research UK. *Kidney Cancer Statistics*. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/risk-factors> [Accessed 13 March 2018]
- ⁹ Cancer Research UK. *Kidney cancer – symptoms*. Available from: <http://www.cancerresearchuk.org/about-cancer/kidney-cancer/symptoms> [Accessed 13 March 2018]
- ¹⁰ Macmillan Cancer Support. *Understanding Kidney Cancer*. June 2015. 9th Edition. Available from: [https://www.macmillan.org.uk/documents/be_macmillan/mac11629-kidney-e09-p05-low-res-pdf2-sh-20160503-\(2\).pdf](https://www.macmillan.org.uk/documents/be_macmillan/mac11629-kidney-e09-p05-low-res-pdf2-sh-20160503-(2).pdf) [Accessed 13 March 2018]
- ¹¹ Office for National Statistics. Cancer registration statistics, England 2016. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland> [Accessed 26 March 2018]
- ¹² Cancer Research UK. *Kidney cancer incidence statistics*. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/incidence#heading-Zero> [Accessed 13 March 2018]. Last reviewed 23 January 2018.
- ¹³ Cancer Research UK. *Kidney cancer diagnosis and treatment statistics*. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/diagnosis-and-treatment#heading-Two> [Accessed 13 March 2018]. Last Updated 17 November 2017
- ¹⁴ Motzer RJ, Ravaud A, Patard J, Pandha HS, George DJ, Patel A, et al. Adjuvant Sunitinib for High-risk Renal Cell Carcinoma after Nephrectomy: Subgroup Analyses and Updated Overall Survival Results. *European Urology*. 73 (2018) 62 –68. Available from <http://dx.doi.org/10.1016/j.eururo.2017.09.008> [Accessed 26 March 2018]
- ¹⁵ Office for National Statistics. Cancer Survival in England: adults diagnosed between 2011 and 2015 and followed up to 2016. Available from <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed> [Accessed 26 March 2018]
- ¹⁶ Cancer Research UK. *Kidney cancer survival statistics*. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/survival#heading-Two> [Accessed 13 March 2018]. Last reviewed 28 November 2014.
- ¹⁷ Cancer Research UK. *Kidney cancer mortality statistics*. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/mortality#heading-Five> [Accessed 13 March 2018]. Last reviewed 27 May 2014.
- ¹⁸ Office for National Statistics. Death Registrations Summary Statistics, England and Wales, 2016. Available from <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathregistrationssummarytablesenglandandwalesreferencetables> [Accessed 26 March 2018]
- ¹⁹ Office for National Statistics. *Hospital Episode Statistics. Primary diagnosis: 34 character 2016-17*. Available from: <https://www.ons.gov.uk/> [Accessed 13 March 2018]
- ²⁰ NICE Pathways. *Renal Cancer (CSG2)*. Available from: <https://www.nice.org.uk/guidance/conditions-and-diseases/cancer/renal-cancer> [Accessed 12 March 2018]
- ²¹ National Comprehensive Cancer Network. Kidney Cancer, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology. *Journal of National Comprehensive Cancer Network* 2017;15:804-834. doi: 10.6004/jnccn.2017.0100.
- ²² ESMO. *Renal Cell Carcinoma: ESMO Clinical Practice Guidelines*. September 2016. Available from: <http://www.esmo.org/Guidelines/Genitourinary-Cancers/Renal-Cell-Carcinoma> [Accessed 12 March 2018]
- ²³ European Association of Urology. *Guidelines on Renal Cell Carcinoma*. March 2015. Available from: <https://uroweb.org/wp-content/uploads/EAU-Guidelines-Renal-Cell-Cancer-2015-v2.pdf> [Accessed 12 March 2018]
- ²⁴ Cancer Research UK. *Treatment decisions*. Available from: <http://www.cancerresearchuk.org/about-cancer/kidney-cancer/treatment/decisions> [Accessed 13 March 2018]. Last Updated 20 January 2016
- ²⁵ Cancer Research UK. *Removing part or all of a kidney*. Available from: <http://www.cancerresearchuk.org/about-cancer/kidney-cancer/treatment/surgery/removing-part-all> [Accessed 13 March 2018]. Last updated 04 February 2016
- ²⁶ NICE Pathway. *Renal cancer overview*. Available from: <https://pathways.nice.org.uk/pathways/renal-cancer#content=view-node%3Anodes-first-line-treatment-for-advanced-and-metastatic-renal-cancer> [Accessed 13 March 2018]
- ²⁷ British National Formulary. *AXITINIB*. Available from: <https://www.medicinescomplete.com/mc/bnf/current/PHP18848-axitinib.htm#PHP18848-medicinalForms> [Accessed 12 March 2018]