SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

No-Spa 40 mg tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS

Each tablet contains 40 mg drotaverine hydrochloride.
Excipient with known effect: each tablet contains 52.0 mg lactose monohydrate.

For a full list of excepients see in section 6.1.

3. PHARMACEUTICAL FORM

Tablet
Yellow, greenish or orange-yellow, round tablet with convex surface and identification «spa» engraved on one side.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Smooth muscle spasms associated with biliary tract disorders: cholecystolithiasis, cholangiolithiasis, cholecystitis, pericholecystitis, cholangitis, papillitis.

Smooth muscle spasms associated with urinary tract disorders: nephrolithiasis, ureterolithiasis, pyelitis, cystitis, tenesmus of urinary bladder.

As adjuvant therapy:
In case of smooth muscle spasm associated with gastrointestinal disorders: gastric and duodenal ulcer, gastritis, cardia and pyloric spasm, enteritis, colitis, spastic constipation or meteoristic form of irritable colon.
Tension-type headache.
In gynaecological diseases: dysmenorrhoea.

4.2. Posology and method of administration

Posology

Adults
Recommended daily dose is 120-240 mg (in 2-3 divided doses).

Children
The use of dratovaerine in children has not been established in clinical studies; if drotaverine administration is necessary:
for children between 6 and 12 years of age the maximum daily dose is 80 mg, divided in 2 parts
for children above the age of 12 years the maximum daily dose is 160 mg divided in 2 to 4 parts.
No data are available for children below 6 years of age.

4.3. Contraindications

- Hypersensitivity to the active ingredient or to any of the excipients listed in section 6.1.
- Severe renal or hepatic insufficiency.
- Cardiac insufficiency (low output syndrome).

4.4. Special warnings and special precautions for use

Special caution should be take in the case of hypotension.

Children
No clinical studies have been performed with children.

No-Spa 40 mg tablet contains lactose monohydrate. Patients with rare hereditary problems with galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorbtion should not take this medicine.

4.5. Interaction with other medicinal products and other forms of interaction

Phosphodiesterase inhibitors like papaverine decrease the antiparkinsonian effect of levodopa. When drotaverine is administered concomitantly with levodopa, antiparkinsonian effect decreases and rigidity and tremor may worsen.

4.6. Fertility, pregnancy and lactation

Pregnancy
Per os retrospective human studies, and animal studies did not show any direct or inderect harmful effect exerted on pregnancy, embryonal developement, delivery or postnatal development (see section 5.3.). Nevertheless, caution should be taken when used in pregnant women.

Lactation
The excretion of drotaverine in milk has not been studied in animals. Therefore, its administration during breast-feeding is not recommended.

Fertility
No data are available on human fertility.

4.7. Effects on ability to drive or use machines

Patients should be informed if dizziness is experienced after intake, they should avoid potentially hazardous tasks such as driving or operating machines.

4.8. Undesirable effects

Possible adverse reactions occured in clinical studies in association with drotaverine administration are listed below according to system organ classes: very common (> 1/10); common (> 1/100, < 1/10); uncommon (> 1/1,000, < 1/100); rare (> 1/10,000, < 1/1,000) ; very rare (< 1/10,000), not known: cannot be estimated from the available data:

Immune system disorders
Rare: allergic reactions (angioedema, urticaria, rash, pruritus)

Nervous system disorders
Rarely: headache, dizziness, insomnia.

Cardiac disorders
Rare: palpitation.

Vascular disorders
Rare: hypotension.

Gastrointestinal disorders

Rarely: nausea, obstipation.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 listed in Appendix V.

4.9. OVERDOSAGE

Symptoms
Significant overdose of drotaverine has been associated with heart rhythm and conduction disorders including complete bundle branch block and cardiac arrest, which may be fatal

Management
If overdosed, the patient should closely be monitored, and symptomatic *treatment* is recommended, including emesis and/or gastric lavage.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: drugs for functional bowel disorders. ATC: A03A D02.

Mechanism of action
Drotaverine is an isoquinolin derivative, which exerts its spasmolytic effect directly on smooth musculature. The inhibition of the phosphodiesterase enzyme and the consequent increase of cAMP level are determinant in its mechanism of action and lead to the smooth muscle relaxation through the myosin light chain kinase enzyme (MLCK) inactivation.
Drotaverine inhibits phosphodiesterase (PDE) IV enzyme *in vitro* without inhibiting isoenzymes PDE III and PDE V. Practically, PDE IV appears to be very important in blockage of the contractile activity of smooth muscles; on the basis of what the selective PDE IV blockage might be useful in the treatment of hypermotility disorders and various diseases accompanied with gastrointestinal smooth muscle spasm. PDE III isoenzyme hydrolyses cAMP in myocardium and vascular smooth muscles; it provides explaination, that drotaverine can be an effective spasmolytic agent without significant cardiovascular adverse effects and strong cardiovascular therapeutic activity.
It is effective in all cases of smooth muscle spasms of both neural and muscular origin. Independently from the type of autonomous innervation, drotaverine acts equally on the smooth musculature of gastrointestinal, biliary, urogenital and the vascular system. Due to its vasodilatator effect it increases the blood supply in tissues.
Its effect is stronger than papaverine's, its absorption is more rapid and more complete, and it bonds less to the serum proteins. Its advantage is that the stimulating adverse effect on respiration observed after parenteral administration of papaverine does not occur with drotaverine administration.

5.2. Pharmacokinetic properties

Absorption
Drotaverine is rapidly absorbed after both oral and parenteral administration.

Distribution
It is highly bound to plasma albumin (95-98%), alfa and beta globulins. Serum peak concentration is reached within 45-60 min. after oral administration.

Biotransformtaion
Following the first pass metabolism of drotaverine the 65% of the administered dose reaches the systemic circulation in unchanged form.
It is metabolised in the liver.

Elimination
Biological half-life of drotaverine is 8-10 hours. Practically, it eliminates from the body within 72 hours, in approximately 50% via the urine and about 30 % in the faeces. It is mainly excreted in the form of metabolites; its unchanged form cannot be detected in the urine.

5.3. Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development. Based on the *in vitro and in vivo* studies, drotaverine did not cause any delay in ventricular repolarisation.

- *In vitro in vivo* genotoxcicity studies (e.i. Ames test, mouse lymphoma test, micronucleus test) drotaverine has not shown any sign suggestive of genotoxicity.
- Drotaverine has no effect on fertility in rats, as well as on embyronic /foetal developement in rats and rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Magnesium stearate, talcum, polividon, maize starch, lactose monohydrate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Store below 25°C, in the original packaging.

6.5. Nature and contens of the container

20 or 24 pcs of No-Spa 40 mg tablets in Alu/Alu or PVC/Alu blisters, in box.

6.6. Special precautions for disposal and other handling

No special requirements.

Note: ✠ (one cross)
Classification: Group I

Medicinal product not subject to medical prescription (VN).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

SANOFI-AVENTIS Zrt.
1045. Budapest, Tó u. 1-5.
Hungary

8. MARKETING AUTHORISATION NUMBER(S)

OGYI-T-6267/03 (PVC/Al blister, 20x)
OGYI-T-6267/05 (PVC/Al blister, 24x)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 1962
Date of latest renewal: 22 January 2008

10. DATE OF REVISION OF THE TEXT

14 August 2016