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.

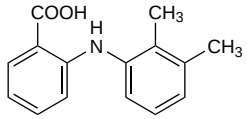
Мефенамовая Кислота

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

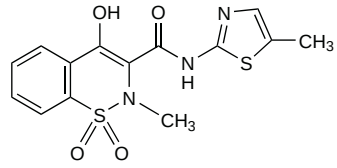
Мелоксикам

$C_{14}H_{13}N_3O_4S_2$ = 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,

including erythema multiforme and Stevens-Johnson syndrome (5). No patients died from skin reactions and most recovered after meloxicam was withdrawn. Other frequently reported reactions were neurological (mostly headache), cardiovascular (oedema and palpitations), dizziness, flushing, and fatigue. A prescription event monitoring study has also analysed events reported with meloxicam use.[2] In a cohort of 19 087 patients who had received meloxicam some time between December 1996 and March 1997, 203 patients had had 252 events considered to be suspected adverse reactions. The majority of reactions were not serious or were labelled adverse effects of meloxicam. Rare, serious suspected adverse reactions included 2 reports of thrombocytopenia and 1 each of interstitial nephritis and idiosyncratic liver abnormality. The most frequent gastrointestinal event was dyspepsia; other more serious gastrointestinal events occurring during meloxicam exposure included upper gastrointestinal bleeding (33 reports) and peptic ulcer (19 reports). However it was considered that the incidence of gastrointestinal disturbance was low in the absence of gastrointestinal risk factors. Adverse drug reactions reported during the first year of marketing of meloxicam to the Swedish Medical Products Agency suggested a similar safety profile to other NSAIDs.[3] Of the 15 reports, 6 were for gastrointestinal disturbances and 5 involved skin reactions.

1. CSM/MCA. Meloxicam (Mobic): gastrointestinal and skin reactions. *Current Problems* 1998; **24:** 13. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023231&RevisionSelectionMethod=LatestReleased (accessed 08/11/07)
2. Martin RM, *et al.* The incidence of adverse events and risk factors for upper gastrointestinal disorders associated with meloxicam use amongst 19 087 patients in general practice in England: cohort study. *Br J Clin Pharmacol* 2000; **50:** 35–42.
3. Anonymous. Meloxicam safety similar to other NSAIDs. *WHO Drug Information* 1998; **12:** 147.

Effects on the gastrointestinal tract. It is generally accepted that inhibition of cyclo-oxygenase-1 (COX-1) plays a role in the adverse gastrointestinal effects of NSAIDs, and that selective inhibition of the other isoform, COX-2, by NSAIDs such as meloxicam may cause less gastrotoxicity than that seen with the non-selective inhibition of traditional NSAIDs. However, there has been little convincing evidence that the risk of severe gastrointestinal events is lower with meloxicam than with other NSAIDs at equi-effective doses.[1] Two large multicentre studies[2,3] have reported a lower incidence of gastrointestinal adverse effects with meloxicam than with non-selective cyclo-oxygenase inhibitors (diclofenac[2] or piroxicam[3]) but in one of these[2] the dose of meloxicam given also appeared to be less effective than the reference drug. A more recent systematic review[4] also found a lower risk of serious gastrointestinal toxicity with meloxicam 7.5 mg daily when compared with diclofenac (100 or 150 mg daily), naproxen (500 mg twice daily), or piroxicam (20 mg daily); however, when given at a dose of 15 mg daily, the risk of toxicity with meloxicam was significantly lower only when compared with piroxicam.

Individual case reports of gastrointestinal toxicity with meloxicam included one of ischaemic colitis associated with high-dose (15 mg daily) meloxicam treatment.[5]

1. Anonymous. Meloxicam—a safer NSAID? *Drug Ther Bull* 1998; **36:** 62–4.
2. Hawkey C, *et al.* Gastrointestinal tolerability of meloxicam compared to diclofenac in osteoarthritis patients. *Br J Rheumatol* 1998; **37:** 937–45.
3. Dequeker J, *et al.* Improvement in gastrointestinal tolerability of the selective cyclooxygenase (COX)-2 inhibitor, meloxicam, compared with piroxicam: results of the safety and efficacy large-scale evaluation of COX-inhibiting therapies (SELECT) trial in osteoarthritis. *Br J Rheumatol* 1998; **37:** 946–51.
4. Singh G, *et al.* Risk of serious upper gastrointestinal and cardiovascular thromboembolic complications with meloxicam. *Am J Med* 2004; **117:** 100–106.
5. Garcia B, *et al.* Ischaemic colitis in a patient taking meloxicam. *Lancet* 2001; **357:** 690.

Precautions

As for NSAIDs in general, p.98.

Meloxicam should be avoided in severe hepatic impairment, in bleeding disorders, and in patients with renal failure unless receiving dialysis. Rectal use should be avoided in patients with a history of proctitis, haemorrhoids, or rectal bleeding.

Renal impairment. The pharmacokinetics of meloxicam were not substantially altered in patients with a creatinine clearance (CC) of 41 to 60 mL/minute compared with those with normal renal function.[1] In those with a CC of 20 to 40 mL/minute, total plasma-meloxicam concentrations were lower but meloxicam free fractions were higher. Such free meloxicam concentrations were similar to the other groups. On the basis of these results, it was suggested that it was not necessary to reduce meloxicam doses in patients with a CC greater than 20 mL/minute.

1. Boulton-Jones JM, *et al.* Meloxicam pharmacokinetics in renal impairment. *Br J Clin Pharmacol* 1997; **43:** 35–40.

Interactions

For interactions associated with NSAIDs, see p.99.

Colestyramine increases the clearance and decreases the half-life of meloxicam.

Pharmacokinetics

Meloxicam is well absorbed after oral or rectal doses with peak plasma concentrations reached in up to 6 hours. It is 99% bound to plasma proteins. Meloxicam has a plasma-elimination half-life of about 20 hours. It is extensively metabolised, mainly by oxidation to its major metabolite, 5′-carboxymeloxicam. *In vitro* studies suggest that the cytochrome P450 isoenzyme CYP2C9 plays an important role in the metabolism of meloxicam with CYP3A4 involved to a lesser degree. Meloxicam, in the form of metabolites, is excreted in similar amounts in the urine and in the faeces; less than 5% of a dose is excreted unchanged. The volume of distribution is increased in renal failure.

◊ References.

1. Narjes H, *et al.* Pharmacokinetics and tolerability of meloxicam after i.m. administration. *Br J Clin Pharmacol* 1996; **41:** 135–9.
2. Türck D, *et al.* Clinical pharmacokinetics of meloxicam. *Arzneimittelforschung* 1997; **47:** 253–8.
3. Davies NM, Skjodt NM. Clinical pharmacokinetics of meloxicam: a cyclooxygenase-2 preferential nonsteroidal anti-inflammatory drug. *Clin Pharmacokinet* 1999; **36:** 115–26.
4. Meineke I, Türck D. Population pharmacokinetic analysis of meloxicam in rheumatoid arthritis patients. *Br J Clin Pharmacol* 2003; **55:** 32–8.
5. Burgos-Vargas R, *et al.* Pharmacokinetics of meloxicam in patients with juvenile rheumatoid arthritis. *J Clin Pharmacol* 2004; **44:** 866–72.

Renal impairment. For reference to the pharmacokinetics of meloxicam in renal impairment, see under Precautions, above.

Uses and Administration

Meloxicam, an oxicam derivative, is an NSAID (p.99). It is reported to be a selective inhibitor of cyclo-oxygenase-2 (COX-2). Meloxicam is used in the management of rheumatoid arthritis, for the short-term symptomatic treatment of acute exacerbations of osteoarthritis, and for the symptomatic treatment of ankylosing spondylitis. It may also be used in the treatment of juvenile idiopathic arthritis.

In the treatment of rheumatoid arthritis and ankylosing spondylitis, meloxicam is given in a usual oral dose of 15 mg daily as a single dose. Those with an increased risk of adverse reactions should be started on 7.5 mg daily. A dose of 7.5 mg daily is recommended for long-term treatment in the elderly. In the treatment of acute exacerbations of osteoarthritis the usual oral daily dose of meloxicam is 7.5 mg, increased if necessary to a maximum of 15 mg daily given as a single dose.

For dosage details in children see below.

Meloxicam may be given by rectal suppository in doses similar to those used orally but use should be limited to the shortest time possible.

For the dose of meloxicam in patients with renal impairment, see below.

Administration in children. In the USA, meloxicam is used in the treatment of juvenile idiopathic arthritis in children aged 2 years and over. The recommended oral dose is 125 micrograms/kg once daily, up to a maximum of 7.5 mg daily. In the UK, licensed product information states that meloxicam should not be used in children aged under 15 years; however, the *BNFC* has suggested the following oral doses, according to body-weight, in those aged 12 to 18 years who are intolerant of other NSAIDs:

- less than 50 kg: 7.5 mg once daily
- over 50 kg: 15 mg once daily

Administration in renal impairment. Meloxicam is normally contra-indicated in patients with severe renal impairment. However, in dialysed patients, meloxicam may be given in a dose of 7.5 mg daily by mouth or by rectal suppository. No dose reduction is required in those with mild to moderate renal impairment (creatinine clearance of greater than 25 mL/min).

Musculoskeletal and joint disorders. Meloxicam is used in the treatment of osteoarthritis (see p.11), rheumatoid arthritis (see p.11) including juvenile idiopathic arthritis (p.10), and ankylosing spondylitis (see Spondyloarthropathies, p.13). However, in the UK, the use of meloxicam and other selective cyclo-oxygenase-2 (COX-2) inhibitors is limited to those patients with good cardiovascular health and at high risk of developing serious gastrointestinal problems if given a non-selective NSAID (see p.97).

References.

1. Lemmel EM, *et al.* Efficacy and safety of meloxicam in patients with rheumatoid arthritis. *J Rheumatol* 1997; **24:** 282–90.
2. Yocum D, *et al.* Safety and efficacy of meloxicam in the treatment of osteoarthritis: a 12-week, double-blind, multiple-dose, placebo-controlled trial. The Meloxicam Osteoarthritis Investigators. *Arch Intern Med* 2000; **160:** 2947–54.
3. Combe B, *et al.* Comparison of intramuscular and oral meloxicam in rheumatoid arthritis patients. *Inflamm Res* 2001; **50** (suppl 1): S10–16.
4. Fleischmann R, *et al.* Meloxicam. *Expert Opin Pharmacother* 2002; **3:** 1501–12.

Veterinary use. For the suggestion that meloxicam should be used as an alternative to diclofenac in cattle in South Asia (to reduce toxicity to vultures who may consume their carcasses), see under Precautions of Diclofenac, p.45

Preparations

BP 2008: Meloxicam Tablets;
USP 31: Meloxicam Oral Suspension; Meloxicam Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Bronax; Dominadol; Flexidol; Flexium; Loxitenk; Meloxid†; Merapiran†; Mextran; Miogesil†; Miolox; Mobic; Skudal†; Telaroid; Tenaron; ***Austral.:*** Mobic; Movalis; Moxicam; ***Austria:*** Melodyn; Meloxistad; Metosan; Movalis; ***Belg.:*** Docmeloxi; Mobic; ***Braz.:*** Alivian; Artritec†; Bioflac; Diatec†; Dormelox; Flamatec; Inicox; Leutrol; Lonaflam†; Loxam; Loxiflan; Melocox; Melonan†; Melonax†; Melotec; Meloxigran; Meloxil; Mevamox; Movacox†; Movatec; Movoxicam; ***Canad.:*** Mobicox; ***Chile:*** Anposel; Ecax; Hyflex; Isox; Melic; Melodol; Mexan; Mexilal; Mibloc FT; Mobex; Sition; Tenaron; Zix†; ***Cz.:*** Artrilom; Duplicam; Galoxiway; Melobax; Melocox; Melovis; Meloxistad; Movalis; Recoxa; ***Denm.:*** Mobic; ***Fin.:*** Latonid; Mobic; ***Fr.:*** Mobic; ***Ger.:*** Mobec; ***Gr.:*** Arsitec; Arthrox; Auroxicam; Brosiral; Doctinon; Examel; Farmelox; Flumidon; Iamaxicam; Iaten; Iconal; Infomel; Loxitan; Mecalox; Medoxicam; Melice; Melocalm; Melock; Melocox; Melodin; Meloprol; Melorilif; Melotec; Melotop; Meloxil; Meloxitor; Meomel; Movatec; Movaxin; Moxalid; Notpel; Partial; Philipon-S; Rentilox; Reumotec; Reumotherm; Sanetron; Saniflam; Starmelox; Supercad; Transantor; Tropofin; Valoxin; Vexicam; Zametrixal; Zerelin; ***Hong Kong:*** Melflam; Melox; Mobic; ***Hung.:*** Camelox; Melodyn; Melogen; Meloxan; Meloxep; Movalis; Moxicam; Noflamen; ***India:*** Mel-OD; Melflam; Melstar†; ***Indon.:*** Artrilox; Flamoxi; Loxinic; Mecox; Meloxin; Mevilox; Mexpharm; Mobiflex; MoviCox; Movix; Moxam; Moxic; Nulox; Ostelox; Velcox; X-Cam; ***Irl.:*** Areloger; Melcam; Mobic; Mobiglan; Movox; ***Ital.:*** Leutrol; Mobic; ***Jpn:*** Mobic; ***Malaysia:*** Mel-OD; Melocam; Melox; Mobic; Rafree; ***Mex.:*** Aflamid; Anflatox†; Anpre; Auricam; Dolocam; Exel; Flexiver; Flexol; Lexpram; Loxam; Loxibach; Loxibest; Masflex†; Mavicam; Maxoflam; Meflen; Melarthryl; Melican; Melosteral; Menflixil; Mobicox; Promotion; Reosan; Retoflam; ***Neth.:*** Movalis; Movicox; ***Norw.:*** Mobic; ***NZ:*** Mobic; ***Philipp.:*** Melora; Mobic; ***Pol.:*** Aglan; Aspicam; Lormed; Meloksam; Melokssia; Meloxic; MeloxiLek; Meloxistad; Movalis; ***Port.:*** Marlex; Melpor; Movalis; Ziloxican†; ***Rus.:*** Lem (Лем); Melokan (Мелокан); Melox (Мелокс); Mirlox (Мирлокс); Movalis (Мовалис); Movasin (Мовасин); ***S.Afr.:*** Coxflam; Flexocam; Loxiflam; Melflam; Mobic; ***Singapore:*** Melox; Mobic; ***Spain:*** Aliviodol; Movalis; Parocin; Uticox; ***Swed.:*** Latonid†; Mobic; ***Switz.:*** Mobicox; Zilutrol†; ***Thai.:*** Melcam; Melobic; Melox; Mobic; ***Turk.:*** Exen; Melox; Mobic; Zeloxim; ***UK:*** Mobic; ***USA:*** Mobic; ***Venez.:*** Biomelox; Calmox†; Mecox†; Melonax; Melovax; Mobic; Mowin†; Taucaron.

Multi-ingredient: ***Arg.:*** Flexidol Relax; Mextran Flex; ***India:*** Melodol; ***Mex.:*** Dolocam Plus; Dolocartigen; Dorsal; Flexamol; Nuro-B; Retoflam F.

Meptazinol Hydrochloride

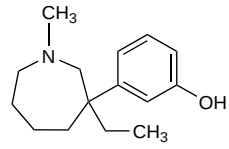
(BANM, USAN, rINNM)

Hidrocloruro de meptazinol; IL-22811 (meptazinol); Meptazinol, Chlorhydrate de; Meptazinoli Hydrochloridum; Wy-22811 (meptazinol). 3-(3-Ethyl-1-methylperhydroazepin-3-yl)phenol hydrochloride.

Мептазинола Гидрохлорид

$C_{15}H_{23}NO,HCl$ = 269.8.

CAS — 54340-58-8 (meptazinol); 59263-76-2 (meptazinol hydrochloride); 34154-59-1 (±-meptazinol hydrochloride).



(meptazinol)

Pharmacopoeias. In *Br.*

BP 2008 (Meptazinol Hydrochloride). A white or almost white powder. Very soluble in water and in methyl alcohol; freely soluble in alcohol; very slightly soluble in acetone; dissolves in dilute solutions of alkali hydroxides. Store at a temperature not exceeding 25°.

Dependence and Withdrawal

As for Opioid Analgesics, p.101.

◊ In assessing the dependence potential of meptazinol, a WHO expert committee[1] noted in 1989 that abrupt discontinuation of chronic meptazinol use precipitated only slight withdrawal signs in *animals* and that meptazinol did not suppress opioid withdrawal signs and symptoms in humans dependent on morphine. Abuse had not been reported. They considered that the likelihood of abuse was moderate and that international control was not warranted at that time.

1. WHO. WHO expert committee on drug dependence: twenty-fifth report. *WHO Tech Rep Ser 775* 1989. Also available at: http://libdoc.who.int/trs/WHO_TRS_775.pdf (accessed 26/06/08)

Adverse Effects, Treatment, and Precautions

As for Opioid Analgesics in general, p.102.

Gastrointestinal adverse effects are commonly reported with meptazinol and include abdominal pain, constipation, dyspepsia, diarrhoea, and nausea and vomiting. Meptazinol is claimed to have a low incidence of respiratory depression; nonetheless, UK licensed prod-