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Ramucirumab (Cyramza) + capecitabine or 5-FU + cisplatin for gastric cancer of GOJ – treatment naïve for palliative chemotherapy

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LAY SUMMARY

Gastric cancer is cancer of the stomach. Gastro-oesophageal cancer is the cancer that develops at the point where the oesophagus (food pipe) meets the stomach. If the cancer has spread to the tissues around the stomach but not to other organs, it is called locally advanced. Advanced gastric cancer (metastatic) means that the cancer has spread to at least one other part of the body, such as the liver. Most gastric cancer cases are diagnosed at a late stage. Metastatic cancers have poor prognosis and it might not be possible to remove the cancer by surgery (unresectable). Some cancers have an overexpression of a protein called human epidermal growth factor receptor 2 (HER2). Those type of cancers are described as HER2-positive and are usually associated with poor prognosis. Cancers that have no or little expression of HER2 are described as HER2-negative.

Ramucirumab is a treatment used for patients with advanced gastric cancer or gastro-oesophageal cancer who have progressed after prior treatment with certain types of chemotherapies. Ramucirumab acts by stopping tumour growth by slowing formation of new blood vessels and the blood supply that feeds tumours. Ramucirumab is being developed to be given in combination with other chemotherapies (capecitabine and cisplatin) to treat unresectable, locally advanced or metastatic gastric cancer of gastro-oesophageal junction which are HER2-negative. Capecitabine and cisplatin are approved in the UK for the treatment of several types of cancers. Therefore, if licensed, ramucirumab, in combination with capecitabine and cisplatin, will offer an additional treatment option for patients with HER2-negative, unresectable, locally advanced, metastatic gastric cancer of gastro-oesophageal junction who did not have a prior chemotherapy for their cancer (treatment naïve for palliative chemotherapy).

TARGET GROUP

Gastric cancer of the gastro-oesophageal junction (HER2-negative, unresectable, locally advanced, metastatic) – treatment naïve for palliative chemotherapy

TECHNOLOGY

DESCRIPTION

Ramucirumab as a single agent is the first and only treatment approved for patients with advanced gastric cancer (cancer of the stomach) or gastro-oesophageal junction (GOJ) adenocarcinoma (cancer of the area where the gullet (oesophagus) meets the stomach) who have progressed after prior fluoropyrimidine or platinum-containing chemotherapy. Ramucirumab is a vascular endothelial growth factor (VEGF) Receptor 2 antagonist that specifically binds VEGF Receptor 2 and blocks binding of VEGF receptor ligands VEGF-A, VEGF-C, and VEGF-D. VEGF Receptor 2 is an important mediator in the VEGF pathway. In an in vivo animal model, ramucirumab inhibited angiogenesis. Angiogenesis is the process of making new blood vessels. This process involves the migration, growth, and differentiation of endothelial cells, which line the inside wall of blood vessels. In a person with cancer, angiogenesis creates new blood vessels that give a tumour its own blood supply, allowing it to grow and spread. Some tumours create proteins called VEGF. These proteins attach to the VEGF receptors of blood vessel cells causing new blood vessels to form around the tumours, enabling growth. Blocking the VEGF protein from linking to the blood vessels helps to inhibit tumour growth by slowing angiogenesis and the blood supply that feeds tumours.[1]

Ramucirumab is available as a concentrate to be made up into a solution for infusion (drip) into a vein.[2] In the clinical trial NCT02314117, ramucirumab (8 milligrams/kilogram (mg/kg) intravenously (IV) on days 1 and 8 of a 21 day cycle) is given in combination with cisplatin and capecitabine (or 5-FU in patients unable to take capecitabine).[3]

Ramucirumab is a cancer medicine that is already approved by the European Medicines Agency (EMA) to treat adult patients with:[2]

- Advanced gastric cancer or GOJ adenocarcinoma. Ramucirumab is used in combination with another medicine, paclitaxel, or on its own if the combination with paclitaxel is not appropriate, in patients whose disease has worsened despite treatment with medicines containing platinum or fluoropyrimidines;
- Metastatic colorectal cancer. Ramucirumab is used with 'FOLFIRI' chemotherapy (a combination of fluorouracil, folinic acid and irinotecan) in patients whose disease has worsened despite treatment with bevacizumab, oxaliplatin and a fluoropyrimidine;
- Non-small cell lung cancer that is advanced or has spread to other parts of the body. Ramucirumab is used in combination with docetaxel in patients whose disease has worsened despite treatment with medicines containing platinum.

The most serious adverse reactions associated with ramucirumab treatment (as a single agent or in combination with cytotoxic chemotherapy) are gastrointestinal perforation, severe gastrointestinal haemorrhage, and arterial thromboembolic events. The most common adverse reactions observed in ramucirumab-treated patients are neutropenia, leukopenia, thrombocytopenia, hypoalbuminaemia, hypertension, epistaxis, gastrointestinal haemorrhage events, stomatitis diarrhoea, proteinuria, fatigue/asthenia, and peripheral oedema.[4]

Capecitabine is an orally-administered chemotherapeutic agent used in the treatment of metastatic breast and colorectal cancers.[5] It is a cytotoxic medicine (a medicine that kills cells that are dividing, such as cancer cells) that belongs to the group 'anti metabolites'. Capecitabine is a 'prodrug' that is

converted to 5-fluorouracil (5-FU) in the body, but more is converted in tumour cells than in normal tissues. 5-FU is an analogue of pyrimidine. Pyrimidine is part of the genetic material of cells (DNA and RNA). In the body, 5-FU takes the place of pyrimidine and interferes with the enzymes involved in making new DNA. As a result, it inhibits the growth of tumour cells and eventually kills them.[6] Studies have shown that after oral administration, capecitabine is rapidly and almost completely absorbed through the gastrointestinal wall, thus avoiding direct intestinal exposure to 5-FU. The tumour-preferential activation of capecitabine reduces systemic exposure to 5-FU and potentially improves efficacy and safety. As an oral agent, capecitabine enables dosing that approximates to continuous infusion 5-FU with improved convenience.[7]

Capecitabine is taken twice a day at doses between 625 and 1,250 mg per m^2 body surface area (calculated using the patient's height and weight). The dose depends on the type of cancer being treated. The doctor will calculate the number of 150 and 500 mg tablets the patient needs to take. Capecitabine tablets should be swallowed with water within 30 minutes after a meal.[6] As a combination treatment with ramucirumab and cisplatin, capecitabine is given in the clinical trial NCT02314117 as 1,000 mg/m^2 orally twice a day on days 1 through 14. Participants that are unable to take capecitabine are given 800 mg/m^2/day fluorouracil (5-FU) IV on days 1 to 5 of each 21 day cycle.[3]

Capecitabine is licensed in the UK for the following indications:[8]

- Stage III colon cancer, adjuvant following surgery (combination therapy)
- Metastatic colorectal cancer (monotherapy)
- Metastatic colorectal cancer (combination therapy)
- Advanced gastric cancer (first-line treatment in combination with a platinum-based regimen)
- Locally advanced or metastatic breast cancer (second-line treatment as monotherapy after failure of a taxane and anthracycline regimen or where further anthracycline treatment is not indicated)
- Locally advanced or metastatic breast cancer (second-line treatment, in combination with docetaxel, where previous therapy included an anthracycline).

The most common side effects with capecitabine (seen in more than 1 patient in 10) are anorexia (loss of appetite), diarrhoea, vomiting, nausea, stomatitis (sores in the mouth), abdominal pain, hand-foot syndrome (a skin reaction with rash and pain on the hands and feet), tiredness and weakness.[6] For further details about adverse events associated with capecitabine, see summary of product characteristics at the electronic Medicines Compendium (eMC).[9]

Cisplatin (cisplatinum, cis-diamminedichloroplatinum II, CDDP) is a platinum-based chemotherapy drug used to treat various types of cancers, including sarcomas, some carcinomas (e.g. small cell lung cancer, and ovarian cancer), lymphomas and germ cell tumours. It was the first member of its class, which now also includes carboplatin and oxaliplatin. Cisplatin is an antineoplastic in the class of alkylating agents. Alkylating agents work by three different mechanisms:

1- attachment of alkyl groups to DNA bases, resulting in the DNA being fragmented by repair enzymes in their attempts to replace the alkylated bases, preventing DNA synthesis and RNA transcription from the affected DNA,
2- DNA damage via the formation of cross-links (bonds between atoms in the DNA) which prevents DNA from being separated for synthesis or transcription,
3- The induction of mispairing of the nucleotides leading to mutations.[10]

Cisplatin is licensed in the UK for the following indications (alone or in combination):[11]

- Testicular cancer
- Lung cancer
- Cervical cancer
- Bladder cancer
- Head and neck cancer

- Ovarian cancer

In the clinical trial NCT02314117, cisplatin is (80 mg/m^2 cisplatin given IV on day 1 of each 21 day cycle (for up to 6 cycles)) is given in combination with ramucirumab, capecitabine (or 5-FU).[3]
Undesirable effects of cisplatin depend on the used dose and may have cumulative effects. The most frequently reported adverse events (>10%) of cisplatin were haematological (leukopenia, thrombocytopenia and anaemia), gastrointestinal (anorexia, nausea, vomiting and diarrhoea), ear disorders (hearing impairment), renal disorders (renal failure, nephrotoxicity, hyperuricaemia) and fever. Serious toxic effects on the kidneys, bone marrow and ears have been reported in up to about one third of patients given a single dose of cisplatin; the effects are generally dose-related and cumulative. Ototoxicity may be more severe in children.[12]

Ramucirumab in combination with capecitabine (or 5-FU) and cisplatin is not licensed for any indication in the EU.

INNOVATION and/or ADVANTAGES

If licensed, ramucirumab, in combination with capecitabine (or 5-FU) and cisplatin, will offer an additional treatment option for patients with HER2 negative, unresectable, locally advanced, metastatic gastric cancer of GOJ who did not have a prior palliative chemotherapy for their cancers (treatment naïve for palliative chemotherapy).

DEVELOPER

Eli Lilly & Co Ltd

PATIENT GROUP

BACKGROUND

Gastric cancer is cancer of the stomach. The stomach is part of the digestive system, and lies just under the lungs. The top of the stomach is joined to the bottom of the oesophagus (food pipe) and the other end is attached to the bowel. Gastric cancer can start anywhere inside the stomach or the stomach wall. Most gastric cancers start in the gland cells (cells that make mucus) in the inner stomach lining. These are called adenocarcinomas. If the cancer develops at the point where the oesophagus meets the stomach (gastro-oesophageal junction (GOJ)), then it is called gastro-oesophageal cancer or cancer of the GOJ. This term is used to describe cancers where the centre of the tumour is less than 5cm above or below where the oesophagus meets the stomach.[13,14]

GOJ cancers are divided into three types according to their location:[13]
- Type 1: is when the cancer spreads down into the gastro oesophageal junction from the lower end of the oesophagus (Barrett's oesophagus)
- Type 2: is when the cancer develops at the actual gastro oesophageal junction
- Type 3: is when the cancer spreads up into the gastro oesophageal junction from the top of the stomach upwards.

Locally advanced cancer is cancer that has spread into the tissues around the stomach but has not spread to other organs. Advanced gastric cancer (metastatic cancer) is cancer that began in the stomach and has spread to at least one other part of the body, such as the liver, lungs, lymph nodes, or the oesophagus. Advanced cancer cannot be cured, but treatment can control it, relieve the symptoms, and give the patient a good quality of life for a while.[15]

Some cancers express a large amount of human epidermal growth factor receptor 2 (HER2) protein and are called HER2 positive cancers. HER2 is a protein that makes cells grow and divide. A sample of the tumour (biopsy) will show if it is HER2 positive.[16] A tumour is described as HER2-negative if it no or little expression of HER2. It has been firmly established that HER2 is overexpressed in adenocarcinoma of the upper gastrointestinal tract.[17] Studies have indicated that HER2 is a negative prognostic factor, suggesting that HER2 overexpression/amplification might be associated with the development of gastric cancer.[18]

Gastric cancer begins with a change (mutation) in the structure of the DNA in cells, which can affect how they grow. This means cells grow and reproduce uncontrollably, producing a lump of tissue called a tumour. It is not known what triggers the changes in DNA that lead to gastric cancer. Some factors increase the risk of gastric cancer such as old age (55 years and older), male gender, smoking, severe chronic atrophic gastritis (long term inflammation of the stomach lining) and peptic ulcer (ulcer of the stomach lining) caused by *Helicobacter pylori* (type of bacteria) infection, diet (such as pickled vegetables, salt, and smoked meat), family history of gastric cancer, having another type of cancer, vitamin B12 deficiency, and history of stomach surgery.[20]

Common symptoms of gastric cancer include blood in stools or black stools, loss of appetite, weight loss, sickness, tiredness, breathlessness, lumpiness and swelling in the stomach (caused by a build-up of fluid), abdominal pain, persistent indigestion (dyspepsia) and burping, anaemia, yellowing of the skin and whites of the eyes (jaundice).[19, 20]

Late complications of gastric cancer may include pathologic peritoneal and pleural effusions (fluid accumulation in the peritoneal and pleural cavity), obstruction of the gastric outlet or gastroesophageal junction, obstruction of the small bowel, bleeding in the stomach from oesophageal varices (abnormal large veins in the oesophagus) or at the anastomosis (cross-connection) after surgery, jaundice caused by hepatomegaly (enlarged liver), weakness and weight loss from not eating.[21] The prognosis of patients with unresectable or metastatic gastric cancer is poor and the median survival time ranges between 6 and 12 months.[22]

CLINICAL NEED and BURDEN OF DISEASE

In 2014, gastric cancer was the 16th most common cancer in the UK. There were around 6,700 new cases of stomach cancer in the UK in 2014, equivalent to 18 cases diagnosed every day.[23] The crude incidence rate in England was 9.8 per 100,000 in 2014. Between 2012 and 2014 around half (51%) of stomach cancer cases in the UK each year were diagnosed in people aged 75 years and over. The proportion of gastric cancer cases in England diagnosed at stage III and stage IV in 2014 were 17% and 34% respectively. According to the data of 2010–2012 in the UK, the largest proportion of gastric cancer cases (34.0% males, 19.7% females) occur in the cardia[24] (The first part of the stomach which is closest to the oesophagus[25]). Around 1 in 5 people (20%) have HER2 positive gastric cancer.[16]

Hospital episode statistics for England 2015/16 show that there were 20,311 hospital admissions for malignant neoplasm of stomach (ICD 10: C16), with 25,799 finished consultant episodes (FCE) resulting in 67,050 FCE bed days. For malignant neoplasms of cardia specifically (ICD10: 16.0), there were 8,593 hospital admissions, 10,261 FCE, and 23,429 FCE bed days.[26]

According to the 2010-2011 data, 19% of people diagnosed with stomach cancer in England and Wales survive their disease for five years or more.[23] Five year survival rates for stage III (A, B, C) gastric cancer were 25%, 20%, and 10% respectively; whereas those for stage IV were 5%.[27]

Gastric cancer was the 12th most common cause of cancer death in the UK in 2014. Crude mortality rate in England was 6.7 per 100,000 in 2014. In the UK, it is the eighth most common cause of cancer death in males, whilst it is the 13th most common cause of cancer death in females. Gastric cancer

mortality is strongly related to age, with the highest mortality rates being in older males and females. In the UK in 2012-2014, on average each year around 6 in 10 (59%) deaths were in people aged 75 and over.[28]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development. Pertuzumab for untreated metastatic HER2-positive gastric or gastro-oesophageal junction cancer (ID1096). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Pembrolizumab for previously treated metastatic gastric or gastro-oesophageal junction cancer (ID1168). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Avelumab for treating gastric or gastro-oesophageal junction cancer after 2 therapies (ID1289). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Nivolumab for previously treated oesophageal cancer (1249). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Nivolumab for previously treated gastric or gastro-oesophageal junction cancer (ID1118). August 2018.
- NICE technology appraisal. Trastuzumab for the treatment of HER2-positive metastatic gastric cancer (TA208). November 2010.
- NICE technology appraisal. Capecitabine for the treatment of advanced gastric cancer (TA191). July 2010.
- NICE technology appraisal. Ramucirumab for treating advanced gastric cancer or gastro–oesophageal junction adenocarcinoma previously treated with chemotherapy (TA378). January 2016.
- NICE guideline in development. Oesophago-gastric cancer (GID-CGWAVE0801). January 2018.
- NICE interventional procedure guidance. Minimally invasive oesophagectomy (IPG407). September 2011.

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Cancer: Oesophageal and gastric (Adult). B11/S/a.
- 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 oesophago-gastric cancers. 16006/P. July 2016

OTHER GUIDANCE

- Gastric Cancer, Version 3. 2016, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network. 2016; 14:1286-1312.[29]
- Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 27 (Supplement 5): v38–v49, 2016.[30]
- LCA Oesophageal and Gastric Cancer Clinical Guidelines. April 2014.[31]
- Guidelines for the management of oesophageal and gastric cancer. Gut 2011; 60: 1449e1472.[32]

CURRENT TREATMENT OPTIONS

The most common treatments for gastric cancers and GOJ cancers are surgery, radiotherapy, and chemotherapy. The patient may have one of these treatments or a combination. If surgery is recommended, the patient may have chemotherapy beforehand. If the patient has a GOJ cancer then they may have radiotherapy before the operation. If it is not possible to remove the tumour, then the treatment focus will be on preventing the tumour from getting any bigger and causing further harm to the body. This can be done by surgery or by chemotherapy. When it is not possible to eliminate the cancer or slow it down, the aim of treatment will be to relieve the symptoms by surgery or radiotherapy.

Chemotherapy is a specialist treatment for cancer that uses medicines, called cytotoxic medicines, to stop cancer cells dividing and multiplying. For stomach cancer, chemotherapy might be given to the patient before surgery to reduce the amount of cancer that has to be removed during the operation. Chemotherapy can also be used after surgery to destroy any remaining cancer cells and prevent the cancer from coming back. The following are recommendations by the National Institute for Health and Care Excellence (NICE) on using the following medicines in gastric cancer or gastro-oesophageal cancer:

- **Capecitabine**

Capecitabine in combination with a platinum-based regimen for the first-line treatment of inoperable advanced gastric cancer.[33]

- **Ramucirumab[34]**

Ramucirumab alone or with paclitaxel is not recommended by NICE within its marketing authorisation for advanced gastric cancer or GOJ adenocarcinoma previously treated with chemotherapy. People whose treatment with ramucirumab was started within the NHS before this guidance was published should be able to continue treatment until they and their clinician consider it appropriate to stop.

- **Trastuzumab[35]**

Trastuzumab, in combination with cisplatin and capecitabine or 5-fluorouracil, is recommended as an option for the treatment of people with HER2-positive metastatic adenocarcinoma of the stomach or GOJ who:

- have not received prior treatment for their metastatic disease and
- have tumours expressing high levels of HER2 as defined by a positive immunohistochemistry score of 3 (IHC3 positive).

People who are currently receiving treatment with trastuzumab for HER2-positive metastatic gastric cancer who do not meet the criteria above should have the option to continue treatment until they and their clinicians consider it appropriate to stop.

EFFICACY and SAFETY

Trial	**RAINFALL, NCT02314117; ramucirumab vs placebo, both in combination with cisplatin and capecitabine; phase III**
Sponsor	Eli Lilly and Company.
Status	Ongoing, not recruiting.
Source of Information	Trial registry.[3]
Location	EU (incl UK), USA, Canada and other countries.
Design	Randomized, double-blind, placebo-controlled, parallel assignment.
Participants	n= 616 (planned); aged 18 years and older; males and females; metastatic gastric or gastroesophageal junction adenocarcinoma; not received any prior first-line systemic therapy; should not be HER2-positive.
Schedule	Randomised to 8 milligrams/kilogram (mg/kg) ramucirumab given intravenously (IV) on days 1 and 8 in combination with 80 mg/square meter (m^2) cisplatin given IV on day 1 of each 21 day cycle (for up to 6 cycles) and 1000 mg/m^2 capecitabine given orally twice a day on days 1 through 14. Participants that are unable to take capecitabine will be given 800 mg/m^2/day fluorouracil (5-FU) IV on days 1 to 5 of each 21 day cycle; or Placebo for blinding given IV on days 1 and 8 in combination with 80 mg/m^2 cisplatin given IV on day 1 of each 21 day cycle (for up to 6 cycles) and 1000 mg/m^2 capecitabine given orally twice a day on days 1 through 14. Participants that are unable to take capecitabine will be given 800 mg/m^2/day 5-FU IV on days 1 to 5 of each 21 day cycle.
Follow-up	Active treatment for 6 cycles (18 weeks), follow-up 42 months.
Primary Outcomes	Progression Free Survival (PFS) [Time Frame: Randomization to Radiological Disease Progression or Death from Any Cause (Approximately 42 months)]
Secondary Outcomes	- Time frame 42 months: - Overall Survival (OS) - Progression Free Survival 2 (PFS2) - Objective Response Rate (ORR) - Disease Control Rate (DCR) - Time to Progression (TTP) - Duration of Response (DoR) - Change from Randomization to 30 Days After Treatment Discontinuation in Quality of Life on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 - Change from Randomization to 30 Days After Treatment Discontinuation in Health Status on the European Quality of Life 5-Dimensions 5 Level Instrument - Time to Deterioration in Eastern Cooperative Oncology Group (ECOG) Performance Status (PS)

	- Pharmacokinetics (PK): Minimum Ramucirumab Concentration (Cmin) and Concentration at 1-Hour Post End of Ramucirumab Infusion [Time Frame: Predose Cycle 1 through Cycle 9 (Approximately 6 Months)] - Number of Participants with Anti-Ramucirumab Antibodies
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date reported as August 2018

ESTIMATED COST and IMPACT

COST

Ramucirumab is already marketed in the UK. The NHS indicative price for Cyramza vials (Eli Lilly and Company Ltd):[36]

- 100mg/10ml concentrate for solution for infusion (1 vial) costs £500
- 500mg/50ml concentrate for solution for infusion (1 vial) costs £2,500

Capecitabine is already marketed in the UK. The NHS indicative price for capecitabine tablets is as follows:[37]

- Capecitabine 150mg tablets (60 tablets) (AAH Pharmaceuticals Ltd) costs £10.40
- Capecitabine 150mg tablets (60 tablets) (Dr Reddy's Laboratories (UK) costs £30.00
- Capecitabine 150mg tablets (60 tablets) (Mylan Ltd) costs £38.90
- Capecitabine 150mg tablets (60 tablets) (medac UK) costs £39.99
- Xeloda 150mg tablets (60 tablets) (Roche Products Ltd) costs £40.02
- Capecitabine 300mg tablets (30 tablets) (medac UK) costs £39.99
- Capecitabine 500mg tablets (120 tablets) (AAH Pharmaceuticals Ltd) costs £52.00
- Capecitabine 500mg tablets (120 tablets) (Actavis UK Ltd) costs £240.00
- Capecitabine 500mg tablets (120 tablets) (Dr Reddy's Laboratories (UK) Ltd) costs £225.72
- Capecitabine 500mg tablets (120 tablets) (Mylan Ltd) costs £262.00
- Capecitabine 500mg tablets (120 tablets) (Sun Pharmaceuticals UK Ltd) costs £265.00
- Capecitabine 500mg tablets (120 tablets) (Zentiva) costs £265.55
- Capecitabine 500mg tablets (120 tablets) (medac UK) costs £260.24
- Xeloda 500mg tablets (120 tablets) (Roche Products Ltd) costs £265.55

Fluorouracil is already marketed in the UK. The NHS indicative price for fluorouracil solution for injection vials is as follows:[38] Fluorouracil 500mg/20ml solution for injection vials (10 vial) (Hospira UK Ltd) costs £64.00

- Fluorouracil 250mg/10ml solution for injection vials (5 vial) (Hospira UK Ltd) costs £24.00
- Fluorouracil 500mg/10ml solution for injection vials (5 vial) (Hospira UK Ltd) costs £32.00
- Fluorouracil 500mg/10ml solution for injection vials (1 vial) (medac UK) costs £6.40
- Fluorouracil 1g/20ml solution for injection vials (1 vial) (medac UK) costs £12.80

The NHS indicative price for fluorouracil solution for infusion vials is as follows:[38]

- Fluorouracil 2.5g/100ml solution for infusion vials (1 vial) (Hospira UK Ltd), (medac UK) costs £32.00
- Fluorouracil 2.5g/50ml solution for infusion vials (1 vial) (Hospira UK Ltd) and (medac UK) costs £32.00

- Fluorouracil 5g/100ml solution for infusion vials (1 vial) (Hospira UK Ltd) and (medac UK) costs £64.00

Cisplatin is already marketed in the UK. The NHS indicative price for cisplatin vials is as follows:[39]

- Cisplatin 100mg/100ml concentrate for solution for infusion vials (1 vial) costs £50.22 (Sandoz, AAH Pharmaceuticals Ltd, Teva UK Ltd) or £55.64 (Hospira UK Ltd).
- Cisplatin 10mg/10ml concentrate for solution for infusion vials (1 vial) costs £5.90 (Sandoz Ltd, AAH Pharmaceuticals Ltd, Teva UK Ltd)
- Cisplatin 50mg/50ml concentrate for solution for infusion vials (1 vial) costs £25.11(Sandoz Ltd) or £25.37 (A A H Pharmaceuticals Ltd, Teva UK Ltd) or £28.11 (Alliance Healthcare (Distribution) Ltd, Hospira UK Ltd)

IMPACT – SPECULATIVE

IMPACT ON PATIENTS AND CARERS

☒ Reduced mortality/increased length of survival

☐ Reduced symptoms or disability

☐ Other:

☐ 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:

☒ 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

☐ Other:

☐ None identified

OTHER ISSUES

☐ Clinical uncertainty or other research question identified

☒ None identified

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