



Medication Policy Manual

Policy No: dru041

Topic: Celebrex[®], celecoxib

Date of Origin: September 2001

Revised/Effective Date: November 13, 2009

Next Review Date: November 2010

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Celecoxib (Celebrex[®]) is a nonsteroidal anti-inflammatory drug (NSAID) used to reduce pain and inflammation.

Policy/Criteria

- I.** Most contracts require prior authorization approval of celecoxib prior to coverage. Celecoxib may be considered medically necessary when either criterion A or B below is met.
- A.** Treatment with at least three generically available prescription NSAIDs was ineffective or not tolerated. At least one of the previously used NSAIDs must be diclofenac, etodolac, meloxicam, nabumetone, or salsalate (see Appendix 1).

OR

- B.** Used to reduce the number of adenomatous colorectal polyps in familial adenomatous polyposis (FAP) as an adjunct to usual care (e.g., endoscopic surveillance, surgery).

II. Administration, Quantity Limitations, and Authorization Period

- A.** Regence considers celecoxib to be a self-administered medication.
- B.** When prior authorization is approved, celecoxib may be authorized in doses up to:
1. 400 mg daily when used in the treatment of chronic pain and/or inflammation.

OR

2. 800 mg daily to reduce the number of adenomatous colorectal polyps in FAP.
- C.** Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

Position Statement

Summary

- Celecoxib is a non-steroidal antiinflammatory drug (NSAID) that is selective for the COX-2 enzyme subtype.
- All NSAIDs, including COX-2 selective NSAIDs, are equally effective treatments for pain and/or inflammation.
- Celecoxib has not demonstrated clinically significant safety advantages when compared with other NSAIDs.

- Please note: two other COX-2 selective NSAIDs, rofecoxib (Vioxx[®]) and valdecoxib (Bextra[®]), have been removed from the market due to safety concerns.

Clinical Efficacy

- Celecoxib 200 mg daily is efficacious for arthritis pain and inflammation. Higher doses are generally not more effective. However, some patients with rheumatoid arthritis may derive additional benefit from 200 mg twice daily.
- Celecoxib reduces the number of adenomatous colorectal polyps in FAP.
- *Prevention and Treatment of Investigational conditions*
 - * There are insufficient clinical data to conclude that NSAIDs are safe and effective as anticancer agents (other than in familial adenomatous polyposis) or agents to prevent Alzheimer's disease.^[33-36, 46-52]
 - * There are insufficient clinical data to conclude that celecoxib is effective:
 - as adjunctive therapy in schizophrenia.^[37]
 - in the prevention of restenosis after coronary angioplasty.^[38]
 - in the prevention of Barrett's Esophagus.^[39]
 - in the treatment of cervical dysplasia.^[40]
 - in the prevention of heterotopic ossification.^[41]
 - in the treatment of metastatic, advanced or unresectable colorectal cancer.^[31,50-52]
 - in the treatment or prevention of non-small cell lung cancer.^[35]
 - in the treatment or prevention of breast cancer.^[49]
 - in the treatment or prevention of pancreatic cancer.
 - in the treatment or prevention of hepatocellular carcinoma.
 - in the treatment or prevention of gastric cancer.
 - in the treatment or prevention of oral cancer.^[47]
 - in the treatment or prevention of meningiomas.
 - in the treatment or prevention of pituitary macroadenomas.

- in the treatment or prevention of malignant mesotheliomas.
- in the treatment or prevention of other advanced malignancies.
- as adjunctive therapy in bipolar disorder. ^[53]
- as adjunctive treatment in chronic periodontitis. ^[54]
- in the treatment of proteinuria in patients with diabetic nephropathy. ^[55]
- as adjunctive treatment in gastric bypass or gastric banding.
- as adjunctive treatment in inflammatory bowel disease. ^[56,57]
- as adjunctive treatment in postoperative spinal fusion ^[60-62]

Safety

GI Safety/Tolerability

- Celecoxib has not demonstrated overall superiority over other NSAIDs in avoiding upper gastrointestinal (GI) events.
- The scientific evidence to date is not sufficient to conclude that celecoxib has potential benefits that are greater than other NSAIDs.
- Celecoxib may not be safe in patients who have a history of gastrointestinal bleeding. In patients with recent history of ulcer bleeding, the rate of recurrent bleeding after treatment with celecoxib for 6 months is 4.9%. ^[28]
- Concomitant use of aspirin and celecoxib resulted in a four-fold increase in the rate of complicated ulcers when compared with celecoxib alone.
- Celecoxib has not demonstrated improved safety than other NSAIDs when used in patients with inflammatory bowel disease. ^[56,57]

Bone remodeling risk

- There is no reliable evidence that bones heal more quickly when celecoxib is used as compared to other NSAIDs ^[58-61]. Common flaws of the trials are:
 - * Retrospective studies.
 - * Non-randomized, open label studies.
 - * Small study populations.

Thrombotic/Cardiovascular Risk

- Current evidence indicates that selective COX-2 inhibitors have important adverse cardiovascular effects that include increased risk for myocardial infarction, stroke, heart failure, and hypertension. ^[42]
- The American Heart Association has stated that COX-2 inhibitors should be the last line of treatment for chronic pain in patients with known heart disease or who have cardiovascular risk. ^[42]
- Selective COX-2 inhibitors in all dosages and nonselective NSAIDs in high dosages increase mortality in patients with previous MI and should therefore be used with particular caution in these patients. ^[43]
- Celecoxib does not affect platelet aggregation and is not a substitute for aspirin in patients requiring cardiovascular prophylaxis.
- Post-marketing experience has uncovered serious bleeding events, some fatal, with concomitant use of celecoxib and warfarin.
- Celecoxib has not demonstrated a more favorable safety profile over non-selective NSAIDs in patients with renal failure or heart failure.

Appendix 1: Generically available prescription nonsteroidal anti-inflammatory drugs (NSAIDs)

Generic Name	Brand Name
Diclofenac	Cataflam [®] , Voltaren [®] , Voltaren [®] XR, Voltaren [®] gel, Solaraze [®] , gel, Flector [®] patch
Diflunisal	Dolobid [®]
Etodolac**	Lodine [®] , Lodine XL [®]
Fenoprofen	Nalfon [®]
Flurbiprofen	Ansaid [®]
Ibuprofen	Advil [®] , Motrin [®] , Nuprin [®] (Also available without prescription)
Indomethacin	Indocin [®]
Ketoprofen	Oruvail [®] , Orudis [®] , Orudis KT [®] (Also available without prescription)
Meclofenamate	Meclomen [®]
Meloxicam	Mobic [®]
Nabumetone	Relafen [®]
Naproxen	Aleve [®] , Anaprox [®] , Naprelan [®] , Naprosyn [®] (Also available without prescription)
Oxaprozin	Daypro [®]
Piroxicam	Feldene [®]
Salsalate*	Disalcid [®]
Sulindac	Clinoril [®]
Tolmetin	Tolectin 600 [®]
*Nonacetylated salicylates such as salsalate and choline magnesium salicylate do not affect platelet function.	
**More "COX-2 selective" than celecoxib. ^[27]	

Appendix 2: COX-1 and COX-2 Selectivity charts for nonsteroidal anti-inflammatory drugs (NSAIDs)

More COX₂ Selective (towards top)

↑	Generic Name	Brand Names
	rofecoxib	Vioxx
	etodolac	Lodine, Lodine XL
	meloxicam	Mobic
	celecoxib	Celebrex
	diclofenac	Cataflam, Voltaren, Arthrotec
	sulindac	Clinoril
	meclofenamate	
	piroxicam	Feldene
	diflunisal	Dolobid
	fenoprofen	Nalfon, Nalfon 200
	ibuprofen	Motrin, Tab-Profen, Vicoprofen* (combined with hydrocodone), Combunox (combined with oxycodone)
	tolmetin	Tolectin, Tolectin DS, Tolectin 600
	naproxen	Naprosyn, Anaprox, Anaprox DS, Naprelan
	aspirin	
	nabumetone	Relafen
	indomethacin	Indocin, Indocin SR, Indo Lemmon, Indomethagan
	ketoprofen	Oruvail
	flurbiprofen	Ansaid
↓	ketorolac	Toradol

More COX₁ Selective (towards bottom)

Modified from ^[44,45]

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Cross References
None

Codes	Number	Description
N/A		