Cancer Association of South Africa (CANSA)

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Fact Sheet on Garlic Use to Reduce the Risk of Cancer

Introduction

Allium sativum, commonly known as garlic, is a species in the onion genus, Allium.

[Picture Credit: Garlic]

Its close relatives include the onion, shallot, leek, chive and rakkyo (*Allium chinense,* commonly known as, Chinese onion, Chinese scallion, Japanese scallion, Kiangsi scallion, and Oriental onion – it is an edible species of onion, native to China and cultivated in many other countries).

With a history of human use of over 7 000 years, garlic is native to central Asia, and has long been a staple in the Mediterranean region, as well as a frequent seasoning in Asia, Africa, and Europe. It was known to Ancient Egyptians, and has been used for both culinary and medicinal purposes.
(Wikipedia).

Garlic Is Highly Nutritious and Has Very Few Kilojoules

Calorie for calorie, garlic is incredibly nutritious.

A twenty-eight grams serving of garlic contains:

- Manganese: 23% of the RDA.
- Vitamin B6: 17% of the RDA.
- Vitamin C: 15% of the RDA.
- Selenium: 6% of the RDA.
- Fibre: 1 gram.
- Substantial amounts of Calcium, Copper, Potassium, Phosphorus, Iron and Vitamin B_1.

[Picture Credit: Garlic Plant]

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Garlic also contains trace amounts of various other nutrients. In fact, it contains a little bit of almost everything we need. This is coming with 176 kilojoules, with 1,8 grams of protein and 9 grams of carbohydrates.
(Authority Nutrition).

The major sulphur-containing compounds in intact garlic are γ-glutamyl-*S*-allyl-L-cysteines and *S*-allyl-L-cysteine sulfoxides (alliin). Both are abundant as sulphur compounds, and alliin is the primary odorless, sulphur-containing amino acid, a precursor of allicin, methiin, (+)-*S*-(*trans*-1-propenyl)-L-cysteine sulfoxide, and cycloalliin. These sulfoxides, except cyloalliin, are converted into thiosulfinates (such as allicin) through enzyme reactions when raw garlic is cut or crushed. Thus, no thiosulfinates are found in intact garlic.
(Amagase, 2006).

Garlic
Garlic is a herb. It is best known as a flavouring for food. Over the years, garlic has also been used as a medicine to prevent or treat a wide range of diseases and conditions. The fresh clove or supplements made from the clove are used for medicine.

Garlic is used for many conditions related to the heart and blood system. These conditions include high blood pressure, high cholesterol, coronary heart disease, heart attack, and atherosclerosis (hardening of the arteries). Some of these uses are supported by science. Garlic actually may be effective in slowing the development of atherosclerosis and seems to be able to modestly reduce blood pressure.

Some people use garlic to prevent colon cancer, rectal cancer, stomach cancer, breast cancer, prostate cancer, and lung cancer. It is also used to treat prostate cancer and bladder cancer.

[Picture Credit: Crushed Garlic]

Garlic has been tried for treating an enlarged prostate (benign prostatic hyperplasia or BPH, diabetes, osteoarthritis, hay fever (allergic rhinitis), traveller's diarrhoea, high blood pressure late in pregnancy (pre-eclampsia), colds and flu. It is also used for building the immune system, preventing tick bites, and preventing and treating bacterial and fungal infections.

Other uses include treatment of fever, coughs, headache, stomach ache, sinus congestion, gout, rheumatism, haemorrhoids, asthma, bronchitis, shortness of breath, low blood pressure, low blood sugar, high blood sugar, and snakebites. It is also used for fighting stress and fatigue, and maintaining healthy liver function.
(WebMD).

Can Garlic Prevent Cancer?
A host of studies provide compelling evidence that garlic and its organic allyl sulphur components are effective inhibitors of the cancer process. These studies reveal that the

benefits of garlic are not limited to a specific species, to a particular tissue, or to a specific carcinogen. Of 37 observational studies in humans using garlic and related allyl sulphur components, 28 studies showed some cancer preventive effect.

The evidence is particularly strong for a link between garlic and reduction of risk of prostate and stomach cancers. However, all of the available information comes from *observational studies* comparing cancer incidence in populations who consume or do not consume garlic (epidemiologic studies), animal models, or observations with cells in culture. These findings have not yet been verified by clinical trials in humans.

Several compounds are involved in garlic's possible anticancer (anti-mutagenic) effects. Garlic contains allyl sulphur and other compounds that slow or prevent the growth of tumour cells. Allyl sulphur compounds, which occur naturally in garlic and onions, make cells vulnerable to the stress created by products of cell division. Because cancer cells divide very quickly, they generate more stressors than most normal cells. Thus, cancer cells are damaged by the presence of allyl sulphur compounds to a much greater extent than normal cells.

The chemistry of garlic is complicated. As a result, the quality of garlic products depends on the manufacturing process. Peeling garlic and processing garlic into oil or powder can increase the number and variety of active compounds. Peeling garlic releases an enzyme called allinase and starts a series of chemical reactions that produce diallyl disulfide (DADS). DADS is also formed when raw garlic is cut or crushed.

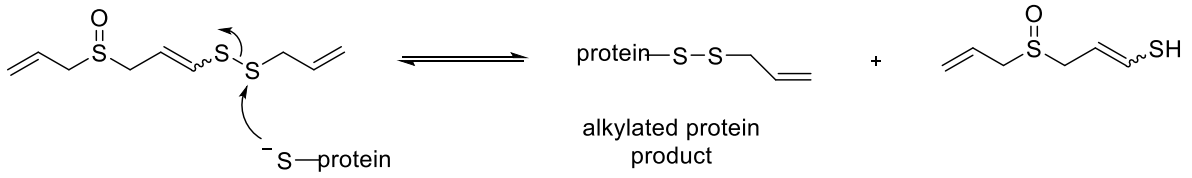
However, if garlic is cooked immediately after peeling, the allinase is inactivated and the cancer-fighting benefit of DADS is lost. Some scientists recommend waiting 15 minutes between peeling and cooking garlic to allow the allinase reaction to occur.

Processing garlic into powder or garlic oil releases other cancer-fighting agents. The inconsistent results of garlic research may be due, at least in part, to problems standardising all of the active compounds within garlic preparations. Some of the garlic compounds currently under investigation are: allin (responsible for the typical garlic odour), alline (odourless compound), ajoene (naturally occurring disulfide), diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DAT), S-allylcysteine (SAC), organosulfur compounds, and allyl sulphur compounds.
(Medicine.Net).

The Cancer Risk Reduction Activity of Dietary Garlic

Garlic has been used for centuries in folk medicine as a natural antibiotic, to stimulate the immune system and in the risk reduction of cancer. Evidence to support the cancer risk reduction potential of garlic comes from numerous epidemiological studies which have demonstrated an inverse relationship between garlic consumption and cancer risk particularly of the stomach and colon. Crushed cloves are rich in allyl sulphur compounds of which E/Z-ajoene is one of the major constituents.

Laboratory studies have demonstrated that ajoene can inhibit the proliferation and induce apoptosis in cancer cells by inducing G2/M cell cycle arrest. In addition, garlic allyl sulphur compounds have been shown to act as anti-mutagenic agents; and to stimulate the immune system which may also contribute to their cancer preventative effects. The specific protein targets and chemistry behind these anti-cancer effects is not well defined although both protein S-thiolation and generation of reactive oxygen species is thought to play a role.



A 4-step synthetic route to ajoene analogues were developed which has enabled us to identify the disulfide functional group as the pharmacophore responsible for inhibition of proliferation, G2/M cell cycle arrest and induction of apoptosis in WHCO1 oesophageal cancer cells.2 In addition, we have found a correlation between the anti-proliferative activity of disulfides and the leaving group stability in a mixed disulfide exchange reaction supporting a mechanism that involves protein S-thiolation. Elevated levels of ROS were not found to be important in the anti-proliferative activity of garlic related disulfides as treatment with ROS scavengers failed to counter these anti-proliferative effects.

Synthesis of two fluorescently-tagged ajoene analogues has enabled us for the first time to identify the endoplasmic reticulum as the target of ajoene in cancer cells. We propose that ajoene may become trapped in the ER through S-thiolation of newly synthesized proteins. We show that protein S-thiolation interferes with folding to result in an accumulation of misfolded protein aggregates; giving rise to an ER stress response.
(Kaschula, 2015).

A Systematic Review of Garlic in the Reduction of Colorectal Cancer Risk
Colorectal cancer (CRC) is a leading cause of cancer death. Environmental factors play important roles in the multiple-stage process of CRC and nutritional intervention has been identified as playing a major role in its prevention.

Nqo *et al*., conducted a systematic review of scientific evidence from studies conducted over the last decade that examined effects of garlic on CRC. Levels of evidence were ranked from level I to level V according to study designs and the quality of each study was assessed against a set of quality criteria based on those used by the National Health and Medical Research Council in Australia.

One randomised controlled trial (RCT, level II) reported a statistically significant 29% reduction in both size and number of colon adenomas in CRC patients taking aged garlic extract. Five of 8 case control/cohort studies (level III) suggested a protective effect of high intake of raw/cooked garlic and 2 of 8 of these studies suggested a protective effect for distal colon.

A published meta-analysis (level III) of 7 of these studies confirmed this inverse association, with a 30% reduction in relative risk. Eleven animal studies (level V) demonstrated a significant anti-carcinogenic (anti-cancer) effect of garlic and/or its active constituents.

There is consistent scientific evidence derived from randomised controlled trials of animal studies reporting protective effects of garlic on CRC despite great heterogeneity of measures of intakes among human epidemiological studies.
(Nqo, *et al*., 2007).

Garlic may strengthen the immune system, helping the body fight diseases such as cancer. In test tubes, garlic seems to kill cancer cells.

[Picture Credit: Health Benefits of Garlic]

Population studies - ones that follow groups of people over time - suggest that people who eat more raw or cooked garlic are less likely to get colon and stomach cancers and cancer of the oesophagus. In fact, researchers who reviewed 7 studies found a 30% reduction in risk of colorectal cancer among people who ate a lot of raw or cooked garlic. Garlic supplements don't seem to have the same effect.

- A large-scale study, called the Iowa Women's Health Study, looked at how much garlic, fruit, and vegetables were in the diets of 41,000 middle-aged women. Results showed that women who regularly ate garlic, fruits, and vegetables had a 35% lower risk of developing colon cancer.

- Garlic may help the immune system function better during times of need such as in cancer. In a study of 50 people with inoperable colorectal, liver, or pancreatic cancer, immune activity improved after they took aged garlic extract for 6 months.

(University of Maryland Medical Center).

Garlic and Cancer of the Stomach

There are suggestions of an anticancer effect of allium vegetables (onions, leeks, shallots, garlic, and chives) and their associated organosulfur components against several cancer types, including cancer of the stomach.

In a study Guercio, et al., summarised findings from epidemiological studies concerning the association between different types of allium vegetables and gastric cancer risk, published up to date.

Available data, derived mainly from case-control studies, suggested a favourable role of high intakes of allium vegetables, mainly garlic and onion, in the aetiology (causation) of gastric cancer. In particular, of 10 studies, 7 suggested a favourable role of high intake of total allium vegetables and gastric cancer.

All 14 of the studies on garlic, and most studies on onion (more than 80%), reported a beneficial role of these allium types against gastric cancer. However several limitations, including possible publication bias and the difficulty to establish a dose-risk relationship, suggest caution in the interpretation. Evidences on other types of allium vegetables, as well as on the influence of different gastric cancer of anatomical and histological types, are less consistent.

(Guercio, *et al*., 2014).

Garlic and Prostate Cancer
Prostate cancer is one of the most common male malignancies worldwide, and benign prostatic hyperplasia (BPH) is a common cause of lower urinary tract symptoms in elderly men. Garlic (Allium sativum) has been known to have anti-inflammatory, anti-cancer and antioxidant effects. Owing to these effects, garlic and its preparations have been used for the treatment of prostate cancer and relief of BPH symptoms for decades.
(Devrim & Durak, 2007).

Garlic and Breast Cancer
Diallyl disulfide (DADS), an important garlic (Allium sativum) derivative, exhibits potential anticancer activity, the molecular mechanism of this activity remains unknown. In a study, the antitumor activity of DADS in triple-negative breast cancer (TNBC) cell lines based in vitro and in vivo models were evaluated.

It was found that treatment with DADS resulted in decreased viability, increased apoptosis, and suppression of metastatic potential in TNBC cells. Furthermore, DADS induced dysregulation of B-cell lymphoma (Bcl)-2 family members, downregulation of matrix metalloproteinase (MMP)-9 and reversal of the epithelial-mesenchymal transition (EMT). DADS significantly inhibited activation of the β-catenin signalling pathway, which regulated Bcl-2 family members, MMP-9 and EMT in TNBC cells.

Results showed that the antitumour effect of DADS on TNBC cells is mediated by the β-catenin pathway, suggesting that DADS could be used as a potential therapeutic agent for treating or preventing breast cancer.
(Huang, *et al*.).

Garlic and Cancer of the Lung
The protective effect of garlic on the development of lung cancer has been reported in the *in vitro* and *in vivo* experimental studies, however, few human epidemiologic studies have evaluated the relationship.
(Jin, *et al.).*

Garlic is rich in antioxidants. In your body, harmful particles called free radicals build up as you age and may contribute to heart disease, cancer, and Alzheimer's disease. Antioxidants like those found in garlic fight off free radicals, and may reduce or even help prevent some of the damage they cause over time.

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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