osteoarthritis and rheumatoid arthritis, in mild to moderate pain, and in dysmenorrhoea and menorrhagia.

Doses of meclofenamate sodium are expressed in terms of the equivalent amount of meclofenamic acid. Meclofenamic acid 100 mg is equivalent to about 113.5 mg of meclofenamate sodium. In arthritic conditions it is given in doses equivalent to 200 to 400 mg daily; daily doses are usually given in 3 or 4 divided doses. For relief of mild to moderate pain doses are 50 to 100 mg every 4 to 6 hours; the daily dose should not exceed 400 mg. The dose in the treatment of dysmenorrhoea and menorrhagia is 100 mg three times daily for up to 6 days during menstruation.

Meclofenamic acid has been given as a rectal suppository and is also used in veterinary medicine.

Preparations

USP 31: Meclofenamate Sodium Capsules.

Proprietary Preparations (details are given in Part 3)
Chile: Meclomen; ***Ital.:*** Lenidolor; Meclodol†; Movens; ***Spain:*** Meclomen†.

Mefenamic Acid *(BAN, USAN, rINN)*

Acide méfénamique; Ácido mefenámico; Acidum mefenamicum; CI-473; CN-35355; INF-3355; Kwas mefenamowy; Kyselina mefenamová; Mefenaamihappo; Mefenamik Asit; Mefenaminsav; Mefenamo rūgštis; Mefenamsyra. *N*-(2,3-Xylyl)anthranilic acid.

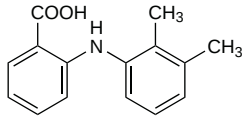
Мефенамовая Кислота

$C_{15}H_{15}NO_2$ = 241.3.

CAS — 61-68-7.

ATC — M01AG01.

ATC Vet — QM01AG01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Mefenamic Acid). A white to almost white, microcrystalline powder. Practically insoluble in water; slightly soluble in alcohol and in dichloromethane; dissolves in dilute solutions of alkali hydroxides.
USP 31 (Mefenamic Acid). A white to off-white, crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in methyl alcohol; sparingly soluble in chloroform; soluble in solutions of alkali hydroxides. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

Treatment should be stopped if diarrhoea and rashes occur. Other effects reported include drowsiness, and effects on the blood such as thrombocytopenia, occasionally haemolytic anaemia, and rarely aplastic anaemia. Convulsions may occur on overdosage.

Mefenamic acid is contra-indicated in patients with inflammatory bowel disease. Licensed product information recommends that blood counts and liver and renal function should be monitored during long-term therapy. Drowsiness may affect the performance of skilled tasks.

Mefenamic acid may give a false positive in some tests for the presence of bile in the urine.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were given mefenamic acid, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding. The *BNF* also considers that the amount of mefenamic acid distributed into breast milk is too small to be harmful to a breast-fed infant. An early study[2] confirms that the distribution of mefenamic acid into breast milk is minimal. However, licensed product information contra-indicates the use of mefenamic acid in nursing mothers.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 08/11/07)
2. Buchanan RA, *et al.* The breast milk excretion of mefenamic acid. *Curr Ther Res* 1968; **10:** 592–6.

Effects on the blood. References to haematological reactions in patients taking mefenamic acid including haemolytic anaemia,[1] leucopenia,[2] neutropenia,[3] and agranulocytosis.[4]

1. Scott GL, *et al.* Autoimmune haemolytic anaemia and mefenamic acid therapy. *BMJ* 1968; **3:** 534–5.
2. Burns A, Young RE. Mefenamic acid induced leucopenia in the elderly. *Lancet* 1984; **ii:** 46.
3. Handa SI, Freestone S. Mefenamic acid-induced neutropenia and renal failure in elderly females with hypothyroidism. *Postgrad Med J* 1990; **66:** 557–9.
4. Muroi K, *et al.* Treatment of drug-induced agranulocytosis with granulocyte-colony stimulating factor. *Lancet* 1989; **ii:** 55.

Effects on the gastrointestinal tract. Reversible steatorrhoea has occurred[1] with mefenamic acid; it may also provoke colitis in patients without a history of this condition.[2]

1. Marks JS, Gleeson MH. Steatorrhoea complicating therapy with mefenamic acid. *BMJ* 1975; **4:** 442.
2. Ravi S, *et al.* Colitis caused by non-steroidal anti-inflammatory drugs. *Postgrad Med J* 1986; **62:** 773–6.

Effects on the kidneys. Nonoliguric renal failure has occurred in elderly patients who had had diarrhoea and vomiting while taking mefenamic acid and had continued to take the drug. It is normally recommended that mefenamic acid be stopped in the event of diarrhoea and it was suggested that in these patients the gastrointestinal toxicity had led to fluid and electrolyte depletion, thus predisposing these patients to mefenamic acid's nephrotoxicity.[1] There has been a subsequent report[2] of nonoliguric renal failure in elderly patients given mefenamic acid for musculoskeletal pain.

1. Taha A, *et al.* Non-oliguric renal failure during treatment with mefenamic acid in elderly patients: a continuing problem. *BMJ* 1985; **291:** 661–2.
2. Grant DJ, MacConnachie AM. Mefenamic acid is more dangerous than most. *BMJ* 1995; **311:** 392.

Effects on the skin. Bullous pemphigoid, together with haemolytic anaemia and diarrhoea,[1] and fixed drug eruptions[2-4] have been associated with the use of mefenamic acid. Additionally, Stevens-Johnson syndrome, together with cholestatic hepatitis and haemolytic anaemia, in one patient has been attributed to mefenamic acid.[5] It is generally recommended that mefenamic acid should be withdrawn if skin reactions develop.

1. Shepherd AN, *et al.* Mefenamic acid-induced bullous pemphigoid. *Postgrad Med J* 1986; **62:** 67–8.
2. Wilson CL, Otter A. Fixed drug eruption associated with mefenamic acid. *BMJ* 1986; **293:** 1243.
3. Long CC, *et al.* Fixed drug eruption to mefenamic acid: a report of three cases. *Br J Dermatol* 1992; **126:** 409–11.
4. Rallis E. 'Dalmatian dog'-like skin eruption (two cases of multifocal fixed drug eruption induced by mefenamic acid). *J Eur Acad Dermatol Venereol* 2005; **19:** 753–5.
5. Chan JCN, *et al.* A case of Stevens-Johnson syndrome, cholestatic hepatitis and haemolytic anaemia associated with use of mefenamic acid. *Drug Safety* 1991; **6:** 230–4.

Overdosage. Mefenamic acid overdose has been associated with CNS toxicity, especially with convulsions.[1] Coma[2,3] has also been reported.

1. Court H, Volans GN. Poisoning after overdose with non-steroidal anti-inflammatory drugs. *Adverse Drug React Acute Poisoning Rev* 1984; **3:** 1–21.
2. Gössinger H, *et al.* Coma in mefenamic acid poisoning. *Lancet* 1982; **ii:** 384.
3. Hendrickse MT. Mefenamic acid overdose mimicking brainstem stroke. *Lancet* 1988; **ii:** 1019.

Pancreatitis. A report of pancreatitis associated with mefenamic acid.[1]

1. van Walraven AA, *et al.* Pancreatitis caused by mefenamic acid. *Can Med Assoc J* 1982; **126:** 894.

Porphyria. Mefenamic acid is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

Interactions

For interactions associated with NSAIDs, see p.99.

Pharmacokinetics

Mefenamic acid is absorbed from the gastrointestinal tract. Peak plasma concentrations occur about 2 to 4 hours after ingestion. The plasma elimination half-life is reported to be about 2 to 4 hours. Mefenamic acid is more than 90% bound to plasma proteins. It is distributed into breast milk. Mefenamic acid is metabolised by the cytochrome P450 isoenzyme CYP2C9 to 3-hydroxymethyl mefenamic acid, which may then be oxidised to 3-carboxymefenamic acid. Over 50% of a dose may be recovered in the urine, as unchanged drug or, mainly, as conjugates of mefenamic acid and its metabolites.

Uses and Administration

Mefenamic acid, an anthranilic acid derivative, is an NSAID (p.99), although its anti-inflammatory properties are considered to be minor.

It is used in mild to moderate pain including headache, dental pain, postoperative and postpartum pain, and dysmenorrhoea, in musculoskeletal and joint disorders such as osteoarthritis and rheumatoid arthritis, and in menorrhagia.

In the UK, the usual oral dose is 500 mg three times daily. US licensed product information recommends an initial dose of 500 mg followed by 250 mg every 6 hours as needed. In addition, in the USA, when mefenamic acid is used in the treatment of mild to moderate pain in adults and adolescents aged 14 years and over, it is also recommended that it should not be given for longer than 7 days at a time.

For doses of mefenamic acid in children, see below.

Administration in children. In the UK, licensed product information states that mefenamic acid may be used in children for the treatment of Still's disease (see Juvenile Idiopathic Arthritis, p.10) and fever; however, the *BNFC* does not recommend mefenamic acid for juvenile idiopathic arthritis, nor for postoperative or mild to moderate pain. A suggested oral dose of mefenamic acid for children over 6 months of age is 25 mg/kg daily in divided doses. Treatment in children should be given for no longer than 7 days unless they are receiving mefenamic acid for juvenile idiopathic arthritis.

Preparations

BP 2008: Mefenamic Acid Capsules; Mefenamic Acid Tablets;
USP 31: Mefenamic Acid Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Ponstil; ***Austral.:*** Mefic; Ponstan; ***Austria:*** Parkemed; ***Braz.:*** Ponstan; Pontin†; ***Canad.:*** Ponstan†; ***Chile:*** Algex; Algifemin; Dolcin†; Flipal; Sicadol; Tanston; Templadol; ***Fin.:*** Ponstan; ***Fr.:*** Ponstyl; ***Ger.:*** Parkemed†; Ponalar†; ***Gr.:*** Acinic; Aidol; Ponstan; Vidan; ***Hong Kong:*** Dyspen†; Hamitan; Hostan; Medicap; Mefa; Mefamic; Mefic; Namic; Napan; Pekaso; Ponstan; Pontacid; Sefmic; ***Hung.:*** Ponmel; ***India:*** Dysmen-500†; Ponstan; ***Indon.:*** Analspec; Asam; Asimat; Benostan; Cetalmic; Corstanal; Datan; Dolfenal; Dolos; Dystan; Femisic; Fensik; Gitaramin; Lapistan; Licostan; Mectan; Mefast; Mefinal; Mefinter; Mefix; Menin; Molasic; Nichostan; Opistan; Ponalar; Poncofen; Pondex; Ponsamic; Ponstan; Ponstelax; Stanalin; Stanza; Stelpon; Topgesic; Tropistan; ***Irl.:*** Mefac; Ponalgic; Ponmel; Ponstan; ***Ital.:*** Lysalgo; ***Malaysia:*** Beafemic; Mefen†; Mefic; Namic; Napan; Pongesic†; Ponstan; Pontalon; ***Mex.:*** Artriden; Namifen; Ponstan; ***NZ:*** Ponstan; ***Philipp.:*** Acidan; Afligec; Analcid; Aprostal; Atmose; Calibral; Dolfenal; Dolmetine; Dolsten; Escandar; Eurostan; Finox; Gardan; Gisfen; Hispen; Inflasic; Istan; Kramon; Laffed; Mecid A; Mefenax; Metaflam; Neostan; Penomor; Ponser; Ponstan; Pontaser; Ralgec; Revalan; Selmac; Senflam; Spegic; Suprazen; Tynostan; Vamgesic; Vandifen; Zanovic; ZapAn; Zestan; ***Pol.:*** Mefacit; ***Port.:*** Ponstan; ***S.Afr.:*** Fenamin; Ponac; Ponstan; Ponstel; ***Singapore:*** Beafemic; Mefacap†; Mefenix; Ponstan†; Pontalon; Ponty†; ***Spain:*** Coslan; ***Switz.:*** mefe-basan†; Mefenacide; Melur; Mephadolor; Ponstan; Spiralgine; ***Thai.:*** Conamic; Dolfen; Dolfenal†; Dyspen†; Femen; Fenamic; Gandin; Manic; Manomic; Masafen; Mednil; Mefa; Mefen; Mefenan; Namic; Painnox; Panamic; Pefamic†; Pondnadysmen; Ponnesia; Ponstan; Prostan; Pynamic; Sefmic; Vestan; ***Turk.:*** Ponstan; Rolan; ***UK:*** Dysman†; Ponstan; ***USA:*** Ponstel; ***Venez.:*** Ponstan.

Multi-ingredient: ***India:*** Cyclo-Meff; Dysmen; Dysmen Forte; Meftal Forte; Spasmonil Forte; Spasmonil Plus; Tranfib MF; Ze-Spas; ***Thai.:*** Difemic; Mainnox; Med-Anspasmic†.

Meloxicam *(BAN, USAN, rINN)*

Meloksikaami; Meloksikam; Méloxicam; Meloxicamum; Meloxikam; UH-AC-62; UH-AC-62XX. 4-Hydroxy-2-methyl-*N*-(5-methyl-2-thiazolyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide.

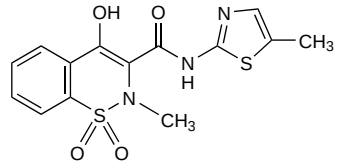
Мелоксикам

$C_{14}H_{13}N_3O_4S_2$ = 351.4.

CAS — 71125-38-7.

ATC — M01AC06.

ATC Vet — QM01AC06.



Pharmacopoeias. In *Br.*, *Chin.*, and *US*.
BP 2008 (Meloxicam). A pale yellow powder. Practically insoluble in water; very slightly soluble in alcohol and in methyl alcohol; slightly soluble in acetone; soluble in dimethylformamide.
USP 31 (Meloxicam). A pale yellow powder. Practically insoluble in water; very slightly soluble in alcohol and in methyl alcohol; slightly soluble in acetone; soluble in dimethylformamide.

Adverse Effects and Treatment

As for NSAIDs in general, p.96.

Incidence of adverse effects. Between September 1996, when meloxicam was first marketed in the UK, and mid-June 1998 the UK CSM had received a total of 773 reports of 1339 suspected adverse reactions for meloxicam.[1] Of all the reactions 41% were gastrointestinal and of these 18% involved gastrointestinal perforation, ulceration and/or bleeding; the mean age of the patients involved was 64 years. Although most patients recovered after withdrawal of meloxicam and/or treatment, 5 died. A total of 193 reactions involved the skin, the most common being pruritus, rash, and urticaria. There were also reports of angioedema (25), photosensitivity (12), and bullous dermatoses,