



Therapeutic Class ReviewSM

Pain & Inflammation –topical diclofenac 1.3% patch (Flector[®]) & 1% gel (Voltaren[®])

June 2008

New Product for Review:

diclofenac (Flector[®]) 1.3% patch [Alpharma]
diclofenac gel (Voltaren) [Novartis/Endo]

Dossier Provided by Manufacturer: Yes for both
Dossier Evaluation: 3

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- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

Executive Summary

- Flector is a topical patch formulation of diclofenac epolamine 1.3%.
 - It was approved by the FDA on January 31, 2007, and launched in January 2008.
 - It is indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions.
 - One patch is applied twice daily.
- Voltaren is a topical gel formulation of diclofenac sodium 1% gel.
 - It is indicated for the relief of pain of osteoarthritis of joints amenable to topical treatment, such as the knees and hands.
 - The gel is applied four times a day.
- It is unclear whether topical diclofenac's lower systemic exposure results in any clinically significant advantages over oral diclofenac.

Evidence

- No evidence was critiqued as useful (Grade A) or possibly useful (Grade B) for either of the topical diclofenac products.
- Safety:
 - Topical NSAID prescribing information contains the same Black Box Warnings as the FDA-approved oral NSAIDs for cardiovascular and gastrointestinal risks.
 - The prescribing information for topical diclofenac lists the same drug interactions as oral diclofenac including: ACE-inhibitors, aspirin, diuretics, lithium, methotrexate, and warfarin.

- Similar to other patches, potential risk exists for a small child or pet to suffer serious adverse effects from chewing or ingesting a new or used diclofenac patch (Flector). Used patches may still contain a large amount of diclofenac (as much as 170 mg).
- Concomitant administration of diclofenac gel (Voltaren) with:
 - Oral NSAIDs or aspirin may result in increased adverse NSAID effects. ^[6]
 - Other topical products, including topical medications, sunscreens, lotions, moisturizers, and cosmetics, on the same skin site has not been tested and should be avoided because of the potential to alter local tolerability and absorption. ^[6]

Decision

Diclofenac patch (Flector) and diclofenac gel (Voltaren) are non-preferred/non-formulary because they add significant cost without adding value over the many generic, preferred brand, and over-the-counter medications options available to suit the needs of most patients.

Products

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^d
celecoxib (Celebrex)	12/1998	5/2014	<ul style="list-style-type: none"> • Ankylosing spondylitis • Familial multiple polyposis syndrome • Juvenile rheumatoid arthritis • Osteoarthritis • Pain, acute • Primary dysmenorrhea • Rheumatoid arthritis 	100-400mg daily (either QD-BID) max 400mg per day	<ul style="list-style-type: none"> • Chronic paroxysmal hemicrania • Schizophrenia; Adjunct • Systemic lupus erythematosus
diclofenac potassium	11/1993	N/A	<ul style="list-style-type: none"> • Osteoarthritis • Pain (Mild to Moderate) • Primary dysmenorrhea • Rheumatoid arthritis 	50 mg ORALLY 2 to 4 times a day, MAX 225 mg/day	<ul style="list-style-type: none"> - General finding of soft tissue – Pain - Gout - Migraine - Post-episiotomy pain
diclofenac (Flector) 1.3% patch	1/2007	1/2010	Pain, acute, Due to minor strains, sprains, and contusions	one topical patch (180 milligrams) applied to the most painful site twice daily	
diclofenac (Voltaren) gel	10/2007	10/2010	treating pain associated with osteoarthritis in joints amenable to topical treatment, such as the knees and those of the hands	Topical gel, 4 g applied to lower extremities 4 times daily; 2 g applied to upper extremities 4 times daily; MAX 16 g/day to any single joint of lower extremity, 8 g/day to any single joint of upper extremity, 32 g/day total over all affected joints	

Products (Continued)

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^d
diclofenac sodium, diclofenac sodium XR	9/1995	N/A	<ul style="list-style-type: none"> Ankylosing spondylitis Osteoarthritis Rheumatoid arthritis 	100-200 mg/day ORALLY in 3 or 4 divided doses (MAX 225 mg/day); Enteric-coated, 100-200 mg/day in divided doses	<ul style="list-style-type: none"> Biliary colic Colorectal cancer; Prophylaxis Fever General finding of soft tissue – Pain Gout Migraine Myalgia Operation on oral cavity – Pain Pain Post-episiotomy pain Primary dysmenorrhea
diflunisal (Dolobid)	4/1982	N/A	<ul style="list-style-type: none"> Osteoarthritis Pain (Mild to Moderate) Rheumatoid arthritis 	250 to 1000 mg PO daily in 2 divided doses; max 1500 mg/day	<ul style="list-style-type: none"> Backache Dysmenorrhea Soft tissue injury
etodolac	1/1991	N/A	<ul style="list-style-type: none"> Juvenile rheumatoid arthritis Osteoarthritis Rheumatoid arthritis Pain 	400 to 1000 mg ORALLY once a day; immediate release, 600 to 1000 mg/day ORALLY divided 2 to 4 times; MAX 1200 mg/day	
fenoprofen	Prior to 1982	N/A	<ul style="list-style-type: none"> Osteoarthritis Pain (Mild to Moderate) Rheumatoid arthritis 	300 mg to 600 mg ORALLY 3 to 4 times a day, up to a total of 3,200 mg per day	<ul style="list-style-type: none"> Migraine Tendinitis
flurbiprofen	10/1988	N/A	<ul style="list-style-type: none"> Osteoarthritis: Rheumatoid arthritis: 	200 to 300 mg/day ORALLY given in 2 to 4 divided doses; MAX 100 mg/dose, 300 mg/day	<ul style="list-style-type: none"> Ankylosing spondylitis: Dental pain: Gynecological procedure Migraine Pain in throat
ibuprofen	Prior to 1982	N/A	<ul style="list-style-type: none"> Fever Headache: Migraine: Osteoarthritis Pain Primary dysmenorrhea: Rheumatoid arthritis: 	1200 to 3200 mg/day ORALLY divided in 3 to 4 doses	Cystic fibrosis

Products (Continued)

Drug Products	FDA approval^a	Patent Expiration(s)^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses^d
indomethacin	Prior to 1982	N/A	<ul style="list-style-type: none"> • Ankylosing spondylitis • Osteoarthritis • Rheumatoid arthritis • Gouty arthritis • Pain, acute - Shoulder pain • Patent ductus arteriosus 	25 to 50 mg ORALLY or RECTALLY 2 to 3 times a day, MAX 200 mg/day, 100 mg/dose	<ul style="list-style-type: none"> • Cholecystitis • Dysmenorrhea • Fever • Headache • Hypotension • Male infertility • Neurogenic hyperthermia • Pain • Polyhydramnios • Preterm labor; Prophylaxis • Systemic lupus erythematosus • Toxicity of drug, Muromonab • Ureteric colic
indomethacin SR	2/1982	N/A	<ul style="list-style-type: none"> • Ankylosing spondylitis • Osteoarthritis • Rheumatoid arthritis 	75 mg ORALLY once or twice a day	
ketoprofen	1/1986	N/A	<ul style="list-style-type: none"> • Fever • Osteoarthritis • Pain • Primary dysmenorrhea • Rheumatoid arthritis 	12.5 mg -50 mg ORALLY every 6-8 hours as needed, MAX 300 mg/day	<ul style="list-style-type: none"> • Soft tissue injury
ketoprofen SR	9/1993	N/A	-	100-200 mg ORALLY once a day	
ketorolac	11/1989	N/A	<ul style="list-style-type: none"> • Arthritis • Disorder of soft tissue • Inflammatory disorder • Pain • Rheumatoid arthritis 	<ul style="list-style-type: none"> • IM/IV 15-30mg q6h • PO: 10 mg every 4 to 6 hours prn , max 40mg/day • Max therapy 5 days 	<ul style="list-style-type: none"> • Cholecystectomy - Postoperative pain • Gouty arthritis, acute • Headache • Renal colic
meclofenamate	Prior to 1982	N/A	<ul style="list-style-type: none"> • Dysmenorrhea • Menorrhagia • Osteoarthritis • Pain • Rheumatoid arthritis 	100 to 400 mg/day in 3 to 4 equally divided doses. Max dose 400 mg/day	<ul style="list-style-type: none"> • Ankylosing spondylitis • Episiotomy - Pain • Gout • Nephrotic syndrome
mefenamic acid	Prior to 1982	N/A	<ul style="list-style-type: none"> • Dysmenorrhea • Low back pain • Pain 	500 mg, followed by 250 mg every 6 H	<ul style="list-style-type: none"> • Fever • Menorrhagia • Premenstrual syndrome
meloxicam	4/2000	N/A	<ul style="list-style-type: none"> • Osteoarthritis • Rheumatoid arthritis • Juvenile rheumatoid arthritis, polyarticular - Pauciarticular juvenile rheumatoid arthritis 	7.5 mg ORALLY once a day, MAX 15 mg ORALLY once a day	<ul style="list-style-type: none"> • Sciatica
nabumetone	12/1991	N/A	<ul style="list-style-type: none"> • Osteoarthritis • Rheumatoid arthritis 	1000-2000 mg/day ORALLY divided 1-2 times	<ul style="list-style-type: none"> • Soft tissue injury

Products (Continued)

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^d
naproxen/naproxen sodium	Prior to 1982	N/A	<ul style="list-style-type: none"> Ankylosing spondylitis Bursitis Fever Gout, acute Headache Osteoarthritis Pain Primary dysmenorrhea Rheumatoid arthritis Tendinitis 	<ul style="list-style-type: none"> 250-500 mg ORALLY twice a day; MAX 1500 mg/day OR 200-400mg every 6 to 8 hours as needed 	<ul style="list-style-type: none"> Cancer - Fever Colorectal cancer; Prophylaxis Disorder of musculoskeletal system Inflammatory disorder Menorrhagia Primary degenerative dementia of the Alzheimer type, presenile onset, uncomplicated; Prophylaxis Radiation esophagitis Soft tissue injury Systemic lupus erythematosus
oxaprozin	10/1992	N/A	<ul style="list-style-type: none"> Osteoarthritis: Rheumatoid arthritis Juvenile rheumatoid arthritis 	1200 mg ORALLY once a day, MAX 1800 mg/day or 26 mg/kg/day	<ul style="list-style-type: none"> Bursitis – Tendonitis Dental pain
piroxicam	4/1982	N/A	<ul style="list-style-type: none"> Osteoarthritis Rheumatoid arthritis 	20 mg/day ORALLY, may give in a single daily dose or divide and give twice daily	<ul style="list-style-type: none"> Cancer pain; Adjunct Dental pain Dysmenorrhea Gouty arthritis Post-episiotomy pain Postop pain Soft tissue injury
sulindac	Prior to 1982	N/A	<ul style="list-style-type: none"> Ankylosing spondylitis Gouty arthritis, acute Osteoarthritis Rheumatoid arthritis Shoulder pain 	150 mg -200 mg ORALLY twice a day, MAX 400 mg/day	<ul style="list-style-type: none"> Familial multiple polyposis syndrome Familial multiple polyposis syndrome; Prophylaxis
tolmetin	Prior to 1982	N/A	<ul style="list-style-type: none"> Osteoarthritis: Rheumatoid arthritis Juvenile rheumatoid arthritis 	200 to 600 mg ORALLY three times a day, maximum 1800 mg/day	<ul style="list-style-type: none"> Colorectal cancer; Prophylaxis

^a Date applies to approval date for the original brand name medication where there are now generics available.

^c Based on patents listed in Orange Book as of 04/30/2008.

^d As listed in © 1974 - 2008 Thomson MICROMEDEX database or as referenced.

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