

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Dipentum 250mg hard Capsules

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 250mg olsalazine sodium.

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Capsule, hard.

Beige, opaque, hard gelatin size 1 capsule radially printed "DIPENTUM 250 mg" in black.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Treatment of mild to moderate acute ulcerative colitis with or without corticosteroids. The drug may also be used in the long term maintenance or remission of ulcerative colitis. It is particularly useful where patients cannot tolerate sulphasalazine because of sulpha intolerance.

### 4.2 Posology and method of administration

To be taken in divided doses with meals.

#### General

Olsalazine taken on an empty stomach may sometimes lead to loose stools or diarrhoea. By taking the drug at the end of a meal, this may be avoided.

#### Acute Mild Disease

*Adults including the elderly:* Commence on 1 g daily in divided doses taken at the end of meals. Depending on the patient's response, the dose may be titrated upwards over a period of one week to a maximum of 3g daily. Concomitant oral or rectal steroids may be used. In the event of drug related diarrhoea occurring, it may be transient. If it is not, dose may be reduced; where diarrhoea continues despite this reduction the drug should be stopped.

A single dose should not exceed 1 g.

#### Long-term maintenance of remission

*Adults, including the elderly:* Two capsules may be taken twice daily with food.

*Children and infants:* No specific recommendations are made.

### 4.3 Contraindications

Patients hypersensitive to olsalazine or other salicylates or any of the excipients. Severe renal impairment.

### 4.4 Special warnings and precautions for use

It is recommended to monitor patients with impaired kidney or liver function.

Patients suffering from severe allergy or asthma should be observed for signs of worsening of these conditions.

In-vitro and in-vivo laboratory studies do not suggest pharmacogenetic problems associated with the drug.

It is recommended to monitor renal function in patients receiving olsalazine, by estimating serum creatinine before treatment, every 3 months for the first year, every 6 months for the next 4 years, and annually after 5 years of treatment.

Haematological investigations should be performed if the patient develops unexplained bleeding, bruising, purpura, anaemia, fever, sore throat or mouth ulcers. Treatment should be stopped if there is a suspicion or evidence of a blood dyscrasia.

Patients or their carers should be instructed how to recognise the signs of haematotoxicity and should be advised to contact their physicians immediately if the symptoms such as fever, sore throat, mouth ulcers, bruising, or bleeding develop.

#### **4.5 Interaction with other medicinal products and other forms of interactions**

The coadministration of salicylates and low molecular weight heparins or heparinoids may result in an increased risk of bleeding, more specifically hematomas following neuraxial anesthesia. Salicylates should be discontinued prior to the initiation of a low molecular weight heparin or heparinoid. If this is not possible, it is recommended to monitor patients closely for bleeding.

Increased prothrombin time in patients taking concomitant warfarin has been reported.

The coadministration of olsalazine and 6-mercaptopurine or thioguanine may result in an increased risk of myelosuppression. If coadministered with 6-mercaptopurine, it is recommended to use the lowest possible doses of each drug and to monitor the patient, especially for leukopenia. In case of coadministration with thioguanine, careful monitoring of blood counts is recommended.

It is recommended not to give salicylates for six weeks after the varicella vaccine to avoid a possible increased risk of developing Reye's syndrome.

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy:

Olsalazine has been shown to produce fetal developmental toxicity as indicated by reduced fetal weights, retarded ossifications and immaturity of the fetal visceral organs when given during organogenesis to pregnant rats in doses 5 to 20 times the human dose (100 to 400 mg/kg).

There are no adequate and well-controlled studies in pregnant women. Olsalazine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

##### Lactation:

Small amounts of the active metabolite of olsalazine (5-ASA) may pass into breast milk. Harmful infant effects (diarrhea) have been reported when 5-ASA was used during breastfeeding. Unless the benefit of the treatment outweighs the risks, olsalazine should not be taken by breast-feeding women, or patients should be advised to discontinue breastfeeding if using olsalazine.

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

On the basis of the pharmacodynamic profile and reported adverse events, olsalazine does not appear to produce any effects on ability to drive and use machines.

#### **4.8 Undesirable effects**

Frequency estimate: very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

The most common side effect is diarrhoea which is usually transient.

In addition, the following undesirable effects have been reported:

General disorders and administration site conditions:

Common: headache

Uncommon: pyrexia

Blood and lymphatic system disorders:

Uncommon: thrombocytopenia

Not known: aplastic anaemia, eosinophilia, haemolytic anaemia, leukopenia, neutropenia, pancytopenia

Gastrointestinal disorders:

Common: diarrhoea, nausea

Uncommon: vomiting, dyspepsia

Not known: abdominal pain upper, pancreatitis

Hepatobiliary disorders:

Uncommon: hepatic enzyme increased

Not known: hepatitis, increased bilirubin

Skin and subcutaneous tissue disorders:

Common: rash

Uncommon: pruritus, alopecia, photosensitivity reaction, urticaria

Not known: angioneurotic oedema

Cardiac disorders:

Uncommon: tachycardia

Not known: myocarditis, palpitations, pericarditis

Renal and urinary disorders:

Not known: interstitial nephritis

Respiratory, thoracic and mediastinal disorders:

Uncommon: dyspnoea

Not known: interstitial lung disease

Musculoskeletal and connective tissue disorders:

Common: arthralgia

Uncommon: myalgia

Nervous system disorders:

Uncommon: dizziness paraesthesia

Not known: peripheral neuropathy

Psychiatric disorders:

Uncommon: depression

Eye disorders:

Not known: vision blurred

## 4.9 Overdose

The knowledge of overdosage is limited. Possible overdose symptoms include nausea, vomiting and diarrhoea. It is recommended to check hematology, acid-base, electrolyte, liver and kidney status, and to provide supportive treatment. There is no specific antidote to Dipentum.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group:**

## 5.2 Pharmacokinetic properties

Olsalazine sodium was developed as a pro-drug for the release of 5- aminosalicylic acid in the colon by bacterial azo reduction. Neither substance is significantly absorbed, but the 5ASA which is taken up is largely acetylated in the gut wall, and urinary excretion is principally as the acetylated form. Olsalazine undergoes enterohepatic circulation with a T<sub>1/2</sub> of 5-7 hours.

## 5.3 Preclinical safety data

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Magnesium stearate (E572)

### Printing Ink

Shellac

Black iron oxide (E172)

Propylene glycol

Postassium hydroxide (only in ink sourced from Tek)

### Capsule Shell

Caramel (E150)

Titanium dioxide (E171)

Gelatin

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

5 years.

## 6.4 Special precautions for storage

Do not store above 25°C.

Keep the container tightly closed in order to protect from moisture.

## 6.5 Nature and contents of container

White, HDPE bottle sealed by a foil inner-seal and tamper-evident LDPE cap, containing 112 capsules.

## 6.6 Special precautions for disposal

No special requirements for disposal.

# 7 MARKETING AUTHORISATION HOLDER

Atnahs Pharma Netherlands B.V.

Copenhagen Towers,  
Ørestads Boulevard 108, 5.tv  
DK-2300 København S,  
Denmark

**8 MARKETING AUTHORISATION NUMBER**

PA22657/001/001

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

Date of first authorisation: 12 July 1995

Date of latest renewal: 12 July 2010

**10 DATE OF REVISION OF THE TEXT**

December 2020