

PROFESSIONAL INFORMATION RELEASE ARTIGEST IBS

D 33.6 Western Herbal Medicine. Complementary Medicines: Discipline-Specific Traditional Claims. This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS: S0

1. NAME OF MEDICINE:

Artigest IBS (capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each **Artigest IBS** capsule contains 100 mg *Cynara scolymus* L. (Artichoke) [leaf, 12:1 extract containing 2,5 % cynarin] and 20 mg *Zingiber officinale* Roscoe (Ginger) [root; extract containing 25 % gingerols].

Free of Sucrose and Glucose. For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules (30's)

Grey vegetarian capsule.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications

Artigest IBS contains *Cynara scolymus* L. (Artichoke) and *Zingiber officinale* Roscoe (Ginger) which has been shown to reduce gastric motility symptoms related to irritable bowel syndrome (IBS)^{1,2} and dyspepsia.²⁻⁴ Symptoms include bloating,¹⁻⁴ abdominal pain,^{1,2,4} gastric fullness^{2,4} and nausea.¹⁻⁴ **Artigest IBS** is indicated for adults 18 years and older.

4.2 Posology and method of administration

Posology

Adults: Take one to two capsules daily before food.

Method of administration

Take **Artigest IBS** orally.

4.3 Contraindications

• Hypersensitivity to *Cynara scolymus*, *Zingiber officinale*, other plants from the *Compositae/Asteraceae* family or other excipients listed under section 6.1.

4.4 Special warnings and precautions for use

Use with caution in patients with biliary obstructions or gallstones, as *Cynara scolymus* may worsen these conditions.² Use with caution in patients who are at a high risk of bleeding, or in patients taking antiplatelet medication, as *Zingiber officinale* may increase the risk of bleeding.¹ *Zingiber officinale* may decrease blood glucose levels and should be used with caution in patients with hypoglycaemia or in patients taking hypoglycaemic medication.¹

4.5 Interaction with other medicines and other forms of interaction

Interactions with Medicines

Anticoagulants/Antiplatelets: *Zingiber officinale* is suggested to inhibit thromboxane synthase, consequently decreasing platelet aggregation. When used concomitantly with anticoagulants/antiplatelet medication, such as aspirin, clopidogrel, dalteparin, enoxaparin, heparin, ticlopidine, nifedipine, phenprocoumon, warfarin and others, or anticoagulant/antiplatelet herbs such as angelica, clove, danshen, garlic, ginkgo, Panax ginseng, red clover, turmeric and others, it may theoretically increase the risk of bleeding.¹

Antibiotics: The concomitant use of *Zingiber officinale* and metronidazole may theoretically increase metronidazole levels by increasing its absorption and plasma half-life and decreasing its elimination rate.¹

Antidiabetics: The concomitant use of *Zingiber officinale* and antidiabetic medications such as glimepiride, glyburide, insulin, metformin, pioglitazone, rosiglitazone, etc., or antidiabetic herbs such as devil's claw, fenugreek, guar gum, Panax ginseng, Siberian ginseng, etc., may theoretically increase insulin levels/and or decrease blood glucose levels.¹

Antihypertensives: The concomitant use of *Zingiber officinale* and angiotensin receptor blockers (such as losartan) or calcium channel blockers (such as nifedipine, verapamil, diltiazem, isradipine, felodipine and amlodipine), may theoretically have an additive blood glucose lowering effect.¹

Cytochrome substrates: *Cynara scolymus* may theoretically inhibit cytochrome P450 (CYP2B6/CYP2C19) activity, consequently increasing the level of substrates metabolized by these cytochromes.² CYP2B6 substrates include bupropion, cyclophosphamide, efavirenz, methadone, sertraline, nevirapine, tamoxifen, valproic acid, etc., and CYP2C19 include substrates include proton pump inhibitors (omeprazole, lansoprazole and pantoprazole), diazepam, carisoprodol, nelfinavir and others.²

Interactions with Diseases/Impairments

Bile duct obstruction/Gallstones: *Cynara scolymus* may theoretically increase bile flow, consequently worsening bile duct obstruction and gallstones.²

Cross-allergenicity: Individuals sensitive to the *Asteraceae/Compositae* family (chrysanthemums, daisies, ragweed, marigolds, etc.) should use *Cynara scolymus* with caution as it might cause an allergic reaction.²

Bleeding conditions: *Zingiber officinale* may theoretically increase the risk of bleeding by inhibiting thromboxane synthase.¹

Hypoglycaemic conditions: *Zingiber officinale* may theoretically cause hypoglycaemia, by increasing insulin levels and/or decreasing blood glucose levels.¹

Surgical procedures: Due to the hypoglycaemic and antiplatelet properties of *Zingiber officinale*, discontinue use 2 weeks prior to surgical procedures¹ (see section 4.4).

Interactions with Foods

No known interactions.

4.6 Fertility, pregnancy and lactation

Cynara scolymus: Insufficient reliable information on fertility, pregnancy and lactation.

Zingiber officinale: Did not cause malformities or fetoneonatal toxicity in pregnant women (n = 490).³ Insufficient reliable information with respect to reproductive toxicity.

In the absence of sufficient data, the use during pregnancy, and lactation is not recommended.

4.7 Effects on ability to drive and use machines

Artigest IBS may affect the ability to drive or operate machinery, as it may cause sedation,¹ drowsiness¹ or dizziness.¹

Please exercise care until you are certain that your ability to perform such activities is not affected.

4.8 Undesirable effects

4.8 a Summary of safety profile

Cynara scolymus is generally well tolerated and possibly safe when used orally and appropriately in medicinal amounts.²

Zingiber officinale is generally well tolerated and likely safe when used orally and appropriately.¹

4.8 b Summary of adverse reactions

Gastrointestinal disorders (Frequent): Abdominal discomfort/pain,¹⁻⁴ constipation,¹ diarrhoea,^{1,2} heartburn,^{1,4} nausea,¹⁻⁴ belching,^{1,3} dry mouth,¹ dry retching,¹ vomiting,¹ burning/tingling sensation and numbness of tongue/throat.¹

Dermatological disorders (Less frequent): Redness in face² and sweating.²

Dermatological disorders (Frequency unknown): Hives,¹ bruising,¹ flushing¹ or rash.¹

Gastrointestinal disorders (Frequency unknown): Flatulence² and hunger.²

Neurological disorders (Frequency unknown): Sedation,¹ drowsiness¹ or dizziness.¹

Pulmonary disorders (Frequency unknown): Asthma symptoms or exacerbation,² chest tightness,² cough² and dyspnea.²

4.8 c Description of selected adverse reactions

Adverse reactions associated with *Zingiber officinale* (abdominal discomfort/pain, constipation, diarrhoea, heartburn, nausea, belching, dry mouth, dry retching, vomiting, burning/tingling sensation and numbness of tongue/throat) seems to be dose dependant. Higher dosages (5 grams per day) may reduce *Zingiber officinale* tolerability and increase the risk of side effects.¹

4.8 d Paediatric Population

Due to lack of adequate data, **Artigest IBS** is not recommended for use in children.⁴

4.8 e Other special populations

No clinical data are available on the effects of **Artigest IBS** on other special populations.

4.9 Overdose

No known side effects were reported for overdose of *Cynara scolymus* or *Zingiber officinale*.¹⁻⁴ Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties

Mechanism of action:

Cynara scolymus: The reduction in dyspepsia can be ascribed to the constituents cynarin, chlorogenic acid and scolymoside which are thought to be responsible for the choleric effect of *Cynara scolymus*.²

Zingiber officinale: According to preliminary research, the gastroprotective effects of *Zingiber officinale* may be ascribed to an increase of protective prostaglandins in the gut wall.¹ The constituent, 6-shogaol, may also improve gastrointestinal motility.¹

Pharmacodynamic effects:

Cynara scolymus is a perennial plant, used for dyspepsia,^{2,4} bloating,^{2,4} abdominal pain,^{2,4} gastric fullness,^{2,4} and nausea.^{2,4}

Zingiber officinale is a perennial plant, used for dyspepsia,³ bloating,^{1,3} abdominal pain¹ and nausea.^{1,3}

5.2 Pharmacokinetic properties

Cynara scolymus:

Absorption: The active phenolic constituents of *Cynara scolymus*, including luteolin and caffeoylquinic acids are not present in the plasma after consumption, however, metabolites of the constituents are present.²

Metabolism: The caffeoylquinic acid metabolites, caffeic acid, ferulic acid, isoferulic acid, dihydrocaffeic acid and dihydroferulic acid is metabolized to sulfates or glucuronides. The peak plasma concentration of caffeic acid, ferulic acid and isoferulic acid is reached within one hour, whereas peak levels of dihydrocaffeic acid and dihydroferulic acid is reached after 6-7 hours.²

Elimination: Caffeic acid, ferulic acid, isoferulic acid, dihydrocaffeic acid and dihydroferulic acid is excreted in the urine mainly as glucuronides or sulfates.²

Zingiber officinale:

Absorption: Once consumed, the main constituents of ginger, 6-, 8-, 10-gingerol and 6-shogaol are quickly absorbed in the serum followed by the formation of glucuronide and sulfate conjugates.⁵ The majority of constituents are present as glucuronide metabolites.⁵

Distribution: It is unclear whether gingerols/shogaols are conjugated to glucuronides in the liver, intestinal mucosa or both.⁵ It is also unclear whether the free or conjugated form of gingerols/shogaols enters the liver, and are further conjugated with sulfate to form glucuronide/sulfate conjugates.⁵

Metabolism: Once consumed, gingerols and 6-shogaols are conjugated to glucuronide or sulfate conjugates.^{1,5}

Excretion: The half-life of 6-, 8-, 10-gingerol and 6-shogaol is approximately 1-3 hours in the human plasma.¹

5.3 Preclinical safety data

No preclinical findings of relevance have been reported.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients

- Magnesium stearate (vegetable grade)
- Maltodextrin

6.2 Incompatibilities

In the absence of compatibility studies, **Artigest IBS** must not be mixed with other medicines.

6.3 Shelf life

23 months

6.4 Special precautions for storage

Store in a cool, dry place at or below 25 °C.

Do not use after expiry date.

Protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents

Artigest IBS: 30's: Grey coloured vegetable size 0 capsules are available in PVDC/aluminium blister strips. Each blister strip contains 10 capsules. Each carton of 30 capsules contains 3 blister strips.

6.6 Special precautions for disposal

Return all unused **Artigest IBS** to your pharmacist. Do not dispose of unused **Artigest IBS** in drains or sewerage systems (e.g. toilets).

7. HOLDER OF CERTIFICATE OF REGISTRATION

RELEASE PHARMACEUTICALS (PTY) LTD

14 De Vreugde Crescent

Dal Josaphat

Paarl

7646

Tel: +27 (21)001 9748

Email: info@releasepharma.co.za

8. REGISTRATION NUMBER(S)

To be allocated.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not Applicable

10. DATE OF REVISION OF THE TEXT

May 2021

RP0170/21A

PATIENT INFORMATION LEAFLET ARTIGEST IBS

SCHEDULING STATUS: S0

Artigest IBS (capsules)

Artichoke / Ginger

100 mg / 20 mg

Free of Sucrose and Glucose

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Read all of this leaflet carefully because it contains important information for you.

Artigest IBS is available without a doctor's prescription, for you to maintain your health. Nevertheless, you still need to use **Artigest IBS** carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Do not share **Artigest IBS** with any other person.
- Ask your healthcare provider or pharmacist if you need more information or advice.
- You must see a doctor if your symptoms worsen or do not improve.

What is in this leaflet

1. What **Artigest IBS** is and what it is used for
2. What you need to know before you take **Artigest IBS**
3. How to take **Artigest IBS**
4. Possible side effects
5. How to store **Artigest IBS**
6. Contents of the pack and other information

1. What Artigest IBS is and what it is used for

Artigest IBS contains *Cynara scolymus* L. (Artichoke) and *Zingiber officinale* Roscoe (Ginger) which has been shown to reduce gastric motility symptoms related to irritable bowel syndrome (IBS)^{1,2} and dyspepsia.²⁻⁴ Symptoms include bloating,¹⁻⁴ abdominal pain,^{1,2,4} gastric fullness^{2,4} and nausea.¹⁻⁴

2. What you need to know before you take Artigest IBS

Do not take Artigest IBS:

- If you are hypersensitive (allergic) to Artichoke, other plants from the *Compositae/Asteraceae* family, Ginger or any of the other ingredients in **Artigest IBS** (listed in section 6).

Warnings and Precautions

Special care should be taken with **Artigest IBS**:

- If you have biliary obstructions or gallstones, as Artichoke may worsen these conditions.²
- If you are at a high risk of bleeding or taking antiplatelet medication, as Ginger may increase the risk of bleeding.¹
- If you have low blood sugar levels or if you are taking medication to lower your blood sugar levels, as Ginger may also decrease your blood glucose levels.¹

Children and adolescents

Artigest IBS is indicated for adults 18 years and older.

Other medicines and healthcare provider

Always tell your healthcare provider if you are taking other medicines, including complementary or traditional medicines.

Consult your doctor if you want to take **Artigest IBS** in combination with medicines or treatments such as:

- Blood thinning/antiplatelet medicines, such as aspirin, clopidogrel, dalteparin, enoxaparin, heparin, ticlopidine, nifedipine, phenprocoumon, warfarin and others, or blood thinning/antiplatelet herbs such as angelica, clove, danshen, garlic, ginkgo, Panax ginseng, red clover, turmeric and others, as it may theoretically increase the risk of bleeding.¹
- Antibiotics, such as metronidazole as it may theoretically increase metronidazole levels.¹
- Antidiabetic medications such as glimepiride, glyburide, insulin, metformin, pioglitazone, rosiglitazone, etc., or antidiabetic herbs such as devil's claw, fenugreek, guar gum, Panax ginseng, Siberian ginseng, etc., as it may theoretically increase insulin levels/and or decrease blood glucose levels.¹
- Blood pressure lowering medicines, such as angiotensin receptor blockers (losartan) or calcium channel blockers (nifedipine, verapamil, diltiazem, isradipine, felodipine and amlodipine), as it may theoretically have an additive blood pressure lowering effect.
- CYP2B6 / CYP2C19 cytochrome substrates, such as bupropion, cyclophosphamide, efavirenz, methadone, sertraline, nevirapine, tamoxifen, valproic acid, proton pump inhibitors (omeprazole,



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