

## **ONCOLOGY (CANCER) MANAGEMENT PROGRAMME**

If you or one of your registered beneficiaries are diagnosed with cancer, it is important to register on the oncology management programme as soon as possible. All oncology treatment requires pre-authorisation and case management.

Once the oncology management team has received your treatment plan from your doctor, your details, disease information and proposed treatment will be captured. Your treatment plan is reviewed and, if necessary, a member of the clinical team will contact your doctor to discuss more appropriate or cost-effective treatment alternatives.

After the treatment plan has been assessed and approved, an authorisation will be sent to your treating doctor. You will also be sent an authorisation letter. The letter will show the treatment authorised, the approved quantities and how long the authorisation is valid for.

Please make sure that your doctor advises the oncology management team of any change in your treatment, as your authorisation will need to be re-assessed and updated. If you fail to do so, your claims may be rejected or paid from the incorrect benefit as there will not be a matching oncology authorisation.

### **Please note:**

You will need pre-authorisation for any hospitalisation, specialised radiology (e.g. MRI scans, CT scans, angiography), stoma requirements or private nursing or hospice services.

### **How to register on the Oncology Management Programme:**

On diagnosis, your treating doctor should fax a copy of your treatment plan and a copy of the histology which confirms the cancer to **0861 004367** or email **oncologyauths@gems.gov.za**.

An oncology case manager will then take the process forward.

You may also contact the oncology management team by calling **0860 00 4367**.

### **Reasons for not funding treatment:**

When registering on the oncology management programme, the clinical pre-authorisation team reviews the treatment proposed by your doctor and compares it to what is often referred to as the "standard of care". Such standard of care refers to what most doctors in South Africa would consider prescribing for a given cancer at a certain level of its growth and/or spread. The clinical managers also assess whether there are adequate funds based on your options' benefits limits, as well as how much money may have already been used during the course of the year.

There are various reasons that all or some of the treatment schedule that is being requested by your doctor may not be supported for purposes of payment.

Common reasons include the following:

1. The treatment for which an application has been submitted is investigational. This means it has not been tested adequately in the clinical setting in which it is being requested.
2. There are less costly treatments that are likely to achieve the same clinical results.
3. Although the treatment may have some accepted clinical benefits, these are very small. If taken together with the potential toxicity of the drug, as well as the drug's significant costs, funding cannot be justified.
4. Available funds are inadequate.

If you and your doctor follow the standard pre-authorization process, you will always be informed whether the treatment planned by your doctor will be funded in your personal situation.

To assist you in your planning, we refer you to some of the common conditions and drugs where funding is limited on the basis that either cheaper treatments that are likely to be equally beneficial are available, or that the potential toxicity and cost of the drug cannot be justified in light of only very small expected clinical benefits associated with the treatment.

This approach ensures that there will be enough money to pay for effective treatments, where and if needed. Please note that other treatments not listed here may also not be reimbursed for reasons listed above.

For a summary of the most common oncology treatments where funding is limited, see below. Policies not listed here are available on request.

If your treating doctor requires further information they may contact the oncology management team by calling 0860004367 or by emailing [oncologyauths@gems.gov.za](mailto:oncologyauths@gems.gov.za)

## Oncology Policies

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A summary of the most common oncology treatments where funding is limited or excluded:

### 1. Breast Cancer

#### 1.1 *Trastuzumab (Herceptin®)*

Biological therapy e.g. trastuzumab (Herceptin®) may be used in the treatment of Human Epidermal growth factor Receptor 2-positive (HER2+) breast cancer in combination with chemotherapy (medicines to treat cancer). This type of breast cancer occurs when the cancer cells have high levels of HER2 protein, which makes the tumour cells grow more quickly. Trastuzumab binds with HER2 and stops it from stimulating the growth of cancer cells.

Trastuzumab is available as an intravenous medicine (injected into the vein) or as a subcutaneous injection (injected into the fat layer of the skin). The subcutaneous injection costs much less than the intravenous form of trastuzumab.

Trastuzumab can be used in the following stages of HER2+ breast cancer:

##### 1.1.1. **HER2-positive early breast cancer**

Trastuzumab is used to treat early breast cancer (when the cancer has spread within the breast or to the glands under the arm but not to other parts of the body) after surgery, chemotherapy (medicines to treat cancer), and radiotherapy (treatment with radiation). It can also be used earlier in treatment (before surgery), in combination with chemotherapy.

Because of its high cost, the funding of trastuzumab (Herceptin®) in patients with HER2-positive early breast cancer is limited to the 9 week treatment protocol and is subject to benefit limits. The subcutaneous form of trastuzumab may be funded.

##### 1.1.2. **HER2-positive metastatic breast cancer**

Trastuzumab is used to treat metastatic breast cancer (cancer that has spread to other parts of the body). It may be used in patients with HER2- positive disease either on its own or preferably in combination with chemotherapy. Trastuzumab (Herceptin®) treatment should be stopped when the cancer continues to grow or spread whilst on treatment with trastuzumab. Trastuzumab (Herceptin®) may be continued in patients when the cancer has continued to grow or spread within the brain, but not anywhere else in the body.

Trastuzumab (Herceptin®) may be funded for HER2-positive metastatic breast cancer up to benefit limits. The subcutaneous form of trastuzumab may be funded.

### **1.2 Bevacizumab (Avastin®)**

Bevacizumab has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, Avastin® stops it having an effect. As a result, the cancer cells cannot develop their own blood supply and are starved of oxygen and nutrients, helping to slow down the growth of tumours.

Bevacizumab (Avastin®) is used with chemotherapy for first-line treatment of patients with locally recurrent (the cancer returns to the same area of the body) or metastatic breast cancer (cancer that has spread to other parts of the body).

However, there is no evidence to show that adding bevacizumab to chemotherapy (medicines for treating cancer) will help patients to live longer or improve their quality of life. It may cause life-threatening side effects such as severe high blood pressure, bleeding, heart attack or heart failure.

Bevacizumab (Avastin®) will therefore **not** be funded for the treatment of locally recurrent or metastatic breast cancer.

### **1.3 Lapatinib (Tykerb®)**

Lapatinib (Tykerb®) is a drug that may be used in the treatment of Human Epidermal growth factor Receptor 2-positive (HER2+) breast cancer. This type of breast cancer occurs when the cancer cells have high levels of HER2 protein, which makes the tumour cells grow more quickly. Lapatinib blocks an enzyme in the HER2 receptor and stops it from stimulating the growth of cancer cells.

Lapatinib is used to treat HER2 positive breast cancer that has advanced or metastasized (grown or spread to other parts of the body) after treatment with other drugs such as trastuzumab (Herceptin®).

However, adding lapatinib to chemotherapy (medicines for treating cancer) provides minimal benefit in prolonging life compared to chemotherapy alone. It may cause serious side effects such as heart problems, severe diarrhoea, increased liver enzymes and low red blood cell count (anaemia).

Lapatinib (Tykerb®) will therefore **not** be funded for the treatment of advanced or metastatic HER2-positive breast cancer

### **1.4 Everolimus (Afinitor®)**

Everolimus (Afinitor®) is an anticancer medicine, which acts by blocking a protein called 'mammalian target of rapamycin' (mTOR). The mTOR protein is involved in the control of cell division and the growth of blood vessels, Everolimus (Afinitor®) thus prevents the division of tumour cells and reduces their blood supply. This slows down the growth and spread of the tumours.

Everolimus is used to treat advanced (has started to spread) breast cancer after failure of hormone treatment.

Everolimus treatment has not been shown to improve survival by much when added to hormone treatment. It may cause serious side effects such as lung problems, low blood counts, diarrhoea, weakness and infections.

Everolimus (Afinitor®) will therefore **not** be funded for the treatment of advanced breast cancer.

### **1.5 Ixabepilone (Ixempra®)**

Ixabepilone (Ixempra®) is expected to block the ability of cells to divide and multiply. Without this ability the cancer cells cannot divide and they eventually die. Ixabepilone is also expected to affect non-cancer cells such as nerve cells, which could cause side effects.

Ixabepilone is used for the treatment of breast cancer that is locally advanced or metastatic (has grown or spread to other parts of the body).

Ixabepilone has not been shown to improve survival when used in combination with chemotherapy compared to chemotherapy on its own.

Ixabepilone (Ixempra®) will therefore **not** be funded for the treatment of locally advanced or metastatic breast cancer, when used in combination with chemotherapy.

Ixabepilone (Ixempra®) may be funded up to benefit limit, for locally advanced or metastatic breast cancer, when it is used on its own, for the treatment of patients who have failed on most other chemotherapy options.

### **1.5 Eribulin (Halaven®)**

Eribulin (Halaven®) works by interrupting the network in the cancer cells which is essential for them to divide and multiply. Without this ability the cancer cells cannot divide and grow.

Eribulin is used in locally advanced (has started to spread within the breast) or metastatic (has started to spread to other parts of the body) breast cancer, after they have tried other therapies.

Eribulin provides minimal benefit in prolonging life and may cause serious side effects such as blood disorders and infections.

Eribulin (Halaven®) will **not** be funded for locally advanced (has started to spread within the breast) or metastatic (has started to spread to other parts of the body) breast cancer.

## 2. Non-Hodgkin's Lymphoma

**Non-Hodgkin's lymphoma is cancer that develops in the lymph system, which is a network of vessels and glands in the body.**

The lymphatic system is part of the immune system. Clear fluid called lymph flows through the lymphatic vessels and contains infection-fighting white blood cells known as lymphocytes. In non-Hodgkin's lymphoma, some lymphocytes start to multiply and collect in your glands. These lymphocytes lose their infection-fighting properties, making you more likely to get an infection. The most common symptom of non-Hodgkin's lymphoma is a painless swelling in a gland (usually in the neck, armpit or groin).

### **2.1 Rituximab (Mabthera®) maintenance**

Rituximab, is a monoclonal antibody (a type of protein), that has been designed to recognise and attach to a specific structure (called an antigen) that is found on certain cells in the body. Rituximab has been designed to target an antigen called CD20, which is present on the surface of B-lymphocytes. When rituximab attaches to the antigen, this causes cell death. This helps in lymphoma, since the cancerous B-lymphocytes are destroyed.

Rituximab may be funded, when used in combination with chemotherapy, for the treatment of non-Hodgkin's lymphoma to induce remission (first-line treatment), subject to benefit limit. However, the long-term benefit of maintenance rituximab (i.e. rituximab used on its own after first-line treatment) is not clear.

Rituximab (Mabthera®) maintenance will therefore **not** be funded for the treatment of non-Hodgkin's lymphomas, in patients who are newly diagnosed after first-line treatment or in patients who have relapsed

### **2.2 Bendamustine (Ribomustin®)**

Bendamustine (Ribomustin®) is an anticancer medicine that damages the DNA of cancer cells, which prevents them from growing and spreading. Bendamustine is also expected to affect non-cancer cells such as bone marrow (spongy tissue inside bones that makes blood cells), which may cause side-effects.

It may be used on its own for the treatment of non-Hodgkin's lymphomas, in patients, who have progressed during or within 6 months following treatment with rituximab or a rituximab containing regimen. However, there is very limited evidence for its use in this setting and no evidence to show that treatment with bendamustine will help patient's live longer than they would if they were treated with standard of care.

Bendamustine and rituximab may be used together as first-line treatment of non-Hodgkin's lymphomas. However there is no evidence that the combination of the therapies will help patient's live longer than they would if they were treated with standard of care. It has been shown to be non-inferior (no better than) standard of care in reducing the number of patients with progressive disease, and is considerably more costly.

It may also be used alone for the first-line treatment of chronic lymphocytic leukaemia (CLL). However, it has not been shown to prolong life when used to treat CLL and was associated with a greater risk of adverse events.

Bendamustine (Ribomustin®) will therefore **not** be funded for the treatment of non-Hodgkin's lymphomas (including chronic lymphocytic leukaemia).

### **2.3 Bortezomib (Velcade®)**

Bortezomib (Velcade®) blocks certain proteins within the cancer cell that are essential for the cell to survive. This results in cell death and slows the growth of the cancer.

It is used in combination with chemotherapy as first-line treatment for mantle cell lymphoma (a particular type of non-Hodgkin lymphoma), for patients who cannot have a blood stem-cell transplant (replaces a person's abnormal stem cells with healthy ones from another person). However, it has not been shown to help prolong the life of patients.

Bortezomib (Velcade®) will therefore **not** be funded for the treatment of non-Hodgkin's lymphomas (specifically mantle cell lymphoma).

## **3. Bowel Cancer (cancer of the intestine/colon and rectum)**

### **3.1 Bevacizumab (Avastin®)**

Bevacizumab (Avastin®) has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, Avastin® stops it having an effect. As a result, the cancer cells cannot develop their own blood supply and are starved of oxygen and nutrients, helping to slow down the growth of tumours.

Bevacizumab (Avastin®) is used to treat metastatic (spread to other parts of the body) bowel cancer.

However, its clinical benefit in prolonging survival is limited. It may cause serious side effects like delayed wound healing, gastrointestinal bleeding, bloody diarrhoea, abdominal pain and vomiting.

Bevacizumab (Avastin®) will therefore **not** be funded for the treatment of metastatic bowel cancer.

### **3.2 Cetuximab (Erbix®)**

Cetuximab (Erbix®) is another monoclonal antibody (type of protein), that is designed to block the epithelial growth factor receptor (EGFR), and slow cancer cell growth.

It is used to treat metastatic (spread to other areas of the body) bowel cancer. However, its clinical benefit in prolonging survival is limited. There are certain genetic markers that may be used to help predict, which patients will not respond to cetuximab treatment.

However, further research is required to show if the use of genetic markers helps to identify a group of patients where cetuximab prolongs life significantly.

Cetuximab (Erbitux®) will therefore **not** be funded for the treatment of metastatic colorectal cancer.

### **3.3 Regorafenib (Stivarga®)**

Regorafenib (Stivarga®) is a 'protein-kinase inhibitor'. It blocks several enzymes that are important for the development of a blood supply to tumours and the growth and development of cancer cells. By blocking the action of these enzymes, it helps to restrict the growth and spread of the cancer.

It is used to treat metastatic (spread to other areas of the body) bowel cancer. However, its clinical benefit in prolonging survival is minimal.

Regorafenib (Stivarga®) will therefore **not** be funded for the treatment of metastatic colorectal cancer.

## **4. Liver Cancer (hepatocellular carcinoma)**

Hepatocellular carcinoma is a primary cancer of the liver. Most cases are caused by viral infection or cirrhosis (healthy liver is replaced by scar tissue).

### **4.1 Sorafenib (Nexavar®)**

Sorafenib (Nexavar®) is a 'protein kinase inhibitor'. It blocks several enzymes that are important for the development of a blood supply to tumours and the growth and development of cancer cells. By blocking the action of these enzymes, it helps to restrict the growth and spread of the cancer.

Sorafenib (Nexavar®) is used for the treatment of advanced hepatocellular carcinoma (type of liver cancer) that cannot be surgically removed.

However, sorafenib (Nexavar®) provides minimal benefit in prolonging life.

Sorafenib (Nexavar®) will therefore **not** be funded for the treatment of advanced hepatocellular carcinoma.

## **5. Non-Small Cell Lung Cancer**

Cigarette smoking is the cause of about 90% of lung cancer cases in men and women. Other causes of lung cancer are chemicals or substances breathed in at work. The most common symptom is a persistent cough. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. There are three types, adenocarcinomas, squamous cell carcinomas and large cell carcinomas.



### **5.1 Bevacizumab (Avastin®)**

Bevacizumab (Avastin®) has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, Avastin® stops it having an effect. As a result, the cancer cells cannot develop their own blood supply and are starved of oxygen and nutrients, helping to slow down the growth of tumours.

Bevacizumab has been registered in South Africa for the treatment of patients with inoperable (not able to remove with surgery), advanced, metastatic (spread to other areas of the body) or recurrent (returns to area of diagnosis) cancer of the lung, in combination with chemotherapy.

However, its clinical benefit in prolonging survival is minimal. It may also have life-threatening side effects such as severe high blood pressure, bleeding, heart attack or heart failure.

Bevacizumab (Avastin®) will therefore **not** be funded for the treatment inoperable, advanced, metastatic or recurrent cancer of the lung.

### **5.2 Maintenance pemetrexed (Alimta®)**

Pemetrexed (Alimta®) is a cytotoxic medicine (a medicine that kills cells that are dividing, such as cancer cells). This results in the division of cancer cells being reduced, helping to slow down the growth of tumours.

Pemetrexed (Alimta®) is used to treat advanced 'non-small-cell' lung cancer in combination with cisplatin in previously untreated patients (induction). It can also be used to maintain remission in patients who have received a platinum-based chemotherapy or pemetrexed/cisplatin combination for induction.

However, there is no convincing evidence showing that maintenance treatment with pemetrexed helps to prolong life. Further studies are required to determine the optimal timing of retreatment.

Pemetrexed (Alimta®) maintenance will therefore **not** be funded for the treatment of patients with non-small cell lung cancer, who have not progressed after induction with platinum based chemotherapy or a combination of pemetrexed and cisplatin.

Pemetrexed (Alimta®) may be considered for funding as second-line treatment for those patients who have progression of disease (cancer grows or spreads) after their initial treatment.

## **6. Renal Cell Carcinoma (kidney cancer)**

It is the most common type of kidney cancer in adults. When the tumour is confined to the kidney, the 5-year survival is 60-70%. The survival is much lower when the cancer has spread beyond the kidney. Kidney cancer may be cured by removing part or the entire affected kidney.

### **6.1 Temsirolimus (Torisel®)**

Temsirolimus (Torisel®) is an anticancer medicine, which acts by blocking a protein called 'mammalian target of rapamycin' (mTOR). The mTOR protein is involved in the control of cell division and the growth of blood vessels, Temsirolimus (Torisel®) prevents the division of tumour cells and reduces their blood supply. This slows down the growth and spread of the tumours.

Temsirolimus (Torisel®) is used to treat advanced renal-cell carcinoma (a type of kidney cancer). 'Advanced' means that the cancer has started to spread.

However, it provides minimal benefit in prolonging life and is very costly. Common side effects are rash, nausea vomiting and diarrhoea, swelling, joint pain, headache, weakness and abnormal liver and kidney function results

Temsirolimus (Torisel®) will therefore **not** be funded for the treatment of renal cell carcinoma.

### **6.2 Everolimus (Afinitor®)**

Everolimus (Afinitor®) is an anticancer medicine, which acts by blocking a protein called 'mammalian target of rapamycin' (mTOR). The mTOR protein is involved in the control of cell division and the growth of blood vessels, Everolimus (Afinitor®) prevents the division of tumour cells and reduces their blood supply. This slows down the growth and spread of the tumours.

Everolimus (Afinitor®) is indicated for the treatment of metastatic (spread to other areas of the body) renal cell carcinoma (a type of kidney cancer) after failure of other targeted therapies.

However, it provides minimal benefit in prolonging life and may cause serious side effects such as lung problems, low blood counts, diarrhoea, weakness and infections.

Everolimus (Afinitor®) will therefore **not** be funded for the treatment of metastatic renal cell carcinoma.

### **6.3 Bevacizumab (Avastin®)**

Bevacizumab (Avastin®) has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, Avastin® stops it having an effect. As a result, the cancer cells cannot develop their own blood supply and are starved of oxygen and nutrients, helping to slow down the growth of tumours.

Bevacizumab (Avastin®), is used to treat advanced or metastatic (spread to other areas of the body) kidney cancer, in combination with interferon alfa-2a.

However, it provides minimal benefit in prolonging life and may be associated with life-threatening side-effects such as high blood pressure, bleeding, heart attack or heart failure.

Bevacizumab (Avastin®) will therefore **not** be funded for the treatment of advanced or metastatic renal cell carcinoma.

## 7. Gastric (Stomach) Cancer

### 7.1 *Trastuzumab (Herceptin®)*

Some stomach cancers are stimulated by a type of protein called **Human Epidermal growth factor Receptor 2 (HER2)**. Trastuzumab works by blocking the effects of this protein. This doesn't cure stomach cancer, but it can slow its growth and increase survival time.

Due to its high cost and minimal survival benefit, trastuzumab in combination with chemotherapy is not funded for the treatment of advanced or metastatic HER2positive gastric or gastro-oesophageal junction cancer.

Trastuzumab (Herceptin®) will therefore **not** be funded for the treatment of advanced or metastatic HER2positive gastric or gastro-oesophageal junction cancer.

## 8. Brain Tumours

Surgery is recommended for most patients with brain tumours. After surgery, treatment with radiotherapy (treatment with radiation) and/or chemotherapy (medicine to treat cancer) may be recommended.

### 8.1 *Carmustine Wafers (Gliadel®)*

Carmustine wafers are placed in the brain during surgery. Carmustine is a medicine that stops or slows down tumour cell growth. However, carmustine wafers (Gliadel®) offer minimal benefit in prolonging life in patients with newly diagnosed high grade brain tumours. They have also not been shown to prolong life when the cancer returns.

Carmustine wafers (Gliadel®) will therefore **not** be funded for the treatment of newly diagnosed high grade brain tumours or for recurrent brain tumours.

### 8.2 *Temozolomide (e.g. Temodal®, Temintas®, Accord-temozolomide®)*

Temozolomide is an anticancer medicine that stops cancer cells dividing and slows tumour growth. It is given in tablet form.

Funding of temozolomide (for up to 6 months) along with radiotherapy (treatment with radiation) may be considered in patients with newly diagnosed Grade IV brain tumours if they are:

- Less than 60 years of age
- And have good functional status
- And most of the tumour has been removed during surgery

Maintenance therapy with temozolomide, beyond the initial 6 months therapy, is not supported

## 9. Head and Neck Cancer

Head and neck cancer is cancer that starts in the [lip](#), mouth, inside the nose, [sinuses](#), [pharynx](#), [larynx](#) or [parotid glands](#). It is strongly associated with certain environmental and lifestyle risk factors, including [tobacco smoking](#) and [alcohol](#) consumption, and [viruses](#), such as [human papillomavirus](#) (HPV).

Surgery and radiation therapy are most commonly used to treat head and neck cancer.

Chemotherapy:

### 9.1 Cetuximab (Erbix<sup>®</sup>)

Cetuximab (Erbix<sup>®</sup>) is another monoclonal antibody (type of protein), that is designed to block the epithelial growth factor receptor (EGFR), and slow cancer cell growth. It has been registered for the treatment of locally advanced (has started to spread to surrounding parts of the body) or metastatic (spread to other parts of the body) head and neck cancer.

However, it provides minimal benefit in prolonging life and its cost is high.

Cetuximab (Erbix<sup>®</sup>) will therefore **not** be funded for the treatment of locally advanced or metastatic head and neck cancer.

## 10. Melanoma (skin cancer)

Melanoma is the most dangerous type of skin cancer and is the leading cause of death from skin disease. If diagnosed at an early stage melanoma has a very high cure rate. Treatment includes surgical removal of the tumour. Once melanomas have recurred or spread to other parts of the body, treatment includes chemo- and immunotherapy, or radiation therapy.

### 10.1 Interferon alfa-2b (e.g. Intron A<sup>®</sup>)

Interferon alfa-2b belongs to the group 'interferons'. Interferons are natural substances produced by the body to help it fight against attacks (for example infections caused by viruses). The exact way that they work in cancer is not fully understood, but it is thought that they act as immunomodulators (substances that modify how the immune system works).

Interferon alfa-2b is registered in South Africa for the treatment of patients with malignant melanoma (a type of skin cancer affecting cells called melanocytes). It is used after surgery in patients whose melanoma could come back.

Interferon alfa-2b has been shown to increase the period of time between surgery and the cancer returning, but it remains uncertain whether treatment with interferon alfa-2b prolongs life. It may also cause severe side-effects, for example severe flu-like symptoms (fever; shaking chills; pain; tiredness; weakness).

Interferon alfa-2b (e.g. Intron A®) will therefore **not** be funded for the treatment of malignant melanoma.

### **10.2 Ipilimumab (Yervoy®)**

Ipilimumab is a 'monoclonal antibody' (a type of protein) that has been designed to recognise and attach to a specific structure (called an antigen) that is found in certain cells in the body. Ipilimumab blocks a particular protein in the body, which leads to the activation of T-cells (a type of white blood cell). The T-cells attack the tumours cells leading to their death.

Ipilimumab is registered in South Africa for the treatment of advanced (begun to spread to other areas of the body) malignant melanoma (a type of skin cancer affecting cells called melanocytes).

However, only a small number of patients respond to treatment with ipilimumab and the cost of treatment is high (close to one million rand). Treatment with ipilimumab is also associated with various severe side effects (e.g. gastrointestinal bleeding; severe diarrhoea; colitis (inflammation of the lining of the colon) requiring treatment; a life threatening skin condition (toxic epidermal necrolysis) and severe neuropathy (nerve damage).

The funding of ipilimumab for the treatment of malignant melanoma is not supported due to its limited clinical benefit; severe side effect profile and very high cost (close to one million rand).

### **10.3 Vemurafenib (Zelboraf®)**

Vemurafenib is a targeted therapy; it is a 'protein-kinase inhibitor'. It blocks specific enzymes, which reduces the growth and spread of the cancer.

Vemurafenib is a high cost chemotherapy (medicines to treat cancer) used for skin cancer that has spread to other parts of the body (metastatic) or for advanced disease that is unresectable (cannot be removed with surgery).

Vemurafenib provides minimal benefit in prolonging life when compared to standard of care and is also associated with serious side effects.

Vemurafenib (Zelboraf®) will therefore **not** be funded for the treatment of skin cancer.

## 11. Gynaecological Cancers

Gynaecological cancers are uncontrolled growth and spread of cancer cells involving the reproductive organs of the female. This may be limited to certain areas such as the ovaries or the cervix for example or spread to more than one area.

### **11.1 Ovarian Cancer**

Ovarian cancer is a malignant growth arising from the ovary. Symptoms are frequently very vague early on and may include bloating, pelvic pain, difficulty eating and frequent urination, and are easily confused with other illnesses. Ovarian cancer is often only diagnosed at an advanced stage as symptoms of the disease are non-specific.

#### **11.1 .1 Trabectedin (Yondelis®)**

Trabectedin is a chemotherapy drug that stops cancer cells from growing and multiplying.

It is registered in South Africa for use in patients with ovarian cancer (cancer of the ovaries) that has relapsed (come back after previous treatment) in combination with another chemotherapy drug.

However, its clinical benefit in prolonging life is minimal and it is associated with severe side effects, including an increased risk of infection, low red blood cell count (anaemia), nausea, vomiting and liver damage.

Trabectedin (Yondelis®) will therefore **not** be funded for the treatment of relapsed ovarian cancer.

#### **11.1.2 Bevacizumab (Avastin®)**

Bevacizumab (Avastin®) has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, Avastin® stops it having an effect. As a result, the cancer cells cannot develop their own blood supply and are starved of oxygen and nutrients, helping to slow down the growth of tumours.

It is registered in Europe and the USA for use in patients with ovarian cancer (cancer of the ovaries) that has relapsed (come back after previous treatment).

However, its clinical benefit in prolonging life is minimal and it may cause life-threatening side effects such as severe high blood pressure, bleeding, heart attack or heart failure.

Bevacizumab (Avastin®) will therefore **not** be funded for the treatment of relapsed ovarian cancer.

## 11.2 Cervical Cancer

Cervical cancer occurs when there is a growth of abnormal cells in the uterus or in the cervix of the female body. Early stages of cervical cancer may not cause symptoms. Symptoms for more advanced (has spread) disease may include abnormal or irregular vaginal bleeding or abnormal vaginal discharge.

### 11.2.1. Bevacizumab (Avastin®)

Bevacizumab has been designed to attach to vascular endothelial growth factor (VEGF), a protein that circulates in the blood and makes blood vessels grow. By attaching to VEGF, Avastin® stops it having an effect. As a result, the cancer cells cannot develop their own blood supply and are starved of oxygen and nutrients, helping to slow down the growth of tumours.

It is registered for use with chemotherapy (medicine to treat cancer) for the treatment of persistent, recurrent (the cancer returns to the same area of the body) or metastatic (cancer that has spread to other parts of the body) cancer of the cervix.

However, its clinical benefit in prolonging survival is minimal. It may also have life-threatening side effects such as severe high blood pressure, bleeding, heart attack or heart failure.

Bevacizumab (Avastin®) will therefore **not** be funded for the treatment of locally recurrent or metastatic (has spread to other parts) cervical cancer.

## 12. Prostate Cancer

Prostate cancer is a form of cancer that develops in the prostate, a gland in the male reproductive system. Although it is one of the most common types of cancer in men, many never have symptoms, undergo no treatment, and eventually die of other causes. This is because cancer of the prostate is, in most cases, slow-growing, symptom-free, and since men with the condition are older, they often die of causes unrelated to the prostate cancer, such as heart/circulatory disease, pneumonia, other unconnected cancers, or old age.

However, some cases of prostate cancer can be aggressive. Prostate cancer can spread to other parts of the body, particularly the bones. Many factors, including genetics and diet, have been implicated in the development of prostate cancer. The presence of prostate cancer may be indicated by symptoms, physical examination, prostate-specific antigen (PSA) or biopsy. The PSA test increases cancer detection but does not result in less men dying from prostate cancer.

Treatment for prostate cancer may involve monitoring for tumour progression or symptoms, surgery (i.e. radical prostatectomy), radiation therapy, oral and or intravenous chemotherapy, hormonal therapy, or combination treatment.

### **12.1 Cabazitaxel (Jevtana®)**

Cabazitaxel is an anticancer medicine that works by blocking the ability of cancer cells to divide and multiply. Cabazitaxel may also affect non-cancer cells, such as blood and nerve cells, which can cause side effects.

Cabazitaxel is used when the prostate cancer has spread to other parts of the body (metastatic) and has stopped responding to hormonal treatment (hormone-refractory). It is used in combination with prednisone or prednisolone (anti-inflammatory medicines) in patients who have previously been treated with docetaxel (another cancer medicine). Men with metastatic castration-resistant (cancer that keeps growing even when testosterone levels in the body have been reduced to very low levels) prostate cancer are usually treated with docetaxel plus prednisone. No treatments have been approved for patients with disease progression after these treatments.

In clinical trials the survival benefit in patients receiving cabazitaxel was minimal and the side effects were severe (blood in urine, difficulty in breathing, diarrhoea, nausea, vomiting, gastrointestinal bleeding, and anaemia (low red blood cell count).

Cabazitaxel (Jovani®) will therefore **not** be funded for the treatment of hormone refractory, metastatic, castration resistant prostate cancer.

### **12.2 Abiraterone (Zytiga®)**

Abiraterone blocks the production of testosterone. Because the cancer needs a supply of testosterone to survive and grow, by reducing the production of testosterone, abiraterone acetate may slow the growth of the prostate cancer. It is given in tablet form.

It may be used to treat metastatic (spread to other areas of the body) prostate cancer which has continued to progress even when male hormone levels in the body have been reduced to low levels either before or after treating with chemotherapy.

While it has been shown to improve survival by more than 3 months when compared to placebo, the cost of the drug is very high and as a result funding is not recommended.

Abiraterone (Zytiga®) will therefore **not** be funded for the treatment of hormone refractory, metastatic, castration resistant prostate cancer before or after chemotherapy.

### **12.3 Enzalutamide (Xtandi®)**

Enzalutamide blocks androgen (a type of hormone) from binding to the receptors on the prostate cancer cells. By blocking the androgen, the growth of the cells are slowed down.

It may be used to treat metastatic (spread to other areas of the body) prostate cancer which has continued to progress even when male hormone levels in the body have been



reduced to low levels after treating with chemotherapy and surgery is not possible (castration).

While it has been shown to improve survival by more than 3 months when compared to placebo, the cost of the drug is very high and as a result funding is not recommended.

Enzalutamide (Xtandi<sup>®</sup>) will therefore **not** be funded for the treatment metastatic, castration-resistant prostate cancer after chemotherapy.

#### **12.4 Lutetium-177 - PSMA (e.g. Lu-177-PSMA) (Section 21)**

Lutetium-177-PSMA is a radioactive treatment (molecule that emits radiation) and targets particular cancer cells in the body. It acts by directly targeting the cancer cells and prevents them from growing.

There is no evidence showing improved survival using lutetium-177-PSMA over standard therapy. It is a very costly agent for which there is no long term safety evidence either.

Lutetium-177-PSMA is considered a high cost, experimental therapy (benefit not proven) and is not registered in South Africa for prostate cancer.

Lutetium-177-PSMA will therefore **not** be funded for the treatment of prostate cancer.

#### **12.5 Radium-223 dichloride (Xofigo<sup>®</sup>)**

Radium-223 dichloride is a radioactive treatment (molecule that emits radiation) and targets particular cancer cells. It is used for prostate cancer where the cancer has spread to the bone and surgery is not possible.

Radium-223-dichloride has shown minimal benefit in prolonging life and is very costly. Treatment with radium-223 dichloride may affect the bone marrow (spongy tissue inside bones that makes blood cells), which may cause serious side-effects.

Radium-223-dichloride will therefore **not** be funded for the treatment of prostate cancer where surgery is not possible.

### **13. Soft-tissue Sarcoma**

Soft-tissue sarcomas are relatively uncommon cancers. They account for less than 1% of all new cancer cases each year. In their early stages, soft-tissue sarcomas usually do not cause symptoms. Because soft tissue is relatively elastic, tumours can grow rather large, pushing aside normal tissue, before they are felt or cause any problems. The first noticeable symptom is usually a painless lump or swelling. As the tumour grows, it may cause other symptoms, such as pain or soreness, as it presses against nearby nerves and muscles.

### **13.1 Trabectedin (Yondelis®)**

Trabectedin is a chemotherapy drug that stops the cancer cells from growing and multiplying.

It is registered in South Africa for the treatment of advanced soft-tissue sarcoma, a type of cancer that develops from the soft, supporting tissues of the body. 'Advanced' means that the cancer has started to spread. Trabectedin is used when treatment with other cancer medicines have stopped working, or in patients who cannot be given these medicines

However, its clinical benefit in prolonging life is minimal and it is associated with severe side effects, including an increased risk of infection, low red blood cell count (anaemia), nausea, vomiting and liver damage.

Trabectedin (Yondelis®) will therefore **not** be funded for the treatment of advanced soft-tissue sarcoma.

### **13.2 Pazopanib (Votrient®)**

Pazopanib (Votrient®) is a targeted therapy; it is a 'protein-kinase inhibitor'. It blocks specific enzymes, which reduces the growth and spread of the cancer.

Pazopanib is used to treat certain forms of soft-tissue sarcoma, a type of cancer that develops from the soft, supporting tissues of the body. It is used in patients who have been previously treated with chemotherapy (medicines to treat cancer) because their cancer had spread, or in patients whose cancer has progressed within 12 months of the anticancer medicine they received before or after surgery.

However, its clinical benefit in prolonging life is minimal and it has not been shown to improve patients' quality of life.

Pazopanib (Votrient®) will therefore **not** be funded for the treatment of previously treated advanced soft-tissue sarcoma.

## **14. Gastrointestinal stromal tumours (GIST)**

Gastrointestinal stromal tumours are a type of cancer that occurs in the tissue of the digestive tract. Chemotherapy (medicine to treat the cancer) is recommended when the cancer has spread from the digestive tract to other parts of the body.

### **14.1. Imatinib (Gleevec®)**

Imatinib (Gleevec®) is a targeted therapy; it is a 'protein-kinase inhibitor'. It blocks specific enzymes, which reduces the growth and spread of the cancer.

Imatinib is used to treat Kit-receptor positive stomach or bowel cancers. It may be given after the tumour is removed with surgery but there is a high risk of it coming back or when the cancer has spread to other parts of the body (metastatic).

Imatinib (Gleevec<sup>®</sup>) may be funded for gastrointestinal stromal tumors where there is a high-risk of the disease recurring or advanced disease that is unresectable (cannot be removed with surgery).

#### **14.2. Sunitinib (Sutent<sup>®</sup>)**

Sunitinib (Sutent<sup>®</sup>) is a targeted therapy; it is a 'protein-kinase inhibitor'. It blocks specific enzymes, which reduces the growth and spread of the cancer.

Sunitinib is used for the treatment of gastrointestinal stromal tumours where the tumour cannot be removed using surgery and after treatment with imatinib has failed. It may cause serious side effects such as heart and thyroid problems, which will require monitoring.

Sunitinib (Sutent<sup>®</sup>) may be funded up to benefit limit, as second-line treatment of unresectable (not able to be surgically removed) and / or metastatic gastrointestinal stromal tumors where imatinib has failed.

#### **14.3 Regorafenib (Stivarga<sup>®</sup>)**

Regorafenib (Stivarga<sup>®</sup>) is a targeted therapy; it is a 'protein-kinase inhibitor'. It blocks specific enzymes, which reduces the growth and spread of the cancer.

Regorafenib is used in advanced (has started to spread) gastrointestinal stromal tumors where first-line imatinib and second-line sunitinib have both failed. However, it provides minimal benefit in prolonging life and is very costly. It is also associated with severe side effects, such as infections, low red blood cell count (anaemia), liver damage and bleeding.

Regorafenib (Stivarga<sup>®</sup>) will therefore **not** be funded for the treatment of unresectable and / or metastatic gastrointestinal stromal tumors.

### **15. Myelodysplastic Syndromes (MDS)**

Myelodysplastic syndromes (MDS) are a rare group of disorders that affect the ability of the body to make healthy blood cells. This means people with MDS may be at risk of infection, low red blood cell count (anaemia) and bleeding. Some patients may require frequent platelet transfusions, or a blood stem-cell transplant (replaces a person's abnormal stem cells with healthy ones from another person) or even chemotherapy (medicines for treating cancer).

MDS can develop as a result of previous medication (treatment-related MDS) particularly those used to treat other cancers.

### **15.1. Azacitidine (Vidaza®)**

Azacitidine (Vidaza®) is a chemotherapy (medicines for treating cancer) that targets the abnormal blood cells that do not work properly. It is registered for certain types of MDS.

In patients who are not able to have a blood stem-cell transplant (replaces a person's abnormal stem cells with healthy ones from another person), azacitidine has been shown to improve survival; however, its use in clinical practice is complicated by the lack of a marker that may predict which patients respond to azacitidine, the fact that it has not been shown to improve patient quality of life, and its high cost. There is insufficient benefit to cover the total cost of treatment.

In patients who can have a blood stem-cell transplant (replaces a person's abnormal stem cells with healthy ones from another person), there is no evidence to show that using azacitidine prior to transplant will help patients to live longer or improve their quality of life.

There is also no evidence to show that using azacitidine in those who have developed MDS as a result of other medication (treatment-related MDS) will help patients to live longer or improve their quality of life.

Azacitidine (Vidaza®) will therefore **not** be funded for the treatment of MDS.

### **15.2. Lenalidomide (Revlimid®)**

Lenalidomide (Revlimid®) is an oral chemotherapy (medicines for treating cancer) that works by slowing down the growth of the cancer cells. It is also used to treat patients with certain types of MDS and low red blood cell count (anaemia), where patients would normally need frequent transfusions (replacement of blood and platelets).

Lenalidomide has been shown to reduce patients need for transfusions, but its effect on survival remains uncertain. It may cause serious side effects such as severe bleeding, severe blood disorders and could lead to other cancers as well. There will not be enough benefit to cover the total cost of lenalidomide treatment.

Lenalidomide will therefore **not** be funded for the treatment of patients with transfusion-dependent, low- or -intermediate-1 risk (IPSS), del5(q) myelodysplastic syndrome, with or without additional cytogenetic abnormalities

## **16. Acute Myeloid Leukaemia (AML)**

Acute myeloid leukaemia (AML) is a cancer of the blood whereby a certain component of the blood is affected. White blood cells start to grow rapidly and accumulates (collects) in the bone marrow. This then affects the production of normal blood cells.

### **16.1. Azacitidine (Vidaza®)**

Azacitidine (Vidaza®) is a chemotherapy (medicine for treating cancer) that targets the abnormal blood cells that do not work properly. This helps the bone marrow to grow normal blood cells. Azacitidine is a high-cost treatment used for a group of blood

disorders such as low red blood cell count (anaemia) not responding to treatment (refractory).

It is not registered in South Africa for AML and there is no evidence to show that using azacitidine in AML will help patients to live longer or improve their quality of life.

Azacitidine (Vidaza®) will therefore **not** be funded for the treatment of AML.

### **16.2. Decitabine (Dacogen®)**

Decitabine (Dacogen®) is a chemotherapy (medicines for treating cancer) that targets the abnormal blood cells that do not work properly. This helps the bone marrow to then grow normal blood cells.

Decitabine has been registered in South Africa for the treatment of AML in patients 65 years old or older. Decitabine is very costly and the benefit in prolonging life or improving the quality of life is still unclear.

Decitabine (Dacogen®) will therefore **not** be funded for the treatment of AML.

## **17. Multiple Myeloma**

Multiple myeloma is a condition whereby a type of white blood cells (plasma cells) abnormally starts to increase in amount by continuously making new cells. This can lead to bone destruction and bone marrow failure. It in severe cases it can lead to organ damage.

### **17.1. Bendamustine (Ribomustin®)**

Bendamustine (Ribomustin®) is an anticancer medicine that damages the DNA of cancer cells, which prevents them from growing and spreading. Bendamustine is also expected to affect non-cancer cells such as bone marrow (spongy tissue inside bones that makes blood cells), which may cause side-effects.

It has been registered in South Africa for the treatment of multiple myeloma, and should be used with prednisone (an oral steroid medication). It has shown to improve the quality of life in patients, but it has not been shown to help prolong the life of patients.

Bendamustine will therefore **not** be funded for the treatment of multiple myeloma.

### **17.2 Lenalidomide (Revlimid®)**

Lenalidomide (Revlimid®) is an oral chemotherapy (medicines for treating cancer) that works by slowing down the growth of the cancer cells.

Lenalidomide is registered in South Africa for the treatment of multiple myeloma after at least one other therapy has been tried. It has not been proven to be better than other therapies that may be used for multiple myeloma. It may also cause serious side effects such as severe bleeding, severe blood disorders and could lead to other cancers as well.

Lenalidomide will therefore **not** be funded for multiple myeloma.

## **18. Neuroendocrine Gastro-entero-pancreatic Cancer**

Neuroendocrine tumors occur from cells in the endocrine (hormone) and nervous systems, and may therefore occur in many different parts of the body. They may cause over production of hormones with related symptoms (e.g. diarrhea).

### **18.1. Everolimus (Afinitor®)**

Everolimus (Afinitor®) is an anticancer medicine that blocks the production of the protein needed for the growth and survival of the tumor cells.

It is used in the treatment of advanced (has spread) neuroendocrine cancers where the cancer originally started in the pancreas.

However, it provides minimal benefit in prolonging life and may cause serious side effects such as lung problems, low blood counts, diarrhoea, weakness and infections.

Everolimus (Afinitor®) will therefore **not** be funded for the treatment of advanced neuroendocrine gastro-entero-pancreatic cancer.

### **18.2. Lutetium-177-Dotatate (Section 21)**

Lutetium-177-Dotatate is a type of peptide receptor radionuclide therapy (PRRT). It consists of lutetium-177, a radioactive isotope or radionuclide, attached to a somatostatin analogue, which allows radiotherapy to be delivered to targeted cancer cells.

It is not registered for use in South Africa; therefore it requires special approval for each patient to be used locally.

In patients with neuroendocrine tumours of the mid-gut, it has been shown to reduce the number of patients experiencing progression of their disease, but there is no evidence showing it prolongs life. There is no evidence to show it improves disease progression or prolongs life in patients with neuroendocrine tumours of the pancreas.

It may cause serious adverse events, such as secondary cancers and delayed renal toxicity.

Lutetium-177-Dotatate will therefore **not** be funded for the treatment of advanced neuroendocrine gastro-entero-pancreatic cancer.