Cancer Association of South Africa (CANSA)

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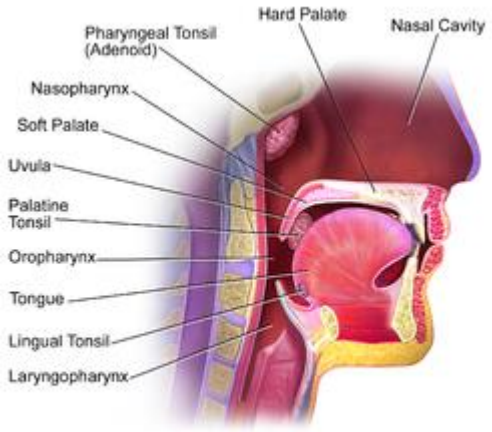
Fact Sheet on Cancer of the Tonsils

Introduction

Tonsils are collections of lymphoid tissue facing into the aerodigestive tract. The set of lymphatic tissue known as Waldeyer's tonsillar ring includes the adenoid tonsil, two tubal tonsils, two palatine tonsils, and the lingual tonsil.

[Picture Credit: Tonsils and Throat]



Tonsils and Throat

When used unqualified, the term most commonly refers specifically to the palatine tonsils, which are masses of lymphatic material situated at either side at the back of the human throat. The palatine tonsils and the nasopharyngeal tonsil are lymphoepithelial tissues located near the oropharynx and nasopharynx (parts of the throat).
(Wikipedia).

Tonsils are part of the lymphatic system and protect the body from harmful germs and contaminants. They lie strategically, just behind the mouth and nose, and form the first station of defense against all ingested and inhaled pollutants. The loose pieces of hanging tissue located on either side of the throat are called palatine tonsils. Those that lie within the throat, near the posterior opening of the nasal cavity are the adenoids, or pharyngeal tonsils. The paired structured that lie at the base of the tongue are called lingual tonsils.

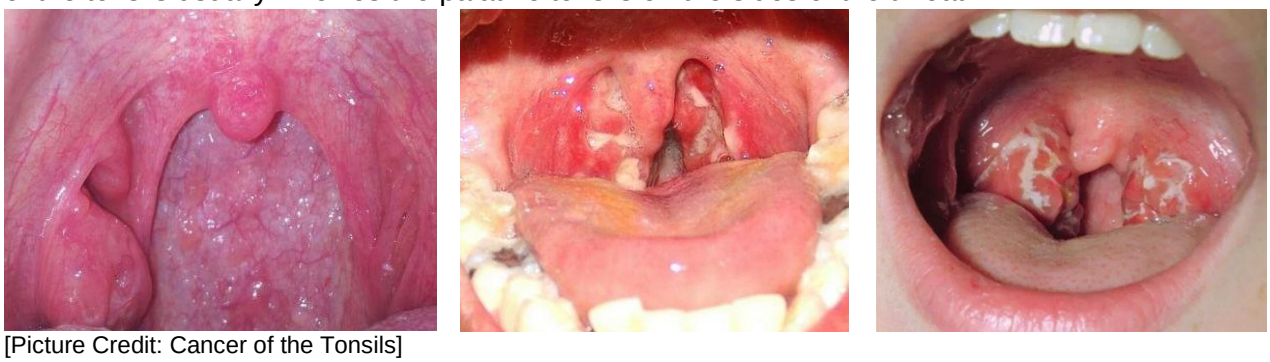
Provide Immunity - tonsils function to trap bacteria and antigens and allow the body to produce antibodies against them. The primary function of the tonsils is to provide local immunity. They trap viruses, bacteria and other infectious contaminants and hold on to them before the immune system goes in for the kill.

Process Lymphatic Fluid - tonsils process lymphatic or lymph fluid in unison with other lymphoid tissue. Lymph fluid is circulated in the tissues of the lymphatic system. The lymphatic system functions to remove interstitial fluid from tissues and adjacent organs, to absorb fatty acids and transport them into the circulatory system, and to transport immune cells to and from lymph nodes. Lymph fluid contains fats, proteins and lymphocytes, which

are a type of white blood cells. It plays a primary role in filtering and destroying germs and toxins.

Produce Antibodies - tonsils produce antibodies that neutralise respiratory infections (e.g. pneumonia, bronchitis, ear infections, laryngitis, sinusitis and rhinitis) that enter through the throat, mouth or nose. Antibodies (or immunoglobulins) are proteins that are found in the blood and other bodily fluids. They are produced by various components of the body's immune system and provide protection against chemicals, viruses, parasites, fungi and bacteria. They produce specific antibodies against staphylococcus aureus, haemophilus influenzae, streptococcus pneumoniae, poliovirus and diphtheria toxoid.
(eHow).

Cancer of the Tonsils
Cancer of the Tonsils occurs when there is uncontrolled division of the tonsillar cells. Cancer of the tonsils usually involves the palatine tonsils on the sides of the throat.



[Picture Credit: Cancer of the Tonsils]

Most tonsil cancers are squamous cell carcinomas but some are lymphomas.
(Cedars-Sinai).

Incidence of Cancer of the |Tonsils in South Africa
The National Cancer Registry (2012) does not provide any information regarding the incidence of cancer of the tonsils.

Signs and Symptoms of Cancer of the Tonsils
Patients with cancer of the tonsils may have one or more of the following symptoms:

- A sore in the back of the mouth that will not heal
- One tonsil is larger on one side
- Blood in the saliva
- Mouth pain
- Difficulty chewing, swallowing or speaking
- Persistent sore throat
- Intolerance to eating or drinking citrus foods
- Sever ear pain
- A lump in the neck
- A pain in the neck
- Pain when swallowing (dysphagia)

- Bad breath

(Cancer Treatment Centers of America; Cedars-Sinai).

Causes and Risk Factors for Cancer of the Tonsils

Men are diagnosed with tonsil cancer three to four times more often than women. Cancer of the tonsils are diagnosed at age 50 or older, although it can develop at any age. The most significant risk factors for tonsil cancers are:

- Tobacco use
- Smokeless tobacco (snuff and betel nut) use
- Alcohol consumption

Other potential causes include people with certain infections or decreased immunity such as:

- Exposure to human papilloma virus (HPV), especially strains 16 and 18
- Organ transplant recipients
- People with Human Immunodeficiency Virus (HIV) disease

(Cancer Research UK; Cedars-Sinai).

Staging of Cancer of the Tonsils

The TNM classifications for oropharyngeal and hypopharyngeal cancers are provided below, along with histologic grades and anatomic stages.

Primary tumour (T)	
Oropharynx:	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour =2cm in greatest dimension
T2	Tumour >2cm but not more than 4cm in greatest dimension
T3	Tumour >4cm in greatest dimension or extension to lingual surface of the epiglottis
T4a	Moderately advanced, local disease Tumour invades the larynx, deep/extrinsic muscle of the tongue, medial pterygoid, hard palate, or mandible
T4b	Very advanced, local disease Tumour invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases the carotid artery
Hypopharynx:	

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
T1	Tumour limited to 1 subsite of the hypopharynx and/or =2cm in greatest dimension
T2	Tumour invades more than 1 subsite of the hypopharynx or an adjacent site or measures >2cm but not more than 4cm in greatest dimension, without fixation of the hemilarynx
T3	Tumour >4cm in greatest dimension or with fixation of the hemilarynx or extension to the oesophagus
T4a	Moderately advanced, local disease Tumour invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue (including prelaryngeal strap muscles and subcutaneous fat)
T4b	Very advanced, local disease Tumour invades prevertebral fascia, encases carotid artery, or involves mediastinal structures
Regional lymph nodes (N)	
NX	Regional nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node =3cm in greatest dimension
N2	Metastasis in a single ipsilateral lymph node >3cm but not more than 6cm in greatest dimension; or in multiple ipsilateral lymph nodes, none >6cm in greatest dimension; or in bilateral or contralateral lymph nodes, none >6cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3cm but not more than 6cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none >6cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none >6cm in greatest dimension
N3	Metastasis in a lymph node >6cm in greatest dimension
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

Histologic grade:

Histologic grade (G)	
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

Anatomic stage/prognostic groups:

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3 T4a	N2 N2	M0 M0
IVB	T Any	N3	M0
	T4b	N Any	M0
IVC	T Any	N Any	M1

(Medscape).

Treatment of Cancer of the Tonsils

Patients may have either surgery or radiotherapy to treat early tonsil cancer. Early means a small tumour that is still contained within the tonsil. If one has a cancer that is larger, has grown throughout the tonsil, or has started to grow outside it, one may have surgery followed by radiotherapy. More advanced cancers that have grown outside the tonsil may need shrinking before they can be removed. One may have chemotherapy or radiotherapy or both to try to shrink the cancer. This is called down staging. If the cancer does shrink, one may then be able to have an operation to remove it.

Advanced cancers cause symptoms such as pain, bleeding and difficulty swallowing. Patients are given radiotherapy or chemotherapy or both to help control symptoms.

There are other experimental treatments being investigated, for example, photodynamic therapy (PDT). For this treatment, patients have to take a drug that concentrates in the cancer cells. The drug is harmless until a bright light is shone onto the cancer cells. This then kills the cells.

Treatment depends on how far the cancer has grown.

The first step is to find out:

- How far the cancer has grown into local tissues
- Whether it has spread to nearby lymph glands
- Whether it has spread to any other part of the body

This is called staging the cancer. The doctor will be able to tell which treatment is best once the cancer has been staged.

A common treatment for tonsil cancer involves using radiation therapy in combination with chemotherapy.

Surgery – the patient may be able to have an operation to remove the part of the throat that contains the cancer. There are different types of operation. The part of the throat removed depends on the exact site of the tumour. If the cancer is very small, the patient may only need a very simple operation. This can be done using local anaesthetic or with laser surgery, and overnight stay in the hospital.

For larger more extensive cancers one may need a more complicated operation and need to stay in hospital for a while. For the most complicated surgery, one may have to have part of the soft palate or the back of the tongue removed. The surgeon will rebuild this with tissue taken from another part of the body.

All types of treatments have side effects. Sometimes surgery to the throat causes a lot of swelling in the area and makes it difficult to breathe normally. If this is the case then the surgeon may need to make a hole in the patient's windpipe, at the base of the neck. This hole is called a tracheostomy and will allow the patient to breathe while the swelling is there. It is usually only temporary and will be removed once the wound has healed.

Some operations on the throat can affect speech. We take it for granted that it is easy to speak, but it is actually a very complicated process. To produce sound humans use their throat, soft palate, lips, nose, mouth and tongue. If one has surgery to any of these, speech may change. This may not be very noticeable and may only be temporary. But sometimes the change is permanent. If a patient has any speech difficulties at all, a speech and language therapist can help you manage.

Radiotherapy – patients may have radiotherapy:

- On its own to treat a small tonsil cancer
- Either before or after surgery to treat a larger cancer
- To help relieve the symptoms of advanced tonsil cancer

Doctors may use both external radiotherapy and internal radiotherapy (brachytherapy) to treat tonsil cancer. External radiotherapy treatment is usually given once a day for a few weeks. Brachytherapy is most likely to be used for small cancers. Patients may have

brachytherapy if the cancer has come back after earlier treatment with external beam radiotherapy.

There are several types of radiation used in radiation therapy such as :

- High-energy X-rays
- Electron beams
- Radioactive isotopes

Chemotherapy - chemotherapy uses anti-cancer (cytotoxic) drugs to destroy cancer. Chemotherapy has not always been a treatment of choice for tonsil cancer. But recent research has suggested that combining chemotherapy with radiotherapy may help as much as surgery for large cancers of the head and neck, including tonsil cancer. Further research is needed in this area.

If one has tonsil cancer, one may have chemotherapy before the main treatment to help shrink the cancer. This is called neo adjuvant treatment. When a cancer is shrunk before further treatment, this is called down staging. The drugs most commonly used to treat cancer of the tonsil are

- Fluorouracil
- Cisplatin

It has been found that using these 2 drugs together is more effective in shrinking the cancer than using one of them alone. Other chemotherapy drugs and combinations have been tested but none has yet produced results as good as cisplatin and fluorouracil.
(Cancer Research UK; Cancer Treatment Centers of America; Tonsil Cure).

About Clinical Trials

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials

Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have

had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including
other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different "phase" in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.
In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or "control" interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial

might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.
Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.
The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific condition or situation. Readers of this document should seek appropriate medical advice prior to taking or refraining from taking any action resulting from the contents of this Fact Sheet. As far as permissible by South African law, the Cancer Association of South Africa (CASNA) accepts no responsibility or liability to any person (or his/her dependants/estate/heirs) as a result of using any information contained in this Fact Sheet.

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