Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dipentum 500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500 mg olsalazine sodium.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

Yellow capsule-shaped tablet debossed with 'D500' on one side and a score line on the other.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

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 of remission of ulcerative colitis. It is particularly useful where patients cannot tolerate sulphasalazine because of sulpha intolerance.

4.2 Posology and method of administration

Oral

Recommended dosage schedules

To be taken in divided doses, with meals.

Acute mild disease

Adults including the elderly: Commence on 1 gram daily in divided doses depending on patient responses titrate dosage upwards to the maximum of 3 g daily over 1 week. Concomitant oral or rectal steroids may be used. In the event of drug related diarrhoea occurring, it may be transient. If it is not, the 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

Adults including the elderly: One tablet 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.

Serious blood dycrasias have been reported very rarely with olsalazine. Hematological 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 blood dycrasia.

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 (≥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).

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 anemia, 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:
ATC Code: A07E C 03, Aminosalicylic acid and similar agents

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 T½ 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)
Colloidal Anhydrous Silica
Povidone (E1201)
Crospovidone

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 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 with white polypropylene cap and foil inner seal.

Pack size: 60 tablets.

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

PA22657/001/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 May 1995

Date of latest renewal: 18 May 2010

10 DATE OF REVISION OF THE TEXT

December 2020