Meclomen advertisement.

[s.l.]: [s.n.], 1984

IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS*

POWER OVER PAIN WITH RAPID AVAILABILITY[1]

Equal to aspirin in five parameters of rheumatoid arthritis therapy*—superior to aspirin in two.
Equal to indomethacin in osteoarthritis.*
Low potential for upper GI ulceration.
Peak plasma levels reached within ½ to 1 hour after a single dose.
Flexible dosing with 50-mg and 100-mg capsules.

MECLOMEN®

50-mg and 100-mg capsules

(meclofenamate sodium capsules, USP)

*Aspirin is considered the preferred initial agent for management of rheumatoid arthritis and osteoarthritis.[2] MECLOMEN is not recommended for initial therapy. Its selection requires careful assessment of the benefit/risk ratio.

Please see next page for brief summary of prescribing information and references.

PARKE-DAVIS

MECLOMEN®

(meclofenamate sodium capsules, USP)

50-mg and 100-mg capsules

RELIABLE OPTION AFTER ASPIRIN*
RAPID AVAILABILITY WITH PROVEN EFFICACY[1]
FLEXIBLE DOSING

*Aspirin is considered the preferred initial agent for management of rheumatoid arthritis and osteoarthritis.[2]
MECLOMEN is not recommended for initial therapy. Its selection requires careful assessment of the benefit/risk ratio.

References: 1. Data on file, Medical Affairs Dept, Parke-Davis.
2. AMA Department of Drugs: AMA Drug Evaluations, ed 4. New York, John Wiley & Sons, Inc, 1980, pp 88, 93.

Meclomen® (meclofenamate sodium capsules, USP)

Before prescribing, please see full prescribing information. A Brief Summary follows:

INDICATIONS AND USAGE: Meclomen is indicated for relief of the signs and symptoms of acute and chronic rheumatoid arthritis and osteoarthritis. Meclomen is not recommended as the initial drug for treatment because of gastrointestinal side effects, including diarrhea which is sometimes severe. Selection of Meclomen requires a careful assessment of the benefit/risk ratio. (See Precautions, Warnings and Adverse Reactions sections.)

The safety and effectiveness of Meclomen have not been established in those patients with rheumatoid arthritis who are designated by the American Rheumatism Association as Functional Class IV (incapacitated, largely or wholly bedridden, or confined to a wheelchair, little or no self-care).

Meclomen is not recommended in children because adequate studies to demonstrate safety and efficacy have not been carried out.

CONTRAINDICATIONS: Meclomen should not be used in patients who have previously exhibited hypersensitivity to it.

Because the potential exists for cross-sensitivity to aspirin or other nonsteroidal antiinflammatory drugs, Meclomen should not be given to patients in whom these drugs induce symptoms of bronchospasm, allergic rhinitis, or urticaria.

WARNINGS: In patients with a history of upper gastrointestinal tract disease, Meclomen should be given under close supervision and only after consulting the Adverse Reactions section. Peptic ulceration and gastrointestinal bleeding, sometimes severe, including one fatality, have been reported in patients receiving Meclomen.

Diarrhea, gastrointestinal irritation and abdominal pain may be associated with Meclomen therapy. Dosage reduction or temporarily stopping the drug have generally controlled these symptoms. (See Adverse Reactions and Dosage and Administration sections.)

PRECAUTIONS: General: Patients receiving nonsteroidal antiinflammatory agents, such as Meclomen, should be evaluated periodically to insure that the drug is still necessary and well tolerated. (See other Precautions, Warnings and Adverse Reactions.)

Decreases in hemoglobin and/or hematocrit levels have occurred in approximately 1 of 6 patients, but rarely required discontinuation of Meclomen therapy. The clinical data revealed no evidence of increased chronic blood loss, bone marrow suppression, or hemolysis to account for the decreases in hemoglobin or hematocrit levels. Patients who are receiving long-term Meclomen therapy should have hemoglobin and hematocrit values determined if anemia is suspected on clinical grounds.

If a patient develops visual symptoms (see Adverse Reactions) during Meclomen therapy, the drug should be discontinued and the patient should have a complete ophthalmologic examination.

When Meclomen is used in combination with steroid therapy, any reduction in steroid dosage should be gradual to avoid the possible complications of sudden steroid withdrawal.

Adverse effects are seen more commonly in the elderly, therefore a lower starting dose and careful follow-up are advised.

As with other nonsteroidal antiinflammatory drugs, borderline elevations of one or more liver tests may occur in some patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Meaningful (3 times the upper limit of normal) elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with Meclomen. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with other nonsteroidal antiinflammatory drugs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (eg, eosinophilia, rash), Meclomen should be discontinued.

Information for Patients: Patients should be advised that nausea, vomiting, diarrhea and abdominal pain have been associated with the use of Meclomen. The patient should be made aware of a possible drug connection and accordingly should consider discontinuing the drug and contacting his or her physician if any of these conditions are severe.

Meclomen may be taken with meals or milk to control gastrointestinal complaints. Concomitant administration of an antacid (specifically, aluminum and magnesium hydroxides) does not interfere with the absorption of the drug.

Laboratory Tests: Patients receiving long-term Meclomen therapy should have hemoglobin and hematocrit values determined if signs or symptoms of anemia occur.

Low white blood cell counts were rarely observed in clinical trials. These low counts were transient and usually returned to normal while the patient continued on Meclomen therapy. Persistent leukopenia, granulocytopenia, or thrombocytopenia warrants further clinical evaluation and may require discontinuation of the drug.

When abnormal blood chemistry values are obtained, follow-up studies are indicated.

Elevations of serum transaminase levels and of alkaline phosphatase levels occurred in approximately 4% of patients. An occasional patient had elevations of serum creatinine or BUN levels.

Drug Interactions:

1. **Warfarin:** Meclomen enhances the effect of warfarin. Therefore when Meclomen is given to a patient receiving warfarin, the dosage of warfarin should be reduced to prevent excessive prolongation of the prothrombin time.
2. **Aspirin:** Concurrent administration of aspirin may lower Meclomen plasma levels, possibly by competing for protein-binding sites. The urinary excretion of Meclomen is unaffected by aspirin, indicating no change in Meclomen absorption. Meclomen does not affect serum salicylate levels. Greater fecal blood loss results from concomitant administration of both drugs than from either drug alone.
3. **Propoxyphene:** The concurrent administration of propoxyphene hydrochloride does not affect the bioavailability of Meclomen (meclofenamate sodium capsules, USP).
4. **Antacids:** Concomitant administration of aluminum and magnesium hydroxides does not interfere with absorption of Meclomen.

Carcinogenesis: An 18-month study in rats revealed no evidence of carcinogenicity.

Usage in Pregnancy: Meclomen like aspirin and other nonsteroidal antiinflammatory drugs causes fetotoxicity, minor skeletal malformations, eg, supernumerary ribs, and delayed ossification in rodent reproduction trials, but no major teratogenicity. Similarly, it prolongs gestation and interferes with parturition and with normal development of young before weaning. Meclomen is not recommended for use during pregnancy, particularly in the 1st and 3rd trimesters based on these animal findings. There are, however, no adequate and well-controlled studies in pregnant women.

Usage in Nursing Mothers: It is not known whether Meclomen is excreted in human milk. Because of the effects on suckling rodents and the fact that many drugs are excreted in human milk, Meclomen is not recommended for nursing women.

Pediatric Use: Safety and effectiveness in children below the age of 14 have not been established.

ADVERSE REACTIONS

Incidence Greater than 1%.

The following adverse reactions were observed in clinical trials and included observations from more than 2,700 patients, 594 of whom were treated for one year and 248 for at least two years.

Gastrointestinal: The most frequently reported adverse reactions associated with Meclomen involve the gastrointestinal system. In controlled studies of up to six months' duration, these disturbances occurred in the following decreasing order of frequency with the approximate incidences in parentheses: diarrhea (10%-33%), nausea with or without vomiting (11%), other gastrointestinal disorders (10%), and abdominal pain.* In long-term uncontrolled studies of up to four years' duration, one third of the patients had at least one episode of diarrhea some time during Meclomen therapy.

In approximately 4% of the patients in controlled studies, diarrhea was severe enough to require discontinuation of Meclomen. The occurrence of diarrhea is dose related, generally subsides with dose reduction, and clears with termination of therapy. The incidence of diarrhea in patients with osteoarthritis is generally lower than that reported in patients with rheumatoid arthritis.

Other reactions less frequently reported were pyrosis,* flatulence,* anorexia, constipation, stomatitis and peptic ulcer. The majority of the patients with peptic ulcer had either a history of ulcer disease or were receiving concomitant antiinflammatory drugs, including corticosteroids which are known to produce peptic ulceration.

Cardiovascular: edema
Dermatologic: rash,* urticaria, pruritus
Central Nervous System: headache,* dizziness*
Special Senses: tinnitus

*Incidence between 3% and 9%. Those reactions occurring in 1% to 3% of patients are not marked with an asterisk.

Incidence Less than 1%.
Probably Causally Related

The following adverse reactions were reported less frequently than 1% during controlled clinical trials and through voluntary reports since marketing. The probability of a causal relationship exists between the drug and these adverse reactions.

Gastrointestinal: Bleeding and/or perforation with or without obvious ulcer formation
Renal: Renal failure
Hematologic: Neutropenia, thrombocytopenic purpura, leukopenia, agranulocytosis, hemolytic anemia, eosinophilia, decrease in hemoglobin and/or hematocrit
Dermatologic: Erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis
Hepatic: Alteration of liver function tests
Allergic: Lupus and serum sickness-like symptoms

Incidence Less than 1%.
Causal Relationship Unknown

Other reactions have been reported but under conditions where a causal relationship could not be established. However, in these rarely reported events, that possibility cannot be excluded. Therefore, these observations are listed to alert physicians.

Cardiovascular: palpitations
Central Nervous System: malaise, fatigue, paresthesia, insomnia, depression
Special Senses: blurred vision, taste disturbances, decreased visual acuity, temporary loss of vision, reversible loss of color vision, retinal changes including macular fibrosis, macular and perimacular edema, conjunctivitis, iritis
Renal: nocturia
Gastrointestinal: paralytic ileus
Dermatologic: erythema nodosum, hair loss
Storage: Store at a room temperature below 30°C (86°F). Protect from moisture and light.

0268G130

PARKE-DAVIS
Division of Warner-Lambert Company
Morris Plains, New Jersey 07950

PD-07-JA-1452-P-2(11-83)

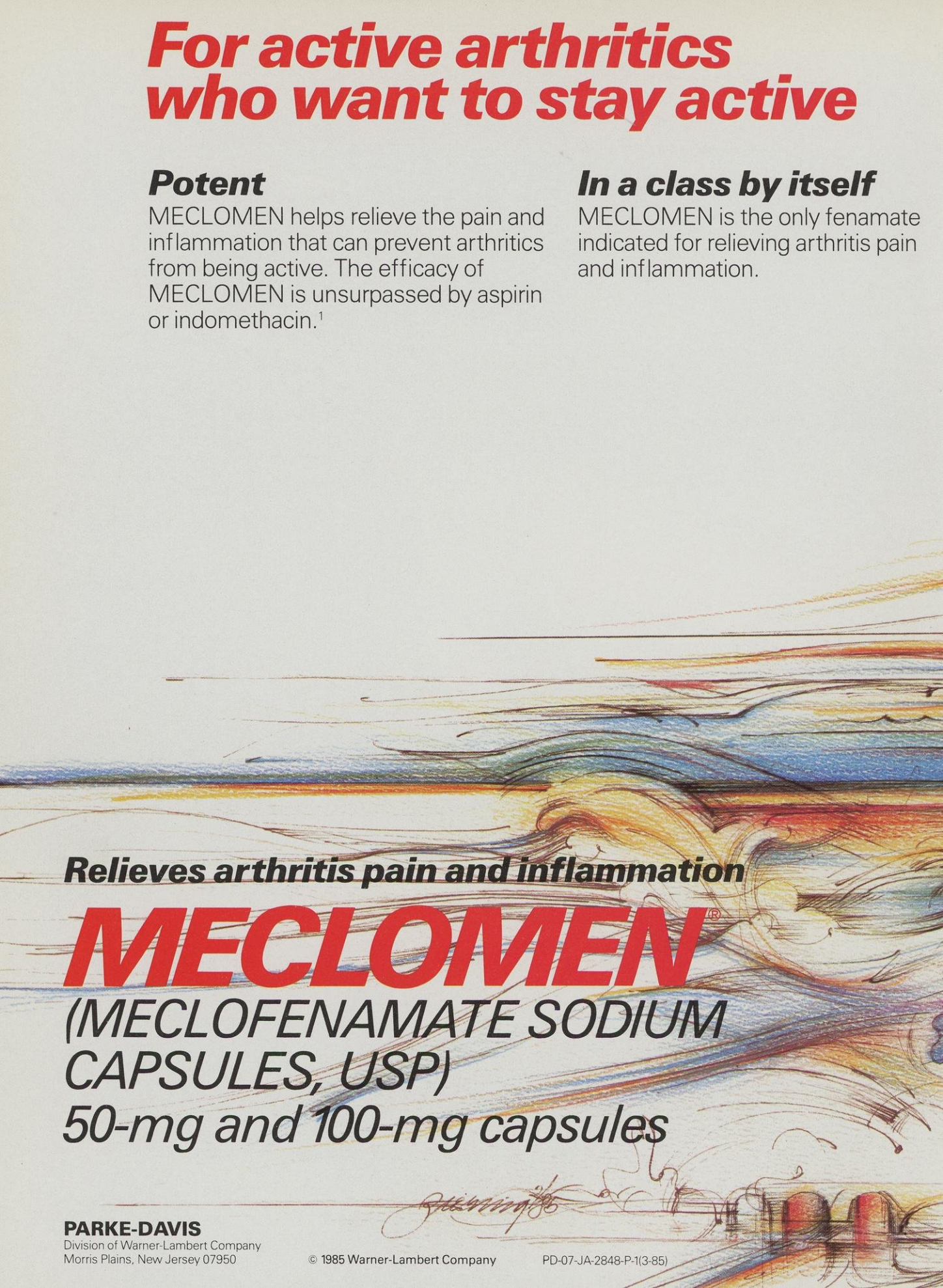
For active arthritics who want to stay active

Potent

MECLOMEN helps relieve the pain and inflammation that can prevent arthritics from being active. The efficacy of MECLOMEN is unsurpassed by aspirin or indomethacin.[1]

In a class by itself

MECLOMEN is the only fenamate indicated for relieving arthritis pain and inflammation.



Relieves arthritis pain and inflammation

MECLOMEN®

(MECLOFENAMATE SODIUM CAPSULES, USP)

50-mg and 100-mg capsules

PARKE-DAVIS
Division of Warner-Lambert Company
Morris Plains, New Jersey 07950

PD-07-JA-2848-P-1(3-85)

Dosage flexibility

MECLOMEN reaches peak plasma levels in as little as 30 minutes and has a single-dose half-life of just two hours, permitting rapid dosage adjustment. Although improvement may be seen in a few days, two to three weeks of treatment may be necessary to obtain optimum therapeutic benefit.

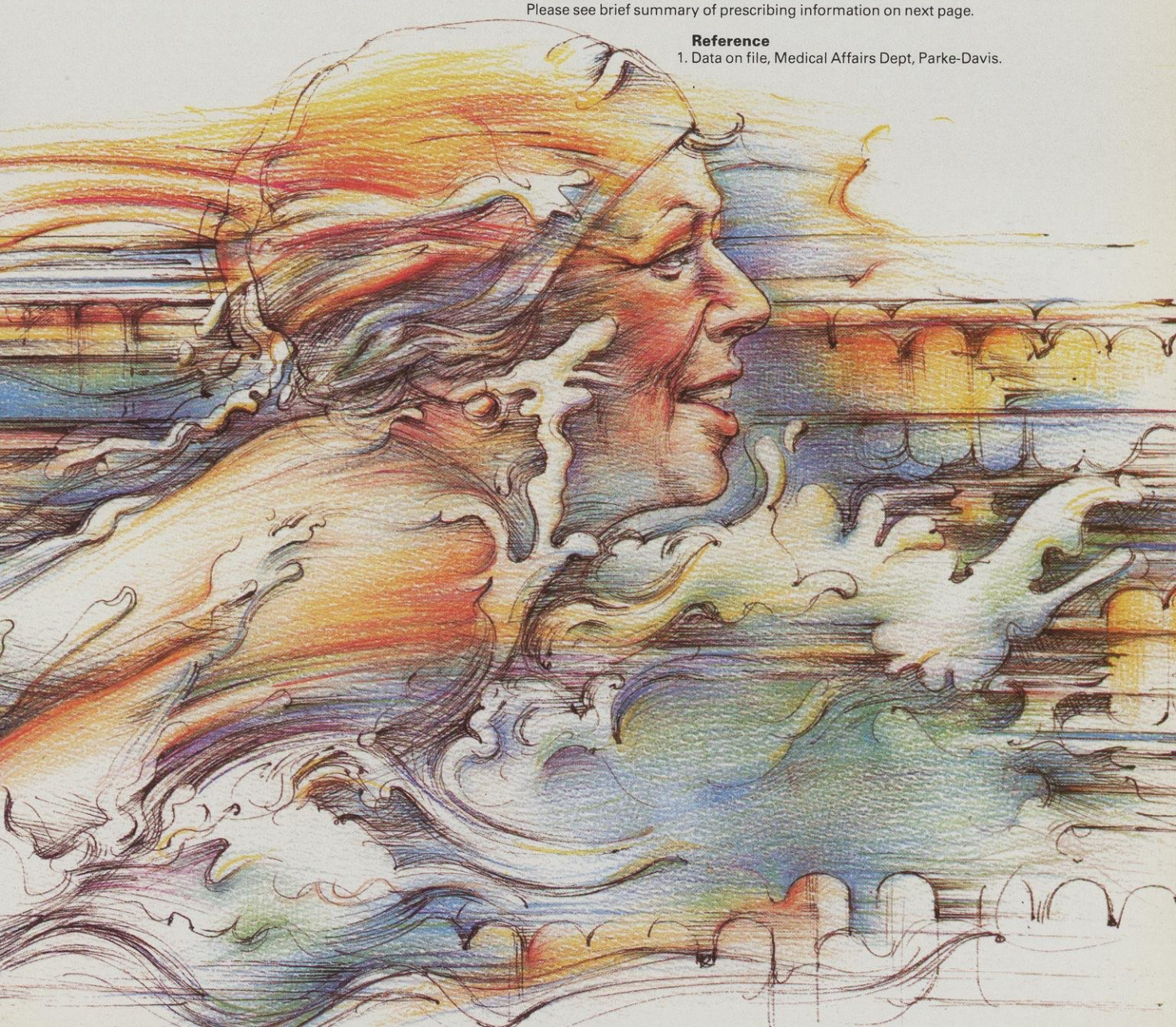
Tolerability

MECLOMEN has demonstrated a low potential for upper GI ulceration.[1] At 200 to 300 mg per day, MECLOMEN has a side effect profile that promotes compliance and successful therapy. Prescribe MECLOMEN as a therapeutic regimen for patients who are not responding adequately to current therapy.

Please see brief summary of prescribing information on next page.

Reference

1. Data on file, Medical Affairs Dept, Parke-Davis.



Relieves arthritis pain and inflammation

MECLOMEN® (MECLOFENAMATE SODIUM CAPSULES, USP)

50-mg and 100-mg capsules

Meclomen® (meclofenamate sodium capsules, USP)
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Renal Effects: As with other nonsteroidal antiinflammatory drugs, long-term administration of meclofenamate sodium to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome.

A second form of renal toxicity has been seen in patients with prerenal conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly. Discontinuation of NSAID therapy is typically followed by recovery to the pretreatment state.

Since Meclomen is eliminated primarily by the kidneys, patients with significantly impaired renal function should be closely monitored; a lower daily dosage should be anticipated to avoid excessive drug accumulation.

Information for Patients: Patients should be advised that nausea, vomiting, diarrhea and abdominal pain have been associated with the use of Meclomen.The patient should be made aware of a possible drug connection and accordingly should consider discontinuing the drug and contacting his or her physician if any of these conditions are severe.

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2. **Aspirin:** Concurrent administration of aspirin may lower Meclomen plasma levels, possibly by competing for protein-binding sites. The urinary excretion of Meclomen (meclofenamate sodium capsules, USP) is unaffected by aspirin, indicating no change in Meclomen absorption. Meclomen does not affect serum salicylate levels. Greater fecal blood loss results from concomitant administration of both drugs than from either drug alone.
3. **Propoxyphene:** The concurrent administration of propoxyphene hydrochloride does not affect the bioavailability of Meclomen.
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Carcinogenesis: An 18-month study in rats revealed no evidence of carcinogenicity.

Usage in Pregnancy: Meclomen like aspirin and other nonsteroidal antiinflammatory drugs causes fetotoxicity, minor skeletal malformations, eg, supernumerary ribs, and delayed ossification in rodent reproduction trials, but no major teratogenicity. Similarly, it prolongs gestation and interferes with parturition and with normal development of young before weaning. Meclomen is not recommended for use during pregnancy, particularly in the 1st and 3rd trimesters based on these animal findings. There are, however, no adequate and well-controlled studies in pregnant women.

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ADVERSE REACTIONS: Incidence Greater than 1%.

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In approximately 4% of the patients in controlled studies, diarrhea was severe enough to require discontinuation of Meclomen. The occurrence of diarrhea is dose related, generally subsides with dose reduction, and clears with termination of therapy. The incidence of diarrhea in patients with osteoarthritis is generally lower than that reported in patients with rheumatoid arthritis.

Other reactions less frequently reported were pyrosis,* flatulence,* anorexia, constipation, stomatitis and peptic ulcer. The majority of the patients with peptic ulcer had either a history of ulcer disease or were receiving concomitant antiinflammatory drugs, including corticosteroids which are known to produce peptic ulceration.

Cardiovascular: edema
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Central Nervous System: headache,* dizziness*
Special Senses: tinnitus

*Incidence between 3% and 9%. Those reactions occurring in 1% to 3% of patients are not marked with an asterisk.

Incidence Less than 1%.
Probably Causally Related

The following adverse reactions were reported less frequently than 1% during controlled clinical trials and through voluntary reports since marketing. The probability of a causal relationship exists between the drug and these adverse reactions.

Gastrointestinal: Bleeding and/or perforation with or without obvious ulcer formation, colitis, cholestatic jaundice
Renal: Renal failure
Hematologic: Neutropenia, thrombocytopenic purpura, leukopenia, agranulocytosis, hemolytic anemia, eosinophilia, decrease in hemoglobin and/or hematocrit
Dermatologic: Erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis
Hepatic: Alteration of liver function tests
Allergic: Lupus and serum sickness-like symptoms

Incidence Less than 1%.
Causal Relationship Unknown

Other reactions have been reported but under conditions where a causal relationship could not be established. However, in these rarely reported events, that possibility cannot be excluded. Therefore, these observations are listed to alert physicians.

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Special Senses: blurred vision, taste disturbances, decreased visual acuity, temporary loss of vision, reversible loss of color vision, retinal changes including macular fibrosis, macular and perimacular edema, conjunctivitis, iritis
Renal: nocturia
Gastrointestinal: paralytic ileus
Dermatologic: erythema nodosum, hair loss

OVERDOSAGE: The following is based on the little information available concerning overdosage with Meclomen and related compounds. After a massive overdose, CNS stimulation may be manifested by irrational behavior, marked agitation and generalized seizures. Following this phase, renal toxicity (falling urine output, rising creatinine, abnormal urinary cellular elements) may be noted with possible oliguria or anuria and azotemia. One patient was anuric for about a week before diuresis and recovery occurred.

Management consists of emptying the stomach by emesis or lavage and instilling an ample dose of activated charcoal into the stomach. There is some evidence that charcoal will actively absorb Meclomen, but dialysis or hemoperfusion may be less effective because of plasma protein binding. The seizures should be controlled by an appropriate anticonvulsant regimen. Attention should be directed throughout, by careful monitoring, to the preservation of vital functions and fluid-electrolyte balance. Dialysis may be required to correct serious azotemia or electrolyte imbalance.

Storage: Store at a room temperature below 30°C (86°F). Protect from moisture and light.

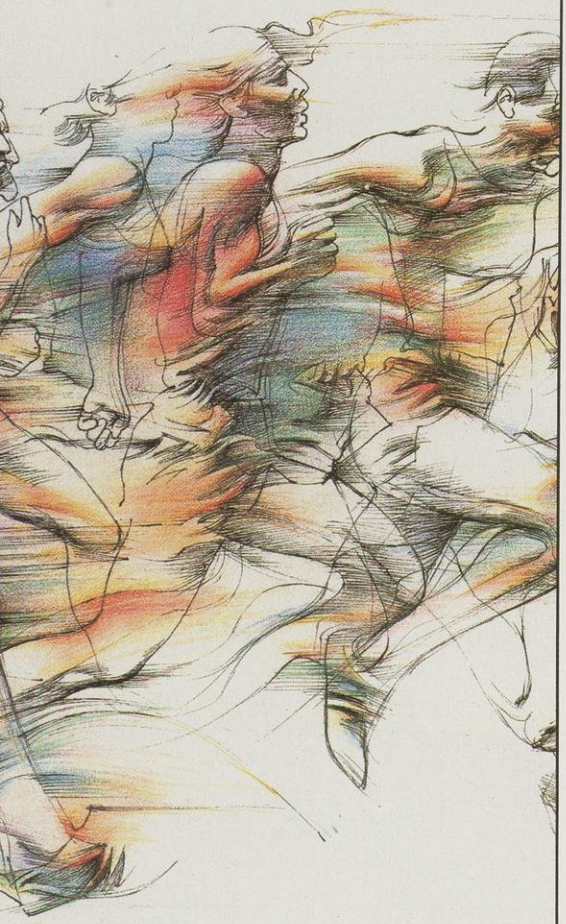
Caution—Federal law prohibits dispensing without prescription.

0268G132

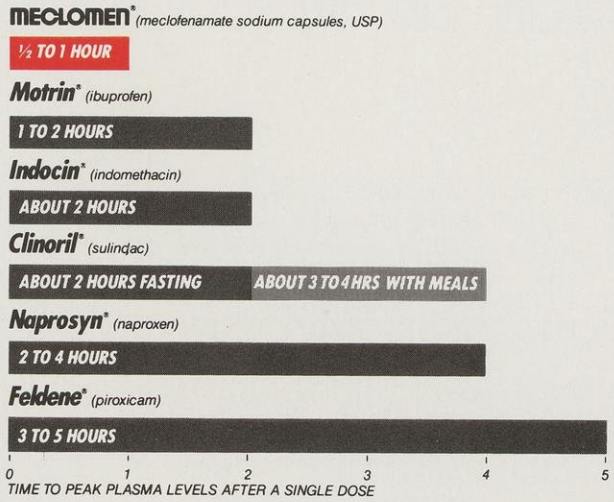
PARKE-DAVIS
Division of Warner-Lambert Company
Morris Plains, New Jersey 07950

PD-07-JA-2848-P-1(9-85)

POTENT RELIEF



The added stress of pleasurable activities can often bring painful consequences for your osteoarthritis patients. Prescribe Meclomen to initiate relief of pain and symptoms of OA. Meclomen is rapidly available—reaching peak plasma levels in as little as 30 minutes.[1]*



Meclomen is as effective as indomethacin in acute and chronic pain of osteoarthritis. Yet it has a low order of upper GI ulceration[2]—promoting successful therapy.

Usual dosage is simple: 50 mg four times a day as needed for the pain of osteoarthritis.†

So let your patients enjoy their pleasure...let Meclomen relieve their arthritis pain.

Please see next page for brief summary of prescribing information.

*Although antiinflammatory improvement may be seen in a few days, two to three weeks of treatment may be necessary to obtain optimum therapeutic benefit.

†Aspirin is considered the preferred initial agent for management of osteoarthritis.[3] Meclomen is not recommended for initial therapy. Its selection requires careful assessment of the benefit/risk ratio.

References 1. Official package inserts. 2. Data on file, Medical Affairs Dept, Parke-Davis. 3. AMA Department of Drugs: AMA Drug Evaluations, ed 4. New York, John Wiley & Sons, Inc, 1980, p 93.

MECLOMEN®
(meclofenamate sodium capsules, USP)

ACTIVE ANALGESIC ACTION FOR ACTIVE ARTHRITICS

PARKE-DAVIS

ACTIVE ANALGESIC ACTION FOR ACTIVE ARTHRITICS

MECLOMEN®
50-mg and 100-mg capsules
(meclofenamate sodium capsules, USP)

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4. **Antacids:** Concomitant administration of aluminum and magnesium hydroxides does not interfere with absorption of Meclomen.

Carcinogenesis: An 18-month study in rats revealed no evidence of carcinogenicity.

Usage in Pregnancy: Meclomen like aspirin and other nonsteroidal antiinflammatory drugs causes fetotoxicity, minor skeletal malformations, eg, supernumerary ribs, and delayed ossification in rodent reproduction trials, but no major teratogenicity. Similarly, it prolongs gestation and interferes with parturition and with normal development of young before weaning. Meclomen is not recommended for use during pregnancy, particularly in the 1st and 3rd trimesters based on these animal findings. There are, however, no adequate and well-controlled studies in pregnant women.

Usage in Nursing Mothers: It is not known whether Meclomen is excreted in human milk. Because of the effects on suckling rodents and the fact that many drugs are excreted in human milk, Meclomen is not recommended for nursing women.

Pediatric Use: Safety and effectiveness in children below the age of 14 have not been established.

ADVERSE REACTIONS

Incidence Greater than 1%.

The following adverse reactions were observed in clinical trials and included observations from more than 2,700 patients, 594 of whom were treated for one year and 248 for at least two years.

Gastrointestinal: The most frequently reported adverse reactions associated with Meclomen involve the gastrointestinal system. In controlled studies of up to six months' duration, these disturbances occurred in the following decreasing order of frequency with the approximate incidences in parentheses: diarrhea (10%-33%), nausea with or without vomiting (11%), other gastrointestinal disorders (10%), and abdominal pain.* In long-term uncontrolled studies of up to four years' duration, one third of the patients had at least one episode of diarrhea some time during Meclomen therapy.

In approximately 4% of the patients in controlled studies, diarrhea was severe enough to require discontinuation of Meclomen. The occurrence of diarrhea is dose related, generally subsides with dose reduction, and clears with termination of therapy. The incidence of diarrhea in patients with osteoarthritis is generally lower than that reported in patients with rheumatoid arthritis.

Other reactions less frequently reported were pyrosis,* flatulence,* anorexia, constipation, stomatitis and peptic ulcer. The majority of the patients with peptic ulcer had either a history of ulcer disease or were receiving concomitant antiinflammatory drugs, including corticosteroids which are known to produce peptic ulceration.

Cardiovascular: edema
Dermatologic: rash,* urticaria, pruritus
Central Nervous System: headache,* dizziness*
Special Senses: tinnitus

* Incidence between 3% and 9%. Those reactions occurring in 1% to 3% of patients are not marked with an asterisk.

Incidence Less than 1%.
Probably Causally Related

The following adverse reactions were reported less frequently than 1% during controlled clinical trials and through voluntary reports since marketing. The probability of a causal relationship exists between the drug and these adverse reactions.

Gastrointestinal: Bleeding and/or perforation with or without obvious ulcer formation
Renal: Renal failure
Hematologic: Neutropenia, thrombocytopenic purpura, leukopenia, agranulocytosis, hemolytic anemia, eosinophilia, decrease in hemoglobin and/or hematocrit
Dermatologic: Erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis
Hepatic: Alteration of liver function tests
Allergic: Lupus and serum sickness-like symptoms

Incidence Less than 1%.
Causal Relationship Unknown

Other reactions have been reported but under conditions where a causal relationship could not be established. However, in these rarely reported events, that possibility cannot be excluded. Therefore, these observations are listed to alert physicians.

Cardiovascular: palpitations
Central Nervous System: malaise, fatigue, paresthesia, insomnia, depression
Special Senses: blurred vision, taste disturbances, decreased visual acuity, temporary loss of vision, reversible loss of color vision, retinal changes including macular fibrosis, macular and perimacular edema, conjunctivitis, iritis
Renal: nocturia
Gastrointestinal: paralytic ileus
Dermatologic: erythema nodosum, hair loss
Storage: Store at a room temperature below 30°C (86°F). Protect from moisture and light.

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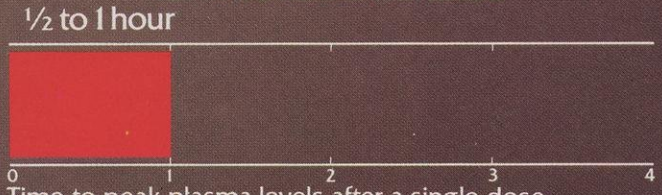

Time to peak plasma levels after a single dose

*Although improvement may be seen in a few days, two to three weeks of treatment may be necessary to obtain optimum therapeutic benefit.

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REFERENCE 1. Data on file, Medical Affairs Dept, Parke-Davis.

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Please see next page for brief summary of prescribing information.