PROFESSIONAL INFORMATION: CONTENT UNDER EACH HEADING

- This product is a Complementary Medicine (Category D33.7);
- and is identified according to its discipline as a Combination Product;
- which is not registered by the Authority.
- **This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.**

SCHEDULING STATUS:

S0

1. NAME OF THE MEDICINE

Progast® FloraCare Plus™ capsules

Strength

≈ 305,262 mg per capsule

Pharmaceutical form

Solid, DR® (delayed-release) capsule, oral

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Lactobacillus acidophilus L.; *Bifidobacterium longum*, *bifidum*, *lactis* L. (Probiotic blend)	1 billion CFUs
Zingiber officinale Roscoe (Ginger) [Root extract, standardised to 5% Gingerol]	150 mg
Cynara scolymus L. (Artichoke) [Leaf, 4:1 extract, standardised to 400mg dried herb equivalent]	100 mg
Zinc gluconate (providing zinc (elemental) 4,9 mg)	35 mg
Selenium bisglycinate (providing selenium (elemental) 20 µg)	10 mg
Manganese bisglycinate (providing manganese (elemental) 1 mg)	10 mg
Folic acid (Vitamin B9)	250 µg
Cholecalciferol (Vitamin D3)	500 IU/IE 12 µg

Excipients:

- Non-essential to proper administration;
- for a full list of excipients and the amounts of each excipient per capsule, see section 6.1

Sugar-free:

- Does not contain sugar.
- Does not contain sweeteners.

3. PHARMACEUTICAL FORM

Solid, DR® (delayed-release) capsule, oral, opaque, 23 mm lock-length, no markings.

4. CLINICAL PARTICULAR

4.1. Therapeutic indications

- Progast® FloraCare Plus Capsules are a dietary supplement that contains a blend of beneficial bacteria (probiotics) and herbal extracts, with vitamins and minerals. With DR®, which stands for delayed-release, capsule technology, Progast® Flora-Care Plus is designed to deliver the active substances where they are most effective. As a combination, DR® capsules offer several benefits over other capsule types, such as:

- Probiotic survival through the harsh acidic environment of the stomach.
- Targeted delivery to the small intestine, as some strains are more beneficial in the small intestine.
- Sustained release that helps optimize the colonization of probiotics in the gut and provides a continuous source of nourishment for the growth of healthy gut bacteria.
- Synergistic effect where the prebiotic nutrients protect and sustain the active probiotics, helping them thrive and multiply in the gut.
- Convenience and stability over very costly or wasteful alternatives, as it is easy-to-take, effective support that safeguards the benefits.
- Overcomes the need for users to refrigerate the product, which many other alternatives may require, as they lack the stability of DR® capsules.
- This health supplement is indicated to support a healthy digestive system, promote gastrointestinal well-being, maintain the balance of gut flora, and support healthy digestion and mental health. It is also indicated to help support the immune system, and symptomatic relief of minor digestive ailments related to gut dysbiosis by maintaining healthy levels of intestinal flora. Progast® Flora-Care Plus Capsules are indicated for self-administration as a low-risk health supplement, although only a healthcare provider may indicate it as an adjunct treatment to an existing treatment regimen for individual persons. It is not indicated as an alternative therapy to replace conventional medicines or any other treatments prescribed by a healthcare provider. It is not indicated as a cure-all or monotherapy for serious conditions because Progast® Flora-Care Plus Capsules are not intended (nor indicated) to diagnose, treat, prevent, or cure diseases.

4.2. Posology and method of administration

Posology

Single dose, ≈ 305,262 mg per capsule.

The potency of this medicine is expressed in capsule units. These units are not interchangeable with the units used to express the potency of other preparations that contain the same active substances. No more than the recommended dosage should be taken, and persons should not take or use a double dose to make up for forgotten individual doses.

Adults over the age of 18 years

1 capsule, 2 times daily, or 2 capsules, 1 time daily. This is the maximum recommended daily and/or total dose.

Method of administration

Oral use only.

4.3. Contraindications

Allergic to the active substances. Hypersensitivity to the active substances. No interactions have yet been observed or reported regarding antidiabetes medications, such as those that have a glycemic effect. Please be cautious when using blood thinners, as it may increase the effects of blood-thinning medication. Based on an existing treatment regimen or pre-existing condition there may be other contraindications (see section 4.5 ‘Interaction with other medicines and other forms of interaction’).

4.4. Special warnings and precautions

In the absence of sufficient data, the use during pregnancy and lactation is not recommended (see section 4.6 ‘Fertility, pregnancy, and lactation’). Progast® FloraCare Plus™ capsules is not established as safe for use in persons younger than 18 years of age. Adequate care must be taken to keep this medicine out of the reach of children. Take special precaution for use with antiplatelet or anticoagulant medication as the coumarins already contained in plant extracts may potentiate the effects of other medicines that contain coumadins such as Warfarin.

The maximum recommended daily and/or total dose should not be exceeded. Progast® FloraCare Plus™ capsules contains coumarins that can act as a plant-based blood-thinning agent. Because of coumarin, those who are using prescription anticoagulants especially on a chronic basis should not use this medicine without consulting their healthcare provider. Avoid blood-thinning medicine at least two weeks before surgery or a dental procedure.

4.5. Interaction with other medicines and other forms of interaction

Recommendations

The use of this medicine with antidiabetes medication has no reported interactions. However, a healthcare practitioner should be consulted. This is an important precaution before using any new health supplement. It is recommended that those who are already using prescription medications observe any and all contraindications of concomitant use provided by those medications and consult their healthcare provider before using this medicine or any other health supplement. Although this medicine is indicated for self-administration, as a low-risk health supplement, and no other forms of interaction have been reported, it is still recommended that a healthcare provider be consulted to avoid patients making any dose adjustments to an existing treatment regimen, where the risks may outweigh the benefits.

4.6. Fertility, pregnancy and lactation

Although it is unlikely to affect fertility, there is no fertility data available. Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended. No adverse effects to fertility, pregnancy, and lactation have yet been reported.

4.7. Effects on the ability to drive and use machines

Although it is unlikely to affect the ability to drive and use machines, no studies on the effect on the ability to drive and use machines have been performed. No adverse effects to the ability to drive or use machines have yet been reported.

4.8. Undesirable effect

No adverse reaction has been reported.

4.9. Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Mechanism of action

Lactobacillus acidophilus L. and *Bifidobacterium species (B. longum, B. bifidum, B. lactis* L.): These are probiotic strains that provide beneficial bacteria to the gut. They promote a healthy balance of gut flora and can help improve digestion and nutrient absorption. Probiotics may also support the immune system and help prevent the growth of harmful bacteria in the gut.

Ginger root extract: Ginger is known for its anti-inflammatory and antioxidant properties. It may help reduce inflammation in the gastrointestinal tract and alleviate symptoms of indigestion, bloating, and gas. Ginger may also support gut motility and promote a healthy digestive process.

Artichoke leaf extract: Artichoke leaf extract is traditionally used for its potential benefits in promoting liver and gallbladder health. It may support the liver's detoxification processes and help with the digestion of fats.

Zinc gluconate: Zinc is an essential mineral that plays a crucial role in various enzymatic reactions in the body, including those related to digestion and immune function. It may support a healthy gastrointestinal lining and contribute to the maintenance of the gut barrier.

Selenium bisglycinate: Selenium is an important antioxidant that can protect cells from oxidative stress. In the gut, it may support the health of the intestinal cells and contribute to overall gut integrity.

Manganese bisglycinate: Manganese is another mineral with antioxidant properties that can help neutralize free radicals. It may assist in the protection of gut tissues from oxidative damage.

Folic acid (Vitamin B9): Folic acid is a B-vitamin essential for DNA synthesis and cell division. In the gut, it may play a role in maintaining healthy intestinal cells and supporting the growth and repair of the intestinal lining.

Cholecalciferol (Vitamin D3): Vitamin D3 is vital for various bodily functions, including calcium absorption and immune regulation. In the gut, it may contribute to a balanced immune response and gut health..

Pharmacodynamic effects

These probiotic strains work by colonizing the gut and promoting a healthy balance of beneficial bacteria. By doing so, they help improve the gut's microbial ecosystem, which can lead to enhanced digestion and absorption of nutrients. Additionally, probiotics can modulate the immune system, promoting a balanced and appropriate immune response in the gut. Ginger's pharmacodynamic effects are mainly attributed to its bioactive compounds, such as gingerols and shogaols. These compounds possess anti-inflammatory properties, which can help reduce inflammation in the gastrointestinal tract and alleviate symptoms of indigestion, bloating, and gas. Ginger may also promote gut motility, supporting healthy digestion. The pharmacodynamic effects of artichoke leaf extract are primarily associated with its high content of bioactive compounds, including cynarin and chlorogenic acid. Artichoke extract is known for its choleretic properties, which means it can stimulate bile production in the liver. Increased bile flow can aid in the digestion of fats and support liver and gallbladder health.

The prebiotic effects of artichoke leaf extract are mainly attributed to its high content of inulin and other fructo-oligosaccharides (FOS). Inulin and FOS are types of dietary fibers that resist digestion in the upper gastrointestinal tract and reach the colon largely intact. Once they reach the colon, they become available as nutrients for the beneficial gut bacteria, particularly Bifidobacteria and Lactobacilli, which are commonly known as probiotics. The prebiotic effects of artichoke leaf extract are mainly attributed to its high content of inulin and other fructo-oligosaccharides (FOS). Inulin and FOS are types of dietary fibers that resist digestion in the upper gastrointestinal tract and reach the colon largely intact. Once they reach the colon, they become available as nutrients for the beneficial gut bacteria, particularly Bifidobacteria and Lactobacilli, which are commonly known as probiotics. By promoting the growth of probiotic bacteria, artichoke leaf extract helps maintain a healthy balance of gut flora. This balance is crucial for optimal gut function, digestion, and overall health. The fermentation of inulin and FOS produces SCFAs, which have several beneficial effects on gut health. SCFAs can improve the gut's barrier function, reducing the permeability of the intestinal lining and preventing the passage of harmful substances into the bloodstream. A healthy and balanced gut flora can enhance the absorption of nutrients from the food we eat, leading to improved overall nutrient uptake and utilization by the body. A well-balanced gut flora, supported by prebiotics like inulin and FOS, can positively influence the immune system, promoting a balanced and appropriate immune response.

Zinc plays a crucial role in numerous enzymatic reactions, including those related to digestion and immune function. In the gut, zinc contributes to the maintenance of the gut barrier, promoting gut integrity and protection against harmful substances. Selenium's pharmacodynamic effects stem from its role as an essential antioxidant. It neutralizes free radicals, which can cause oxidative stress and damage to cells. By supporting antioxidant defenses in the gut, selenium may help protect the intestinal tissues. Manganese, like selenium, acts as an antioxidant in the body. By scavenging free radicals, it can help prevent oxidative damage to the gut tissues and maintain their health.

Folic acid is involved in various cellular processes, including DNA synthesis and repair. In the gut, it may contribute to the growth and maintenance of healthy intestinal cells, supporting gut barrier function. Vitamin D3's pharmacodynamic effects are primarily related to its role in calcium absorption and immune regulation. In the gut, it may support a balanced immune response, promoting gut health.

It is also important to consider the pharmacokinetics of each active substance as opposed to a single abstract pharmacokinetic property for this combination (see section 5.2 'Pharmacokinetic properties').

Clinical safety and efficacy

Administered or used according to the recommended maximum and/or total daily dose is likely safe in adults and children, as the substances are generally well-tolerated. However, insufficient data is available to support safety during pregnancy and lactation. Effectiveness studies on the active substances show plausible therapeutic benefits for patients with constipation symptoms and indigestion-related symptoms as well as bloating. However, these active substances are not used to diagnose, treat, cure, or prevent any disease. This is also understood based on the contraindications (see section 4.3 'Contraindications').

5.2. Pharmacokinetic properties

Probiotics, ginger root extract, and artichoke leaf extract do not have a conventional half-life, as they are not directly metabolized or eliminated in the same way as drugs. It's important to note that the pharmacokinetic properties of each substance can be influenced by various factors, such as individual differences, dose, formulation, and interactions with other substances.

Lactobacillus acidophilus L. and *Bifidobacterium* species (*B. longum, B. bifidum, B. lactis* L.):
- Absorption: Probiotics are living microorganisms that are ingested orally. They are typically encapsulated to survive the acidic environment of the stomach and reach the intestines where they can colonize and exert their effects.
- Distribution: Once in the intestines, probiotics adhere to the gut lining and proliferate, establishing themselves as part of the gut flora.
- Metabolism: Probiotics mainly ferment dietary fibers and other non-digestible compounds, producing beneficial by-products like short-chain fatty acids.
- Excretion: Probiotics are eventually excreted from the body through feces.

Ginger root extract:
- Absorption: Ginger's active compounds, such as gingerols and shogaols, are absorbed through the gastrointestinal tract. Absorption can be influenced by factors such as the presence of fats or other compounds.
- Distribution: Once absorbed, ginger's active compounds circulate through the bloodstream and can reach various tissues in the body, including the gastrointestinal tract.
- Metabolism: Ginger's bioactive compounds may undergo metabolism in the liver and other tissues, eventually leading to the production of metabolites that may exert various effects in the body.
- Excretion: Metabolites and unabsorbed compounds are eliminated through urine and feces.

Artichoke leaf extract:
- Absorption: The bioactive compounds in artichoke leaf extract, such as inulin and other polyphenols, are absorbed in the gastrointestinal tract.
- Distribution: After absorption, these compounds can circulate through the bloodstream and reach various organs and tissues, including the liver and gallbladder.
- Metabolism: Artichoke leaf extract compounds may undergo some metabolism in the liver and other tissues, leading to the formation of metabolites.
- Excretion: Metabolites and unabsorbed compounds are excreted from the body via urine and feces.

Zinc gluconate:
- Absorption: Zinc gluconate is well-absorbed in the gastrointestinal tract, particularly in the small intestine.
- Distribution: After absorption, zinc is transported through the bloodstream and distributed to various tissues throughout the body.
- Metabolism: Zinc is a mineral and does not undergo significant metabolism in the body.
- Excretion: Excess zinc is excreted mainly through feces, with a smaller amount excreted through urine.

Selenium bisglycinate:
- Absorption: Selenium bisglycinate is absorbed in the gastrointestinal tract, and its absorption is likely influenced by dietary factors.
- Distribution: Once absorbed, selenium is transported through the bloodstream and distributed to various tissues.
- Metabolism: Selenium plays a role in various biochemical reactions, but it is not significantly metabolized itself.
- Excretion: Excess selenium is primarily excreted through urine and feces.

Manganese bisglycinate:
- Absorption: Manganese bisglycinate is absorbed in the gastrointestinal tract, and its absorption can be influenced by dietary factors.
- Distribution: Once absorbed, manganese is transported through the bloodstream and distributed to various tissues.
- Metabolism: Manganese participates in various enzymatic reactions but is not significantly metabolized itself.
- Excretion: Excess manganese is primarily excreted through bile, with a smaller amount excreted through urine.

Folic acid (Vitamin B9):
- Absorption: Folic acid is absorbed in the small intestine, where it is converted into its active form, 5-methyltetrahydrofolate (5-MTHF).
- Distribution: 5-MTHF circulates through the bloodstream and is distributed to various tissues in the body.
- Metabolism: Folic acid undergoes enzymatic conversion to its active form, 5-MTHF, which is involved in various biochemical reactions in the body.
- Excretion: Excess folic acid and its metabolites are excreted primarily through urine.

Cholecalciferol (Vitamin D3):

- Absorption: Cholecalciferol is absorbed in the small intestine, facilitated by dietary fats and bile.
- Distribution: Once absorbed, cholecalciferol is transported through the bloodstream to various tissues, including the liver and kidneys.
- Metabolism: Cholecalciferol undergoes hydroxylation in the liver and kidneys to form the active form of vitamin D, calcitriol.
- Excretion: Excess vitamin D and its metabolites are excreted primarily through bile and feces, with a smaller amount excreted through urine.

There is limited data available on the exact pharmacokinetic properties of Progast® FloraCare Plus™ capsules.

5.3. Preclinical safety data

Non-clinical data obtained on the use of the active substances reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction and development. The long-standing and traditional use of the active substances for which studies reveal plausible therapeutic benefits also provides real-world evidence and data. The use of Progast® FloraCare Plus™ capsules is in accordance with low-risk guidelines.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Inactive substances per capsule:

- Microcrystalline cellulose
- Magnesium stearate

6.2. Incompatibilities

Not applicable; solid oral pharmaceutical forms.

6.3. Shelf life

Progast® FloraCare Plus™ capsules has an estimated shelf life of 23 months.

6.4. Special precautions for storage

Protect from direct sunlight or moisture. Do not refrigerate or freeze this product. Store in a cool, dry place at temperatures of 59-77° F, equivalent to 15-25° C, and with ambient humidity between 35% and 65%.

Contents must remain sealed before use, shrink-wrapping, or packing into boxes for transport and storage. For express delivery in smaller batches, the use of specialized containment bins may be used for repacking individual sealed units.

6.5. Nature and contents of the container

Progast® Flora-Care Plus Capsules come in cartons of 10 and 30 capsules. The blister-pack also has the product label printed on the foil for identification purposes. The carton acts as the secondary packaging for storage, also showing the proper labeling. The active substances provide a total of ≈ 305,262 mg per capsule. Inactive substance per capsule are provided also (see section 6.1 ‘List of excipients’).

Progast® Flora-Care Plus Capsules have a solid capsule dosage form with a specific appearance: White capsule with a 23 mm lock length, sealed inside of a blister-pack. The carton acts as the secondary packaging for storage, also showing the proper labeling.

6.6. Special precautions for disposal and other handling

Return all unused medicine to your pharmacist. Do not dispose of remaining medicines in drains or sewerage systems. Please recycle the empty containers. Expired stock of Progast® FloraCare Plus™ capsules is to be quarantined in a special holding facility. Upon quarantine, they must be scheduled for destruction and may accumulate to certain holding levels depending on quarantine capacity.

The expired medicines should be destroyed by those duly authorized to carry out or conduct the destruction.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Tara Pharmaceuticals (Pty) Ltd
36 Sovereign Drive, Route 21 Corporate Park, Irene, Gauteng, 0062, South Africa

8. REGISTRATION NUMBER(S)

Item to be completed by SAHPRA or by the Holder of Certificate of Registration once the authorization has been granted.

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF AUTHORIZATION

Not yet assigned.

10. DATE OF REVISION OF TEXT

Not yet assigned.