# SUMMARY OF PRODUCT CHARACTERISTICS

ANSM (French National Agency for Medicines and Health Products Safety):21/04/2017

## 1. NAME OF THE MEDICINAL PRODUCT

**DUSPATALIN 200 mg, capsule**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Mebeverine hydrochloride 200.00 mg
Per one capsule

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Capsule.
White capsule No. 1 bearing the inscription “254”.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Symptomatic treatment of intestinal pain and discomfort associated with digestive tract and bile duct dysfunction.

### 4.2 Posology and method of administration

Oral route.

**Posology**

Adults

1 capsule, 2 to 3 times a day. The capsule should be swallowed with a glass of water before food.
The capsule must not be chewed as the shell guarantees prolonged release (see section 5.2).

*Specific population:*

No dosing studies have been carried out in elderly patients or patients with renal and/or hepatic impairment. No specific risk has been identified in elderly patients and patients with renal and/or hepatic impairment based on post-marketing data. Consequently, no dose adjustment appears necessary in elderly subjects or in patients with renal and/or hepatic impairment.

### 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

### 4.4 Special warnings and precautions for use

Not applicable.

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

No interaction studies have been performed.

### 4.6 Fertility, pregnancy and lactation

**Pregnancy**
Limited data, if indeed any, are available on the use of mebeverine in pregnant women.
Laboratory animal studies are inadequate and do not provide any conclusive evidence regarding reproductive toxicity (see section 5.3).

DUSPATALIN 200 mg is not recommended during pregnancy.

**Lactation**

It is not known whether mebeverine or its metabolites are excreted in breast milk. The excretion of mebeverine in milk has not been studied in animals.
DUSPATALIN 200 mg must not be used during breast-feeding.

**Fertility**
No clinical data are available regarding male or female fertility. However, laboratory animal studies have not highlighted any harmful effects of mebeverine (see section 5.3).

### 4.7 Effects on ability to drive and use machines

No studies have been carried out on the ability to drive and use machines. However, no effect likely to alter the ability to drive and use machines is anticipated with this product.

### 4.8 Undesirable effects

The following undesirable effects have been reported spontaneously since market launch. Precise frequency cannot be estimated from the data available.

Immune system disorders

Acute hypersensitivity mainly comprising urticaria, angioedema, facial oedema and skin rash, with or without pruritus. Isolated cases of more severe, anaphylactic reaction have been reported.

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: Agence Nationale de Sécurité du Médicament et des Produits de Santé (French National Agency for Medicines and Health Products Safety) (ANSM) and the Centres Régionaux de Pharmacovigilance (Regional Pharmacovigilance Centres) – Internet site: www.ansm.sante.fr.

### 4.9 Overdose

Very rare cases of convulsions have been reported with mebeverine overdose. Treatment will be based on medical monitoring and symptomatic treatment.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic class: synthetic anticholinergics: esters with tertiary amine group, ATC code: A03AA04.**

**Mechanism of action and pharmacodynamic effects**

Mebeverine is a musculotropic antispasmodic with a direct effect on smooth muscle in the gastrointestinal tract. Since this effect is not mediated by the autonomous nervous system, there are no anticholinergic adverse events.

### 5.2 Pharmacokinetic properties

**Absorption**
Mebeverine is absorbed completely and rapidly after oral administration.

**Distribution**

No significant accumulation occurs after administration of repeated doses.

**Biotransformation**

Mebeverine hydrochloride is mainly metabolised by veratric acid esterases and mebeverine alcohol.
The principal plasma metabolite is DMAC (demethylated carboxylic acid).
The half-life of DMAC at steady-state is 5.77 h. During administration of repeated doses (200 mg, twice daily), the DMAC Cmax is 804 ng/ml and the tmax is approximately 3 hours.
Relative bioavailability of the capsule seems optimal with a mean ratio of 97%.

**Elimination**
Mebeverine is completely metabolised. The metabolites are virtually completely eliminated. Veratric acid and mebeverine alcohol are eliminated in the urine, partly in the form of carboxylic acid (MAC) and partly as demethylated carboxylic acid (DMAC).

**Paediatric population**
No pharmacokinetic study has been carried out in children.

### 5.3. Preclinical safety data

During the development phase, the substance, mebeverine, was tested on several animal species during acute, sub(chronic) and reproductive toxicity studies.
In single or repeated oral toxicity studies, effects on the central nervous system including behavioural excitation (mainly tremor and convulsions) were observed in rats, rabbits and dogs. In dogs, the convulsions were observed at doses equivalent to 1 to 2 times the clinical dose in man. In rats and rabbits, these effects were observed only at doses considerably higher than those used in man (e.g. in rats, at 15 times the maximum human dose).
Although inadequately studied in animals, no teratogenic effect has been observed in rats and rabbits up to doses of 100 mg/kg per day. However, mebeverine proved embryotoxic in rats at a twice daily dose of 50 mg/kg, which is equivalent to one to two times the human dose.
In an oral fertility study conducted in male and female rats, no effect was observed in the F0 generation and up to three F1 generations including administration of the dose corresponding to once the human dose.
Mebeverine was devoid of genotoxic effects in standard *in-vitro* and *in-vivo* genotoxicity tests. No carcinogenicity study has been carried out.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Magnesium stearate, methacrylic acid and ethyl acrylate copolymer (1:1) (dispersion) 30 percent (Eudragit L 30D), talc, hypromellose, polyacrylate (dispersion) 30 percent (Eudragit NE 30D), triacetin.
Capsule shell: gelatine, titanium dioxide (E171).
Composition of printing ink: shellac, propylene glycol, concentrated ammonia solution, potassium hydroxide, black iron oxide.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

36 months.

### 6.4 Special precautions for storage

Store at a temperature exceeding +5°C.
For packaging in heat-sealed (PVC/aluminium) blister packs:
Store at a temperature not exceeding +25°C.
For packaging in heat-sealed (aluminium/aluminium) blister packs:
Store at a temperature not exceeding +30°C.

### 6.5 Nature and contents of container

Heat-formed (PVC/aluminium) blister packs
Heat-formed (aluminium/aluminium) blister packs
Boxes of 20, 30 or 60 capsules.
Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

No special requirements.

**7. MARKETING AUTHORISATION HOLDER**

**MYLAN MEDICAL SAS**
42, RUE ROUGET DE LISLE
92150 SURESNES

**8. MARKETING AUTHORISATION NUMBER(S)**

- 34009 349 426 7 9: 20 capsules in heat-sealed (PVC/Aluminium) blister packs
- 34009 349 427 3 0: 30 capsules in heat-sealed (PVC/Aluminium) blister packs
- 34009 349 429 6 9: 60 capsules in heat-sealed (PVC/Aluminium) blister packs
- 34009 363 426 0 6: 20 capsules in heat-sealed (Aluminium/Aluminium) blister packs
- 34009 363 427 7 4: 30 capsules in heat-sealed (Aluminium/Aluminium) blister packs
- 34009 363 428 3 5: 60 capsules in heat-sealed (Aluminium/Aluminium) blister packs.

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

[to be completed subsequently by the holder]

**10. DATE OF REVISION OF THE TEXT**

[to be completed subsequently by the holder]

**11. DOSIMETRY**

Not applicable.

**12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS**

Not applicable.

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**CONDITIONS FOR SUPPLY AND USE**

List II