Optimising Care for Patients on Targeted Therapy for Metastatic Renal Cell Carcinoma

Developing a Pharmacist-led Clinic

SUTENT® (sunitinib malate), INLYTA® (axitinib) and TORISEL® (temsirolimus)

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1. Evolving role of the clinical pharmacist

- The modern clinical pharmacist role is evolving, with responsibilities including:
  - Running independent clinics, as part of agreed care pathways
  - Increased involvement in patient counselling, funding and reimbursement of medicines
  - The development of guidelines

- Several courses have been designed to support clinical pharmacists, such as non-medical prescribing (independent and supplementary prescribing), communication skills and consultation

1.1 The clinical pharmacist as an integral member of the multidisciplinary team

- Clinical pharmacists are acknowledged experts in medicinal products, who are ideally suited to advise on drug therapy to patients and other healthcare professionals (HCPs). Consequently, they now work in close collaboration with other members of the multidisciplinary team to optimise patient care

1.2 Benefits of integrating a clinical pharmacist in the patient care pathway

- Involving clinical pharmacists in direct patient care has several advantages, by helping to:
  - Reduce drug-related adverse events
  - Reconcile medicines
  - Increase compliance
  - Increase patient education and support
  - Improve the patient’s quality of life
  - Provide a multidisciplinary, patient-centred approach
  - Reduce morbidity and mortality
  - Improve health and economic outcomes

2. Key steps to setting up a pharmacist-led clinic

Setting up a pharmacist-led clinic should broadly follow the same process as developing a nurse-managed service. The clinic could be run in isolation or as part of a combined nurse and pharmacist-led clinic, under an agreed patient care pathway. Consider the following steps when developing your clinic:

Step 1: The business case
• Identify the service need and develop a business proposal to explain in logical steps why the service is needed and the resources that are required:
  – Developing a business case requires leadership and you may need managerial support

• Map out all stakeholder relationships to determine the availability of all resources, identify supportive groups and evaluate the impact of setting up a pharmacist-led service
  – It is useful to set up a small steering group to work with you

**Step 2: Aims and objectives**

• Clarify what services will be offered to patients and other HCPs (include outlines, pathways and treatment plans), as well as the aim of the clinic and the objective for all activities involved. The business case should also detail potential improvements to the current healthcare system, and identify challenges and highlight solutions

• Future audit and evaluation should be considered to enable time and resources for monitoring and improving services

• Below are some questions to consider that may help you prepare the aims and objectives of your pharmacist-led clinic:
  – Are there clear clinic pathways?
  – Which patients will be seen and by whom? (More complicated cases may want to be kept under full consultant-led service)
  – How frequent will clinics be?
  – Will you provide telephone monitoring?
  – How will the consultant/SpR and clinical nurse specialist be involved?
  – How will referrals be managed? When will you refer?
  – What supporting documents will be available to staff and to patients?
  – What will the capacity of the clinic be?
  – How will appointments be structured? (pre-treatment versus follow-up appointments)
  – What level of training, competency and experience will be required? How will you assess or provide this?
  – Is there a development plan?
  – How will funding be provided?
Step 3: Criteria for clinic access

- The aims and objectives from Step 2 should be reiterated for emphasis, and the multidisciplinary team consulted to decide the criteria for access to the clinic. Besides factors for inclusion, consider exclusion criteria for patients/referrals and list services that are not offered (this will deter inappropriate referrals from other HCPs/clinics). It may be best to begin with a smaller clinic and expand as experience grows.

- Determine the origin of patient referral – internal (multidisciplinary team) and/or external (e.g. primary care, GP and community).

Step 4: Support from lead clinician and buy-in from clinical team

- At the planning stage, ensure sufficient time and resources to publicise the clinic to the multidisciplinary team, other HCPs and cancer networks. This should include the existence and location of the clinic, services offered (and not offered) by the clinic, and the role of the pharmacist to patients and other HCPs.

- Involve stakeholders at an early stage, alongside the multidisciplinary team.

Step 5: Location

- Carefully select a suitable place to run the clinic, with appropriate facilities and access. Ideally the clinic should be run alongside the existing consultant-led clinic to ensure easy access to clinicians (and other supporting HCPs and administrative staff), improved communications and easy referrals. The following factors should be discussed and defined in the business case:
  - Primary or secondary care setting
  - Equipment/resource requirements/funding
  - Availability of administrative support (e.g. central booking, secretarial, information technology)
  - Determine if the service will run parallel with other associated clinics (e.g. urology, oncology)
  - Consider frequency and duration of patient visits (these should be defined in clear pathways).

Step 6: Multidisciplinary team support

- Support from the multidisciplinary team is critical in setting up the service. The clinical pharmacist should work closely with the team to share expertise, and readily accept advice from other members of the team when issues arise that are outside of their competence.

Step 7: Professional development
Continual development of competencies is essential to evolve and improve the clinic. It may be helpful to have a competency document outlined as part of the clinical plan/business case. Ensure that appropriate education and training are available, and consider incorporating a credentialing process by an existing prescriber to assess competency.

Plan and build in structures to provide appropriate education and/or training, including forging links with higher education faculty and other health clinics (e.g. local or regional cancer networks) to share experience. A non-medical prescribing course maybe a good way of achieving this.

Step 8: Managing medicines

The prescription and administration of medication is an essential function of the clinic; therefore, decide early on how this will be provided at the clinic.

- Patient group directions (i.e. a written direction that is signed by a clinician and agreed by a pharmacist, which enables a nurse to supply and/or administer prescription-only medicines to patients, without necessarily referring back to a clinician for an individual prescription)
- Independent prescribing
- Dependent prescribing

In addition, identify appropriate supervision and/or support network to advise on challenging cases, including medicines reconciliation.

It is also important to establish whether a home delivery service will be used for some patients, and how this fits into the agreed pathway.

Step 9: Audit and evaluation

Consider how to measure the effectiveness of the service at the outset. The identification of indicators can help to focus the aims and objectives of the clinic, and to find validated audit tools that can be used for future audits.

Coordinate with information technology as part of setting up the clinic location to establish the system used to record data as part of an audit/evaluation programme.

Step 10: Closing the loop

Attention to administrative detail will ensure that the clinic runs smoothly. However, the clinic is an evolving service and the findings from audit/evaluation should be used as the basis of ongoing improvements. Any change in service should be communicated to all relevant stakeholders (i.e. similar to Step 4).

3. Summary
• Clinical pharmacists are an important member of the multidisciplinary team, and a pharmacist-led clinic offers several benefits to patients and healthcare system

• Support from the multidisciplinary team is paramount in developing a successful proposal, setting up the clinic and running the service

4. References

SUTENT® Capsules (sunitinib malate)  
PRESCRIBING INFORMATION – MRCC  
Please refer to the Summary of Product Characteristics (SmPC) before prescribing SUTENT 12.5 mg, 25 mg or 50 mg.

Presentation: Hard gelatin capsules containing sunitinib malate equivalent to 12.5 mg, 25 mg and 50 mg sunitinib. 

Indications: For the treatment of: 
- Advanced and/or metastatic renal cell carcinoma (MCRC) in adults. 
- Metastatic bosutinib-resistant Philadelphia chromosome-positive chronic myeloid leukemia (PC-CHARGE). 

Dosage: Therapy should be initiated by a physician experienced in the administration of anti-cancer agents. The recommended dose of sunitinib is 50 mg taken orally, once daily, with or without food, for 4 consecutive weeks, followed by a 2-week rest period, to comprise a complete cycle of 6 weeks. Dose modifications in 12.5 mg steps may be applied based on individual safety and tolerability. Daily dose should not exceed 75 mg nor be decreased below 25 mg. The use of sunitinib in children and adolescents is not recommended. 

Contra-indications: Hypersensitivity to the active substance or to any of the excipients. Special warnings and precautions for use: 
- Co-administration of potent CYP3A4 inhibitors or inducers should be avoided if possible, or the dose of sunitinib altered.
- Skin discoloration, depigmentation of the hair or skin and occasional rash affecting the palms of hands and soles of feet occur during treatment. 
- Pyoderma gangrenosum, generally reversible after drug discontinuation, has been reported. Severe cutaneous reactions have been reported, including cases of erythema multiforme (EM) and cases suggestive of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) some of which were fatal. If signs or symptoms of SJS, TEN, or EM are present, sunitinib treatment should be discontinued. 
- Gastronomic events, some of which were fatal have been reported. Serious, sometimes fatal gastrointestinal complications have occurred in patients with intra-abdominal malignancies. 
- Hypertension has been reported as a very common adverse reaction in clinical trials. Patients should be screened for hypertension and controlled as appropriate. 
- Temporary suspension is recommended in patients with severe hypertension that is not controlled with medical management. 
- Decreased absolute neutrophil and platelet counts occurred during clinical trials and complete blood counts should be performed at the beginning of each treatment cycle. 
- Cardiovascular events including CHF, cardiomyopathy and myocardial disorders, some of which were fatal, have been reported. 
- Closely monitor for clinical signs and symptoms of CHF and consider the administration of and periodic evaluations of LVF especially in patients with cardiac risk factors and/or history of coronary artery disease. 

- If clinical manifestations of CHF present, discontinuation of sunitinib is recommended. 
- The administration of sunitinib should be interrupted and/or dose reduced in patients without clinical evidence of CHF but with a LVEF <50% and >20% below baseline. 
- Sunitinib should be used with caution in patients with a known history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. 
- Treatment-related venous thromboembolic events have been reported. 
- Arterial thromboembolic events (ATE), sometimes fatal, have been reported including cerebrovascular accident, transient ischaemic attack, and cerebral infarction. 
- Respiratory events have been reported. Baseline lab measurements and 3 monthly routine monitoring of thyroid function during treatment are required, including monitoring for signs and symptoms suggestive of thyroid dysfunction and patients treated as per standard medical practice. 
- Cases of thyroiditis and hyperthyroidism, some followed by hypothyroidism have been uncommonly reported. 
- Pancreatitis and serious pancreatic events, some with fatal outcome have been reported. 
- Hyperglycemia has been observed in patients treated with sunitinib. 
- Monitor liver function tests at baseline and at the start of each cycle of treatment, and as clinically indicated. 
- If symptoms of pancreatitis or hepatic failure are present, treatment with sunitinib should be discontinued and the patient provided with appropriate supportive care. Sunitinib treatment may be associated with cholecystitis, including acalculous and emphysematous cholecystitis. 
- Some cases with fatal outcome have been reported. 
- Cases of renal impairment, renal failure and/or acute renal failure, in some cases with fatal outcome, have been reported. 
- Baseline urinalysis is recommended. Patients should be monitored for the development or worsening of proteinuria. 
- Sunitinib should be discontinued in patients with nephrotic syndrome. 
- If fluid accumulation occurs, treatment with sunitinib should be interrupted. 
- Cases of impaired wound healing have been reported during sunitinib therapy and the decision to resume therapy following a major surgical intervention should be based upon clinical judgment of recovery from surgery. 
- Osteonecrosis of the jaw (ONJ) has been reported, the majority of cases occurred in patients who had received previously concurrent treatment with IV bisphosphonates. 
- Cautions should therefore be exercised when sunitinib and IV bisphosphonates are used either simultaneously or sequentially. 
- Prior to treatment with sunitinib, either alone or subsequent to IV bisphosphonates, a dental examination and appropriate preventative dentistry should be considered. 

- Invasive dental procedures are also an identified risk factor and should be avoided. 
- In case of angioedema due to hypersensitivity, treatment with sunitinib should be interrupted and medical care provided. 
- Seizures with or without radiological evidence of brain metastases have been reported, including a few reports (<1%), some fatal, of seizures with radiological evidence of reversible posterior leukoencephalopathy syndrome (RPLS). Patients with seizures and signs/symptoms consistent with RPLS should be controlled with medical management, including control of hypertension as above and temporary suspension of sunitinib is recommended. 
- Cases of Tumour Lysis Syndrome, some fatal, have been reported. 
- Patients should be monitored closely and treated as clinically indicated, and prophylactic hydration should be considered. 
- Serious infections most commonly involve respiratory, urinary tract, skin infections and sepsis, with or without neutropenia, including some with a fatal outcome, have been reported. 
- Rare cases of necrotising fasciitis, including of the perineum, sometimes fatal, have been reported. 
- Sunitinib therapy should be discontinued in patients who develop necrotising fasciitis, and appropriate treatment should be promptly initiated. 
- During sunitinib treatment, decreases in blood sugar leading to loss of consciousness have been reported. 
- In case of symptomatic hypoglycaemia, sunitinib should be temporarily interrupted. 
- Blood glucose levels in diabetic patients should be checked regularly in order to assess if anti-diabetic drug dosage needs to be adjusted to minimize the risk of hypoglycaemia. 

Other interactions: 
- None. 
- Fertility, pregnancy and lactation: Sunitinib should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus and is not recommended during breast-feeding. 
- Fertility may be compromised during treatment with sunitinib.

Driving and operating machinery: Patients should be advised that they may experience dizziness during treatment with sunitinib. 

Undesirable effects: 
- The most important treatment-related serious adverse reactions associated with sunitinib, some fatal, are renal failure, heart failure, pulmonary embolism, gastrointestinal perforation and haemorrhages (e.g. respiratory tract, gastrointestinal, tumour, urinary tract, and brain haemorrhages). 
- Very common adverse events are viral infections, neutropenia, thrombocytopenia, anaemia, leukopenia, hypertension, decreased appetite, oedema, pre-existing heart failure, anaemia, peripheral oedema, erythema, oedema, lassitude increased, jaundice, transient decreases in absolute neutrophil and platelet counts, lipase increased, platelet count decreased, hemoglobin decreased, hyperuricemia, chest pain, pain, influenza like illness, chills, white blood cell count increased, blood uric acid increased. Refer to SmPC for full list.

- Common adverse events are chills, fatigue, fatigue, pain, muscle weakness, renal failure, hyperlipidaemia, increased alanine aminotransferase, increased bilirubin, increased alanine aminotransferase increased, blood creatinine increased, blood pressure increased, blood uric acid increased. Refer to SmPC for full list.

Dosage: 
- Please refer to the Summary of Product Characteristics (SmPC) before prescribing SUTENT 12.5 mg, 25 mg or 50 mg.

PRESCRIBING INFORMATION – MRCC
SUTENT
www.mhra.gov.uk/yellowcard
®
Information on 01304616161
Last revised: July 2014 Ref: ST 22_0
Holder:
28, 25 mg capsules [EU/1/06/347/005] £1,569.40, Pack of 28, 50 mg capsules [EU/1/06/347/006] £3,136.80, Marketing Authorisation Holder: Pfizer Limited, Sandwich, Kent, CT13 9NJ, United Kingdom. Further Information is available on request from: Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK. Tel: +44 (0) 1384 616161.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Pfizer Medical Information on 01304616161.
Inlyta® (axitinib) Film-Coated Tablets

PRESENTING INFORMATION

Please refer to the Summary of Product Characteristics (SmPC) before prescribing Inlyta 1 mg or 5 mg film-coated tablets.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions.

Presentation: Each 1 mg, 3 mg, 5 mg and 7 mg film-coated tablet contains 1 mg, 3 mg, 5 mg and 7 mg of axitinib, respectively. For the treatment of adult patients with advanced renal cell carcinoma (RCC) after failure of prior treatment with sunitinib or a cytokine. Dosage: Treatment should be initiated by a physician experienced in the use of anticancer therapeutic antiangiogenic medicinal products. The recommended oral dose is 5 mg twice daily (approximate 12 hours apart) taken with or without food. Dose increase or reduction is recommended based on individual safety and tolerability. Patients who tolerate the starting dose of 5 mg twice daily with no adverse reactions may have their dose increased to 7 mg twice daily unless BP > 150/90 mmHg or patient is receiving anti-hypertensive medication. Subsequently, using the same criteria, patients who tolerate a dose of 7 mg twice daily, may have their dose increased to a maximum of 10 mg twice daily. Management of some adverse drug reactions may require a temporary discontinuation and/or dose reduction. When dose reduction is necessary, the dose may be reduced to 3 mg twice daily and further to 2 mg twice daily. Co-administration with strong CYP3A4/5 inhibitors or inducers may increase or decrease axitinib plasma concentrations respectively. Selection of an alternative concomitant medicine with no or minimal CYP3A4/5 inhibition or induction potential is recommended. If a strong CYP3A4/5 inhibitor must be co-administered, a dose decrease of axitinib to approximately half the dose (e.g. from a starting dose of 5 mg twice daily to a reduced dose of 2 mg twice daily) is recommended. If co-administration of the strong inhibitor is discontinued, axitinib should be recommenced with careful monitoring for toxicity. If co-administration of the strong inducer is discontinued the axitinib dose should be immediately returned to the dose used prior to initiation of the strong CYP3A4/5 inhibitor. No dose adjustment is required in elderly patients or patients with renal impairment or with mild hepatic impairment (Child-Pugh class A). A dose decrease is recommended in patients with moderate hepatic impairment (Child-Pugh class B) (e.g. the starting dose should be reduced from 5 mg twice daily to 2 mg twice daily). Axitinib has not been studied in patients with severe hepatic impairment (Child-Pugh class C) and should not be used in this population. Dose adjustment is not required on the basis of patient age, race, gender, or body weight. The safety and efficacy of axitinib in children (<18 years) have not been established.

Contra-indications: Hypersensitivity to axitinib or to any of the excipients. Special warnings and precautions for use: Some symptoms of cardiac failure should be monitored periodically throughout treatment. Management of cardiac failure events may require temporary interruption or permanent discontinuation and/or dose reduction of axitinib therapy (including cardiac events (including cardiac failure congestive cardiomyopathy failure, left ventricular dysfunction, ejection fraction decreased, and right ventricular failure) were reported in clinical studies. Blood pressure should be well-controlled throughout treatment. Patients should be monitored for hypertension and treated as needed with standard antihypertensive therapy. In the case of persistent hypertension despite use of antihypertensive therapy, the antihypertensive medication should be stopped at least 24 hours prior to scheduled surgery and the decision to resume therapy after surgery should be based on clinical judgment of adequate wound healing. Events of PRES (a neurological disorder which can present with headache, seizure, lethargy, confusion, blindness and other visual and neurologic disturbances; mild to severe visual loss may be present) were reported in clinical studies. MRI is necessary to confirm diagnosis. In patients with signs or symptoms of PRES, temporarily interrupt or permanently discontinue axitinib treatment. The potential for increased severe hypertension may be greater in patients previously experiencing PRES is not known. Proteinuria, including that of Grade 3 severity, was reported in clinical studies. Monitoring for proteinuria before initiation of, and periodically throughout, treatment with axitinib is recommended. In moderate to severe proteinuria reduce the dose or temporarily interrupt treatment. Increases in ALT, AST and bilirubin levels have been reported. Liver function tests should be performed before initiation of, and periodically throughout, treatment. Systemic exposure to axitinib was approximately two-fold higher in subjects with moderate hepatic impairment (Child-Pugh class B) compared to subjects with normal hepatic function. In these patients dose decrease is recommended (see Dosage section). Axitinib has not been studied in patients with severe hepatic impairment (Child Pugh class C) and should not be used in these patients. The use of axitinib in patients with lactose and with galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Other interactions: Axitinib is metabolised primarily by CYP3A4/5 and, to a lesser extent, CYP1A2, CYP2C19, and UGT1A1. A strong CYP3A4/5 inhibitor (e.g. itraconazole, clarithromycin, erythromycin) or strong CYP3A4/5 inducer (St. John’s wort) must be co-administered, a dose adjustment of axitinib is recommended (see Dosage section). In patients taking strong inhibitors of CYP3A4/5 and CYP2C19 caution should be exercised due to the risk of increased axitinib plasma concentrations. Fertility, pregnancy and lactation: Axitinib may cause foetal harm when administered to a pregnant woman. Studies in animals have shown reproductive toxicity including foetal deformations. Axitinib should not be used during breast-feeding and women of childbearing potential must use effective contraceptive methods before and up to 1 week after treatment. Fertility may be impaired during treatment. Driving and operating machinery: Axitinib has a minor influence on the ability to drive and use machines. Advise patients that they may experience dizziness and/fatigue during treatment. Undesirable effects: The most important serious adverse reactions reported in patients receiving axitinib were cardiac failure events, arterial embolic and thrombotic events, venous embolic and thrombotic events, haemorrhage (including gastrointestinal haemorrhage, cerebral haemorrhage and haemoptysis), gastrointestinal perforation and fistula formation, hypertensive crisis, and PRES. Very common (>1/10) adverse events are hypothyroidism, decreased appetite, headache, dizziness, dysgeusia, hypertension, haemorrhage (epistaxis, haematuria, haemoptysis, rectal haemorrhage, gingival bleeding, gastric haemorrhage, cerebral haemorrhage, lower gastrointestinal haemorrhage), dyspnoea, cough, rash, rash, dry skin, urticaria, QT prolonged, paresthesia, hypotension, pulmonary embolism, deep vein thrombosis, and retinal vein occlusion/thrombosis). Adverse effects should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Pfizer Medical Information on 01304616161.
Torisel (temsirolimus)

ABBREVIATED PRESCRIBING INFORMATION – RCC

Before prescribing Torisel please refer to the full Summary of Product Characteristics.

Presentation: Torisel 30 mg concentrate and diluent for solution for infusion. Each vial of Torisel concentrate contains 30 mg temsirolimus dissolved in a total volume of 1.2 ml.

Uses: First-line treatment of patients with advanced renal cell carcinoma who have at least three of six prognostic risk factors.

Dosage: 25 mg infused intravenously over a 30 to 60 minute period once weekly. To be administered under the supervision of a physician experienced in the use of antineoplastic medicinal products. Administer anti-histamine intravenously at least 30 minutes before the start of each dose of temsirolimus. Treatment should continue until the patient is no longer clinically benefiting or unacceptable toxicity occurs. Suspected adverse reactions may require temporary interruption and/or dose reduction. If dose delay is not appropriate then therapy may be reduced by 5 mg/week decrements. In elderly, renal impairment and mild to moderate hepatic impairment patients, there is no specific recommended starting dose adjustment.

Contra-indications: Hypersensitivity to temsirolimus, its metabolites, polysorbate 80 and any of the excipients.

Warnings and Precautions: Not recommended for paediatric patients. Elderly patients may be more likely to experience certain adverse reactions. Use with caution in severe renal impairment patients. Renal failure (including fatal outcomes) has been observed in patients receiving Torisel for RCC and/or with pre-existing renal insufficiency. Use caution when treating patients with hepatic impairment. An increased rate of fatal events has been observed in patients with moderate and severe hepatic impairment. The fatal events included those due to progression of disease; however a causal relationship cannot be excluded. For patients with severe hepatic impairment, the recommended dose for patients who have baseline platelets > 100 x 10⁹/l is 10 mg IV once a week. Live vaccinations should be avoided. Use carefully in patients with CNS tumours and/or those receiving anticoagulation therapy due to an increased risk of intracerebral haemorrhage. Hypersensitivity/Infusion reactions have been associated with the administration of Torisel. In all patients with severe infusion reactions, Torisel infusion should be interrupted and appropriate medical therapy administered. Use with caution in patients with known hypersensitivity to antihistamines or in those who cannot receive antihistamines. Torisel may be associated with an increase in blood glucose levels in diabetic and non-diabetic patients. This may result in the need for an increase in dose of, or initiation of, insulin and/or hypoglycaemic agent therapy. Use of Torisel is associated with increases in serum triglycerides and cholesterol. Torisel has also been associated with abnormal wound healing, so care should be taken in the peri-operative period. Patients may be immunosuppressed and should be carefully observed for the occurrence of infections, including opportunistic infections such as pneumocystis jiroveci pneumonia (PCP). For patients who require use of corticosteroids or other immunosuppressive agents, prophylaxis of PCP may be considered. Cases of non-specific interstitial pneumonitis, including fatal reports, have been reported in patients receiving weekly intravenous Torisel; empiric treatment with corticosteroids and/or antibiotics may be considered. Opportunistic infections such as PCP should be considered in the differential diagnosis. During a clinical study the combination of temsirolimus and sunitinib resulted in dose-limiting toxicity. The concomitant use of Torisel with ACE inhibitors may increase the risk of angioneurotic oedema-type reactions. Torisel contains 35% volume ethanol and this should be considered in patients suffering from alcoholism and high-risk groups, such as patients with liver disease or epilepsy.

Pregnancy and Lactation: Torisel must not be used during pregnancy. Men with partners of childbearing potential should use medically acceptable contraception while receiving Torisel. Breast-feeding should be discontinued during Torisel therapy.

Interactions: Sunitinib, ACE inhibitors, CYP3A inhibitors and inducers, amphotericin agents.

Undesirable Effects: The most serious adverse reactions observed with Torisel in clinical trials are hypersensitivity/infusion reactions (including some life-threatening and rare fatal reactions), hyperglycaemia/glucose intolerance, infections, interstitial lung disease (pneumonitis), hyperlipaemia, intracranial haemorrhage, renal failure (with fatal outcomes), intestinal perforation, wound healing complication, thrombocytopenia, neutropenia (including febrile neutropenia), pulmonary embolism. Very common adverse reactions (≥1/10) include: bacterial and viral infections, pneumonia, neutropenia, thrombocytopenia, anaemia, hyperglycaemia, hypercholesterolaemia, hypertriglyceridaemia, decreased appetite, hypokalaemia, insomnia, dysgeusia, headache, dyspnoea, epistaxis, cough, nausea, diarrhoea, stomatitis, vomiting, constipation, abdominal pain, rash, pruritus, dry Skin, arthralgia, back pain, fatigue, oedema, asthma, mucosal inflammation, pyrexia, pain, chills, chest pain and blood creatinine increased. Other common adverse reactions (≥1/100 to <1/10) include: sepsis, candidiasis, urinary tract infection, upper respiratory tract infection, pharyngitis, sinusitis, rhinitis, folliculitis, leukopaenia, lymphopaenia, hypersensitivity reactions/drug hypersensitivity, diabetes mellitus, dehydration, hypocalcaemia, hypophosphataemia, hyperlipidaemia, depression, anxiety, dizziness, paraesthesia, somnolence, ageusia, conjunctivitis, venous thromboembolism, thrombophlebitis, hypertension, interstitial lung disease (includes pneumonitis, alveolitis, alveolar allergic, pulmonary fibrosis and eosinophilic pneumonia), pleural effusion, gastrointestinal haemorrhage, gastritis, dysphagia, abdominal distension, aphthous stomatitis, oral pain, gingivitis, dermatitis, exfoliative rash, acne, nail disorder, ecchymosis, petechiae, myalgia, renal failure, increased aspartate aminotransferase, increased alanine aminotransferase.

Legal category: POM.

Package Quantities: Pack contains 2 x glass vials, 1 vial x 1.2 ml of concentrate and 1 vial x 2.2 ml of diluent.

Basic NHS Cost: £620.

Marketing Authorisation Holder: Pfizer Limited, Ramsgate Road, Ramsgate, Kent, CT11 8QI, UK.

Marketing Authorisation number(s): EU/1/07/424/001. For full prescribing information and details of other side effects see Summary of Product Characteristics. Further information is available on request from Medical Information Department at Pfizer Limited, Walton Oaks, Docking Road, Tadworth, Surrey, KT20 7NS, UK.

Date of Prescribing Information: June, 2014

Ref: TO 6_2

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Pfizer Medical Information on 01304616161.