Therapy, Vitamin D Reduce Falls, Readmissions

BY KERRI WACHTER

DENVER — Extended physiotherapy significantly reduced the rate of falls among patients with a prior hip fracture, and high-dose vitamin D significantly reduced the rate of hospital readmissions in a study of 173 patients.

A program of extended physiotherapy reduced the fall rate by 25%, compared with standard postfracture physiotherapy; high-dose vitamin D therapy reduced the hospital readmission rate by 39%, compared with a lower dose, the researchers found.

"The extended physiotherapy program, together with 2,000 IU vitamin D, has complementary benefits on post–hip fracture care," Dr. Heike Bischoff-Ferrari said at the annual meeting of the American Society for Bone and Mineral Research.

The researchers enrolled 173 patients after their first acute hip fracture. Of these, most (79%) were women. Their mean age was 84 years, and 77% were living in the community. Half (51%) of the patients had severe vitamin D deficiency with serum 25-hydroxyvitamin D levels below 30 nmol/L; almost all (98%) had serum 25-hydroxyvitamin D levels below 75 nmol/L.

Patients were randomized to receive extended physiotherapy or standard physiotherapy. Extended physiotherapy consisted of supervised therapy for 1 hour per day during acute care, plus an unsupervised home program of exercises to perform regularly for 1 year. The standard therapy consisted of supervised therapy for 30 minutes per day during acute care.

Patients were also randomized to receive vitamin D supplementation at 2,000 IU or 800 IU vitamin D_3 per day. All patients received calcium.

Clinical assessment, which included laboratory tests and functional evaluations, took place at baseline and at 6 and 12 months' follow-up. Falls and readmissions were assessed by monthly calls to patients, patient calls to a hotline, and patient diaries.

The primary end point was the rate of falls over 12 months. The secondary end point was the rate of hospital readmission over 12 months.

In all, 86 participants were included in the high-dose vitamin D group and 87 in the lower-dose group; 87 participants were included in the extensive physiotherapy group, and 86 in the regular physiotherapy group. The groups did not differ by age, gender, BMI, cognitive function, baseline 25-hydroxyvitamin D levels, and Charleston Comorbidity Index scores.

The researchers documented 212 falls in 92 participants. Of these, 41% fell once, 26% fell twice, 19% fell three times, and 14% fell more than three times. The rate of falls per patient-year was 1.43. There were 22 new nonvertebral fractures, 9 of which were in the contralateral hip.

In terms of hospital readmissions, there were 74 readmissions among 54 participants. Of these, 72% had one readmission, 20% had two, and 8% had three. The rate of hospital readmission was 50%.

Extended physiotherapy reduced the rate of falls by 25%, compared with regular physiotherapy, a significant reduction. Similar improvements were seen in function. However, extended physiotherapy did not reduce the rate of hospital readmissions.

There was no difference in the fall rate for the two vitamin D groups, but high-dose vitamin D did reduce the rate of hospital readmission by 39%, which was significant. There was also a significant 60% reduction in fall-related injuries. "This was mainly driven by a nonsignificant reduction in repeat nonvertebral fractures by 52%," said Dr. Bischoff-Ferrari of the Centre on Aging and Mobility at the University Hospital Zurich; she is also a visiting scientist in the Bone Metabolism Laboratory at Tufts University, Boston.

In the first year after a hip fracture, an estimated 5%-10% of patients fracture the other hip and 30% are readmitted to acute care. Half of these patients are left with permanent functional impairment, a quarter require long-term care, and 10%-25% die, she said.

Dr. Bischoff-Ferrari reported that she has no relevant financial relationships. ■

Flector® Patch (diclofenac epolamine topical patch) 1.3%
Brief Summary **Rx only**

Cardiovascular Risk: • NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk (See **WARNINGS** and Full Prescribing Information, **CLINICAL TRIALS**). • Flector® Patch is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see **WARNINGS**).
Gastrointestinal Risk: • NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events (See **WARNINGS**).

INDICATION AND USAGE: Carefully consider the potential benefits and risks of Flector® Patch and other treatment options before deciding to use Flector® Patch. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (see **WARNINGS**).
Flector® Patch is indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions.

CONTRAINDICATIONS: Flector® Patch is contraindicated in patients with known hypersensitivity to diclofenac.
Flector® Patch should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients (see **WARNINGS - Anaphylactoid Reactions**, and **PRECAUTIONS - Preexisting Asthma**).
Flector® Patch is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see **WARNINGS**).
Flector® Patch should not be applied to non-intact or damaged skin resulting from any etiology e.g. exudative dermatitis, eczema, infected lesion, burns or wounds.

WARNINGS: CARDIOVASCULAR EFFECTS: Cardiovascular Thrombotic Events: Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV events and the steps to take if they occur.
There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID does increase the risk of serious GI events (see **GI WARNINGS**).
Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke (see **CONTRAINDICATIONS**).
Hypertension: NSAIDs, including Flector® Patch, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including Flector® Patch, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.
Congestive Heart Failure and Edema: Fluid retention and edema have been observed in some patients taking NSAIDs. Flector® Patch should be used with caution in patients with fluid retention or heart failure.
Gastrointestinal Effects- Risk of Ulceration, Bleeding, and Perforation: NSAIDs, including Flector® Patch, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients, who develop a serious upper GI adverse event on NSAID therapy, is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.
NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a *prior history of peptic ulcer disease and/or gastrointestinal bleeding* who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore, special care should be taken in treating this population.
To minimize the potential risk for an adverse GI event in patients treated with an NSAID, the lowest effective dose should be used for the shortest possible duration. Patients and physicians should remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high risk patients, alternate therapies that do not involve NSAIDs should be considered.
Renal Effects: Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of a nonsteroidal anti-inflammatory drug may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which 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 ACE inhibitors, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.
Advanced Renal Disease: No information is available from controlled clinical studies regarding the use of Flector® Patch in patients with advanced renal disease. Therefore, treatment with Flector® Patch is not recommended in these patients with advanced renal disease. If Flector® Patch therapy is initiated, close monitoring of the patient's renal function is advisable.
Anaphylactoid Reactions: As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to Flector® Patch. Flector® Patch should not be given to patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs (see **CONTRAINDICATIONS** and **PRECAUTIONS - Preexisting Asthma**). Emergency help should be sought in cases where an anaphylactoid reaction occurs.
Skin Reactions: NSAIDs, including Flector® Patch, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.
Pregnancy: In late pregnancy, as with other NSAIDs, Flector® Patch should be avoided because it may cause premature closure of the ductus arteriosus.

PRECAUTIONS: General: Flector® Patch cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.
The pharmacological activity of Flector® Patch in reducing inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed noninfectious, painful conditions.
Hepatic Effects: Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including Flector® Patch. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Notable elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials with NSAIDs. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported.
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 a more severe hepatic reaction while on therapy with Flector® Patch. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), Flector® Patch should be discontinued.
Hematological Effects: Anemia is sometimes seen in patients receiving NSAIDs. This may be due to fluid retention, occult or gross GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including Flector® Patch, should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia.
NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving Flector® Patch who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants, should be carefully monitored.
Preexisting Asthma: Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, Flector® Patch should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.
Eye Exposure: Contact of Flector® Patch with eyes and mucosa, although not studied, should be avoided. If eye contact occurs, immediately wash out the eye with water or saline. Consult a physician if irritation persists for more than an hour.
Accidental Exposure in Children: Even a used Flector® Patch contains a large amount of diclofenac epolamine (as much as 170 mg). The potential therefore exists for a small child or pet to suffer serious adverse effects from chewing or ingesting a new or used Flector® Patch. It is important for patients to store and dispose of Flector® Patch out of the reach of children and pets.
Information for Patients: Patients should be informed of the following information before initiating therapy with an NSAID and periodically during the course of ongoing therapy. Patients should also be encouraged to read the NSAID Medication Guide that accompanies each prescription dispensed.
1. Flector® Patch, like other NSAIDs, may cause serious CV side effects, such as MI or stroke, which may result in hospitalization and even death. Although serious CV events can occur without warning symptoms, patients should be alert for the signs and symptoms of chest pain, shortness of breath, weakness, slurring of speech, and should ask for medical advice when observing any indicative sign or symptoms. Patients should be apprised of the importance of this follow-up (see **WARNINGS, Cardiovascular Effects**). **2.** Flector® Patch, like other NSAIDs, may cause GI discomfort and, rarely, serious GI side effects, such as ulcers and bleeding, which may result in hospitalization and even death. Although serious GI tract ulcerations and bleeding can occur without warning symptoms, patients should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when observing any indicative sign or symptoms including epigastric pain, dyspepsia, melena, and hematemesis. Patients should be apprised of the importance of this follow-up (see **WARNINGS, Gastrointestinal Effects: Risk of Ulceration, Bleeding, and Perforation**). **3.** Flector® Patch, like other NSAIDs, may cause serious skin side effects such as exfoliative dermatitis, SJS, and TEN, which may result in hospitalizations and even death. Although serious skin reactions may occur without warning, patients should be alert for the signs and symptoms of skin rash and blisters, fever, or other signs of hypersensitivity such as itching, and should ask for medical advice when observing any indicative signs or symptoms. Patients should be advised to stop the drug immediately if they develop any type of rash and contact their physicians as soon as possible. **4.** Patients should be instructed to promptly report signs or symptoms of unexplained weight gain or edema to their physicians (see **WARNINGS, Cardiovascular Effects**). **5.** Patients should be informed of the warning signs and symptoms of hepatotoxicity (e.g. nausea, fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy. **6.** Patients should be informed of the signs of an anaphylactoid reaction (e.g. difficulty breathing, swelling of the face or throat). If these occur, patients should be instructed to seek immediate emergency help (see **WARNINGS**). **7.** In late pregnancy, as with other NSAIDs, Flector® Patch should be avoided because it may cause premature closure of the ductus arteriosus. **8.** Patients should be advised not to use Flector® Patch if they have an aspirin-sensitive asthma. Flector® Patch, like other NSAIDs, could cause severe and even fatal bronchospasm in these patients (see **PRECAUTIONS, Preexisting asthma**). Patients should discontinue use of Flector® Patch and should immediately seek emergency help if they experience wheezing or shortness of breath. **9.** Patients should be informed that Flector® Patch should be used only on intact skin. **10.** Patients should be advised to avoid contact of Flector® Patch with eyes and mucosa. Patients should be instructed that if eye contact occurs, they should immediately wash out the eye with water or saline, and consult a physician if irritation persists for more than an hour. **11.** Patients and caregivers should be instructed to wash their hands after applying, handling or removing the patch. **12.** Patients should be informed that, if Flector® Patch begins to peel off, the edges of the patch may be taped down. **13.** Patients should be instructed not to wear Flector® Patch during bathing or showering. Bathing should take place in between scheduled patch removal and application (see Full Prescribing Information, **DOSAGE AND ADMINISTRATION**). **14.** Patients should be advised to store Flector® Patch and to discard used patches out of the reach of children and pets. If a child or pet accidentally ingests Flector® Patch, medical help should be sought immediately (see **PRECAUTIONS, Accidental Exposure in Children**).
Laboratory Tests: Because serious GI tract ulcerations and bleeding can occur without warning symptoms, physicians should monitor for signs or symptoms of GI bleeding. Patients on long-term treatment with NSAIDs, should have their CBC and a chemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (e.g. eosinophilia, rash, etc.) or if abnormal liver tests persist or worsen, Flector® Patch should be discontinued.
Drug Interactions: ***ACE-inhibitors:*** Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors.
Aspirin: When Flector® Patch is administered with aspirin, the binding of diclofenac to protein is reduced, although the clearance of free diclofenac is not altered. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of diclofenac and aspirin is not generally recommended because of the potential of increased adverse effects.
Diuretics: Clinical studies, as well as post marketing observations, have shown that Flector® Patch may reduce the natriuretic effect-of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure (see **WARNINGS, Renal Effects**), as well as to assure diuretic efficacy.
Lithium: NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.
Methotrexate: NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.
Warfarin: The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.
Carcinogenesis, Mutagenesis, Impairment of Fertility: ***Carcinogenesis:*** Long-term studies in animals have not been performed to evaluate the carcinogenic potential of either diclofenac epolamine or Flector® Patch.
Mutagenesis: Diclofenac epolamine is not mutagenic in *Salmonella Typhimurium* strains, nor does it induce an increase in metabolic aberrations in cultured human lymphocytes, or the frequency of micronucleated cells in the bone marrow micronucleus test performed in rats.
Impairment of Fertility: Male and female Sprague Dawley rats were administered 1, 3, or 6 mg/kg/day diclofenac epolamine via oral gavage (males treated for 60 days prior to conception and during mating period, females treated for 14 days prior to mating through day 19 of gestation). Diclofenac epolamine treatment with 6 mg/kg/day resulted in increased early resorptions and postimplantation losses; however, no effects on the mating and fertility indices were found. The 6 mg/kg/day dose corresponds to 3-times the maximum recommended daily exposure in humans based on a body surface area comparison.
Pregnancy: ***Teratogenic Effects. Pregnancy Category C.:*** Pregnant Sprague Dawley rats were administered 1, 3, or 6 mg/kg diclofenac epolamine via oral gavage daily from gestation days 6-15. Maternal toxicity, embryotoxicity, and increased incidence of skeletal anomalies were noted with 6 mg/kg/day diclofenac epolamine, which corresponds to 3-times the maximum recommended daily exposure in humans based on a body surface area comparison. Pregnant New Zealand White rabbits were administered 1, 3, or 6 mg/kg diclofenac epolamine via oral gavage daily from gestation days 6-18. No maternal toxicity was noted; however, embryotoxicity was evident at 6 mg/kg/day group which corresponds to 6.5-times the maximum recommended daily exposure in humans based on a body surface area comparison.
There are no adequate and well-controlled studies in pregnant women. Flector® Patch should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Nonteratogenic Effects: Because of the known effects of nonsteroidal anti-inflammatory drugs on the fetal cardiovascular system (closure of ductus arteriosus), use during pregnancy (particularly late pregnancy) should be avoided.
Male rats were orally administered diclofenac epolamine (1, 3, 6 mg/kg) for 60 days prior to mating and throughout the mating period, and females were given the same doses 14 days prior to mating and through mating, gestation, and lactation. Embryotoxicity was observed at 6 mg/kg diclofenac epolamine (3-times the maximum recommended daily exposure in humans based on a body surface area comparison), and was manifested as an increase in early resorptions, post-implantation losses, and a decrease in live fetuses. The number of live born and total born were also reduced as was F1 postnatal survival, but the physical and behavioral development of surviving F1 pups in all groups was the same as the deionized water control, nor was reproductive performance adversely affected despite a slight treatment-related reduction in body weight.
Labor and Delivery: In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, and decreased pup survival occurred. The effects of Flector® Patch on labor and delivery in pregnant women are unknown.
Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human-milk and because of the potential for serious adverse reactions in nursing infants from Flector® Patch, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Pediatric Use: Safety and effectiveness in pediatric patients have not been established.
Geriatric Use: Clinical studies of Flector® Patch did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.
Diclofenac, as with any NSAID, is known to be substantially excreted by the kidney, and the risk of toxic reactions to Flector® Patch may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken when using Flector® Patch in the elderly, and it may be useful to monitor renal function.

ADVERSE REACTIONS: In controlled trials during the premarketing development of Flector® Patch, approximately 600 patients with minor sprains, strains, and contusions have been treated with Flector® Patch for up to two weeks.
Adverse Events Leading to Discontinuation of Treatment: In the controlled trials, 3% of patients in both the Flector® Patch and placebo patch groups discontinued treatment due to an adverse event. The most common adverse events leading to discontinuation were application site reactions, occurring in 2% of both the Flector® Patch and placebo patch groups. Application site reactions leading to dropout included pruritus, dermatitis, and burning.
Common Adverse Events: Localized Reactions: Overall, the most common adverse events associated with Flector® Patch treatment were skin reactions at the site of treatment.
Table 1 lists all adverse events, regardless of causality, occurring in ≥ 1% of patients in controlled trials of Flector® Patch. A majority of patients treated with Flector® Patch had adverse events with a maximum intensity of "mild" or "moderate."

Table 1. Common Adverse Events (by body system and preferred term) in ≥1% of Patients treated with Flector® Patch or Placebo Patch[1]

	Diclofenac N=572		Placebo N=564	
	N	Percent	N	Percent
Application Site Conditions	64	11	70	12
Pruritus	31	5	44	8
Dermatitis	9	2	3	<1
Burning	2	<1	8	1
Other[2]	22	4	15	3
Gastrointestinal Disorders	49	9	33	6
Nausea	17	3	11	2
Dysgeusia	10	2	3	<1
Dyspepsia	7	1	8	1
Other[3]	15	3	11	2
Nervous System Disorders	13	2	18	3
Headache	7	1	10	2
Paresthesia	6	1	8	1
Somnolence	4	1	6	1
Other[4]	4	1	3	<1

[1] The table lists adverse events occurring in placebo-treated patients because the placebo-patch was comprised of the same ingredients as Flector® Patch except for diclofenac. Adverse events in the placebo group may therefore reflect effects of the non-active ingredients. [2] Includes: application site dryness, irritation, erythema, atrophy, discoloration, hyperhidriosis, and vesicles. [3] Includes: gastritis, vomiting, diarrhea, constipation, upper abdominal pain, and dry mouth. [4] Includes: hypoaesthesia, dizziness, and hyperkinesias.
Foreign labeling describes that dermal allergic reactions may occur with Flector® Patch treatment. Additionally, the treated area may become irritated or develop itching, erythema, edema, vesicles, or abnormal sensation.

DRUG ABUSE AND DEPENDENCE: Controlled Substance Class: Flector® Patch is not a controlled substance.
Physical and Psychological Dependence: Diclofenac, the active ingredient in Flector® Patch, is an NSAID that does not lead to physical or psychological dependence.

OVERDOSAGE: There is limited experience with overdose of Flector® Patch. In clinical studies, the maximum single dose administered was one Flector® Patch containing 180 mg of diclofenac epolamine. There were no serious adverse events.
Should systemic side effects occur due to incorrect use or accidental overdose of this product, the general measures recommended for intoxication with non-steroidal anti-inflammatory drugs should be taken.
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(Telephone: 1-888-840-8884) • www.FlectorPatch.com
Manufactured for: IBSA Institut Biochimique SA, CH-6903 Lugano, Switzerland
Manufactured by: Teikoku Seiyaku Co., Ltd., Sanbonmatsu, Kagawa 769-2695 Japan
Version June 2008 FI/161 1086 Ed. II/06.08