SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
SPAZZI 60 mg/300 mg Soft Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each soft capsule contains;
Active substance(s):
Alverine citrate 60 mg
Simethicone 300 mg
Excipient(s) with known effect:
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Soft capsule.
Oblong, cream-colored, opaque soft capsule.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
It is indicated for the symptomatic treatment of functional bowel diseases especially with meteorism.

4.2. Posology and method of administration
Posology/frequency and duration of administration
For adult use only.
SPAZZI is taken as one capsule 2 or 3 times a day for the specified indications, unless recommended otherwise by the doctor.

Method of administration
SPAZZI is taken orally and before meals.

Additional information on special populations
Renal / Hepatic impairment:
There is no special use.

Pediatric population:
For use in adults only.

Geriatric population:
There is no special use.

4.3. Contraindications
- Paralytic ileus
- Intestinal obstruction
- SPAZZI is contraindicated for use in people with intolerance or history of allergic reactions to the active substances alverine and simethicone or any of the excipients contained in this medicine.

4.4. Special warnings and precautions for use
Other causes of gastrointestinal pathology should be excluded and patients who do not recover after 2 weeks of treatment should be evaluated by a physician.

Liver function
Elevations in ALT (Alanine Aminotransferase) and AST (Aspartate Aminotransferase) exceeding twice the upper limit of normal (ULN) have been reported in patients receiving treatment with alverine/simethicone. These elevations may be associated with a concomitant elevation in total serum bilirubin (see section 4.8). In case of an elevation in hepatic aminotransferases exceeding 3 times the ULN and in the case of jaundice, treatment with alverine/simethicone should be discontinued.

4.5. Interaction with other medicinal products and other forms of interaction
Since the absorption of medicines containing levothyroxine is impaired when taken together with simeticone, these two medicines must be taken with an interval of at least 2 hours.

Additional information on special populations:
No interaction studies have been conducted for special populations.

Pediatric population:
No interaction studies have been conducted for pediatric population.

4.6 Fertility, pregnancy and lactation
General recommendation:
Pregnancy category is C.

Women of childbearing potential / Contraception
The effect of SPAZZI on women of childbearing potential and contraception methods is unknown.

Pregnancy
Animal studies are insufficient in terms of effects on pregnancy and/or embryonal/fetal development and/or birth and/or postnatal development. The potential risk for humans is unknown.

Simethicone: Due to its negligible systemic exposure, no effect of simethicone taken during pregnancy is expected. There are no data from the use of simethicone alone or in combination during pregnancy.

Alverine citrate: Detailed data on teratogenicity in animals are not available. To date, no malformations or fetotoxic effects have clinically been reported. However, follow-up of pregnancies exposed to alverine is insufficient to exclude any risk.
As a precautionary measure, it is advised to avoid the use of SPAZZI during pregnancy.

Lactation
Due to its negligible systemic exposure, no effect of simethicone taken during breastfeeding is expected.
There are no data available on whether alverine is excreted in human milk.
As a precautionary measure, it is advised to avoid the use of SPAZZI during lactation.

Fertility
No effect on fertility has been reported.

4.7. Effects on ability to drive and use machines
SPAZZI has a minor influence on the ability to drive and use machines. Adverse effects such as vertigo have been reported in some patients (see sections 4.8 and 4.9). These types of disorders may

affect the ability to drive and use machines.

4.8 Undesirable effects

The frequencies of the side effects observed with the use of SPAZZI are as follows:
Very common (1/10); common (≥ 1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥ 1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Immune system disorders
Very rare: Anaphylactic type reactions and anaphylactic shock

Nervous system disorders
Not known: Headache

Ear and labyrinth disorders
Not known: Vertigo

Vascular disorders
Very rare: Shock

Respiratory, thoracic, and mediastinal disorders
Very rare: Laryngeal edema

Gastrointestinal disorders
Not known: Nausea

Hepatobiliary disorders
Very rare: Cytolytic hepatitis (see section 4.4)

Skin and subcutaneous tissue disorders
Not known: Angioedema, skin rash, urticaria and pruritus

Investigations
Not known: Elevated levels of transaminases, alkaline phosphatase and bilirubin

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9. Overdose
Cases of vertigo have been reported when a dosage higher than recommended is taken.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Papaverine and derivatives / Antispasmodics and other drugs altering gut motility
ATC code: A03AX58

SPAZZI is a product consisting of two active substances.

Alverine is a substance with antispasmodic properties of musculotropic character with a similar effect to papaverine. This effect is exerted through the smooth muscle fibrils of the gastrointestinal tract. The spasmolytic effect of alverine was found to be greater than that of papaverine, and the side effect was found to be three times less than that of papaverine. Since it does not have a similar effect to atropine, it has no effect on gastric acid. In a pharmacokinetic study with alverine, serum concentrations were found to be very low (below 2.5 ng/ml). This result suggests that when alverine is not reabsorbed or taken together with simethicone, it undergoes a significant first-pass elimination effect in the liver. These results support the specific effect of alverine.

Simethicone is dimethicone activated by added silicon dioxide. Simeticone, which is an inert substance that does not have pharmacological activity, changes the surface tensions of gas bubbles in the gastrointestinal tract, allowing their coalescence and be easily expelled by physiological means (such as belching, flatulation).

5.2. Pharmacokinetic properties

General properties

Absorption:

Alverine citrate is absorbed throughout the gastrointestinal tract after oral administration. It has been reported that simethicone is minimally absorbed. Simethicone is not absorbed from the gastrointestinal tract. Following oral administration, it is excreted unchanged with feces.

Distribution:

Alverine citrate quickly reaches peak plasma concentration within 1-1.5 hours after ingestion of the oral dose.

Biotransformation:

Alverine citrate is rapidly converted to its active metabolite, which reaches peak plasma concentration within 1-1.5 hours after ingestion of the oral dose. It undergoes further biotransformation to get converted into inactive metabolites.

Simethicone does not undergo any metabolism after taken orally. The half-life, plasma protein binding, entry into the brain and other tissues, and excretion in human milk of simethicone are not known.

Elimination:

Alverine citrate metabolites are excreted in the urine by active renal secretion.

Simeticone is excreted in feces without being metabolized.

5.3 Preclinical safety data

Simethicone is chemically inert and is not systemically absorbed. Therefore, systemic toxic effects are not expected.

Classical nonclinical studies on repeated dose toxicity and genotoxicity prove that alverine citrate has no significant systemic toxicity potential.

Animal studies in 2 different species indicate no harmful effects in terms of embryotoxicity.

A study conducted on rats before and after birth did not produce harmful effects on the development of the fetus, at birth, and on the growth and development of offspring during lactation.

No studies assessing carcinogenicity, fertility, and early embryonic development in animals have been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Gelatin (bovine gelatin)
Glycerin
Purified water
Titanium dioxide

6.2. Incompatibilities

Not known

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store at room temperature below 25°C.

6.5. Nature and contents of container

Transparent PVC/PVdC and aluminum foil are used for the blister packs of the product SPAZZI 60 mg/300 mg Soft Capsules. Blisters are presented in cardboard boxes. Each cardboard box contains 40 or 80 capsules and a package leaflet.

6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local disposal regulations.

7. MARKETING AUTHORISATION HOLDER

Deva Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad.
No:1 34303 Küçükçekmece/İSTANBUL/TÜRKİYE

8. MARKETING AUTHORISATION NUMBER(S)

2021/137

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorization: 24.05.2021
Renewal of the authorization:

10. DATE OF REVISION OF THE TEXT