Clinical Policy Title:	diclofenac
Policy Number:	RxA.55
Drug(s) Applied:	Cambia®, Zipsor®, Pennsaid®, Solaraze®, Zorvolex®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

The following are nonsteroidal anti-inflammatory drugs (NSAIDs) requiring prior authorization: diclofenac potassium (Cambia®, Zipsor®), diclofenac sodium (Pennsaid®, Solaraze®), and diclofenac (Zorvolex®).

- Cambia® is indicated for the acute treatment of migraine attacks with or without aura in adults (18 years of age or older).
- Pennsaid® is indicated for the treatment of the pain of osteoarthritis (OA) of the knee(s).
- Solaraze® is indicated for the topical treatment of actinic keratoses. Sun avoidance is indicated during therapy.
- Zipsor® is indicated for relief of mild to moderate acute pain in adults (18 years of age or older).
- Zorvolex® is indicated for management of mild to moderate acute pain and for OA pain.

Limitation(s) of use:

- Cambia® is not indicated for the prophylactic therapy of migraine.
- Safety and effectiveness of Cambia® is not established for cluster headache, which is present in an older, predominantly male population.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
diclofenac potassium (Cambia®)	Migraine	One packet (50 mg) by mouth once daily	50 mg/day
diclofenac sodium (Pennsaid®)	Pain of OA of the knee(s)	40 mg (2 pump actuations) topically twice daily per knee	80 mg/knee/day (4 pumps/knee/ day)
diclofenac sodium (Solaraze®)	Actinic keratoses	Apply to lesion areas twice daily. Normally 0.5 g of gel is used on each 5 cm x 5 cm lesion site.	Not applicable
diclofenac potassium (Zipsor®)	Mild to moderate acute pain	25 mg by mouth four times a day	100 mg/day
diclofenac (Zorvolex®)	Mild to moderate acute pain	18 – 35 mg by mouth three times a day	105 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
	OA	35 mg orally three times a day.	105 mg/day

Dosage Forms

- diclofenac potassium (Cambia®) : Packets: 50 mg in a soluble powder
- diclofenac sodium (Pennsaid®) : Solution: 2% w/w
- diclofenac sodium (Solaraze®) : Topical gel: 3%
- diclofenac potassium (Zipsor®) : Liquid Filled Capsules: 25 mg
- diclofenac (Zorvolex®) : Capsules: 18 mg and 35 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Mild to Moderate Acute Pain (must meet all):

1. Diagnosis of acute pain;
2. Request is for Zipsor® or Zorvolex®;
3. Age ≥ 18 years;
4. Failure of oral generic diclofenac and one other preferred NSAID at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed:
   a. Zipsor®: 100 mg (4 capsules) per day;
   b. Zorvolex®: 105mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Osteoarthritis Pain (must meet all):

1. Diagnosis of OA;
2. Request is for Pennsaid® or Zorvolex®;
3. Age ≥ 18 years;
4. For Pennsaid® requests: Failure of one oral generic NSAID plus failure of either diclofenac 1.5% topical solution or diclofenac 1% topical gel, unless all are contraindicated or clinically significant adverse effects are experienced;
5. For Zorvolex® requests: Failure of oral generic diclofenac and one other preferred NSAID at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed:
   a. Pennsaid®: 80 mg per knee per day (4 pumps per knee per day);
   b. Zorvolex®: 105 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

C. Migraines (must meet all):
1. Diagnosis of migraine attacks;
2. Request is for Cambia®;
3. Age ≥ 18 years;
4. Failure of rizatriptan orally disintegrating tablets at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
5. Documentation supports inability to use oral generic diclofenac;
6. Dose does not exceed 50 mg (1 packet) per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

D. Actinic Keratosis (must meet all):
1. Diagnosis of actinic keratosis;
2. Request is for Solaraze®;
3. Age ≥ 18 years;
4. Failure of topical 5-fluorouracil and topical imiquimod unless both are contraindicated or clinically significant adverse effects are experienced;
5. Quantity does not exceed 1 tube per 30 days;

Approval Duration
Commercial: 90 days
Medicaid: 90 days

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. For Solaraze® requests: additional treatment is for a new lesion or to complete initial treatment (up to 90 days);
4. If request is for a dose increase, new dose does not exceed:
   a. Cambia®: 50 mg per day (1 packet per day);
   b. Pennsaid®: 80 mg per knee per day (4 pumps per knee per day);
   c. Zipsor®: 100 mg per day (4 capsules per day);
   d. Zorvolex®: 105 mg per day.

Approval Duration
Commercial: 12 months (up to 90 days for Solaraze®)
Medicaid: 12 months (up to 90 days for Solaraze®)

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CABG: Coronary artery bypass graft
FDA: Food and Drug Administration
NSAID: Non-steroidal anti-inflammatory drug
OA: Osteoarthritis

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral NSAIDs		
diclofenac (Voltaren®)	50 mg by mouth three times a day	150 mg/day
etodolac (Lodine®)	400 – 500 mg by mouth twice daily	1,200 mg/day
fenoprofen (Nalfon®)	400 – 600 mg by mouth three times a day to four times a day	3,200 mg/day
ibuprofen (Motrin®)	400 – 800 mg by mouth three times a day to four times a day	3,200 mg/day
indomethacin (Indocin®)	25 – 50 mg by mouth BID to three times a day	200 mg/day
indomethacin SR (Indocin SR®)	75 mg by mouth once daily to twice daily	150 mg/day
ketoprofen (Orudis®)	50 mg by mouth QID or 75 mg by mouth three times a day	300 mg/day
meloxicam (Mobic®)	7.5 mg - 15 mg by mouth once daily	15 mg/day
naproxen (Naprosyn®)	250 – 500 mg by mouth twice daily	1,500 mg/day for up to 6 months
naproxen sodium (Anaprox®, Anaprox DS®)	275 – 550 mg by mouth twice daily	1,650 mg/day for up to 6 months
oxaprozin (Daypro®)	600 – 1,200 mg by mouth once daily	1,800 mg/day
piroxicam (Feldene®)	10 – 20 mg by mouth once daily	20 mg/day
salsalate (Disalcid®)	500 – 750 mg by mouth TID, titrated up to 1,000 mg TID or 1500 mg twice daily	3,000 mg/day
sulindac (Clinoril®)	150 mg – 200 mg by mouth twice daily	400 mg/day
tolmetin DS (Tolectin®)	400 mg by mouth twice daily maintenance 200-600 mg three times a day	1,800 mg/day
Topical NSAIDs		
diclofenac 1.5% (Pennsaid®) solution	40 drops four times a day on each painful knee	160 drops/knee/day
diclofenac 1% gel (Voltaren® Gel)	2 – 4 g applied to affected area four times a day	32 g/day
Anti-migraine Agents		
rizatriptan (Maxalt®/Maxalt® MLT)	5 or 10 mg by mouth once daily	30 mg/day

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to diclofenac or any components of the drug product;
  - All agents except Solaraze®: history of asthma, urticarial, or other allergic-type reactions after taking aspirin or other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients;
  - In the setting of coronary artery bypass graft (CABG) surgery;
  - Zipsor® contains gelatin and should not be given to patients with known hypersensitivity to bovine protein.

- Boxed Warning(s):
  - Cardiovascular thrombotic events;
  - All agents except Solaraze®: Gastrointestinal bleeding, ulceration, and perforation.

APPENDIX D: General Information

Different dose strengths and formulations of oral diclofenac are not interchangeable. This difference should be taken into consideration when changing strengths or formulations.

Zipsor® is contraindicated in the setting of coronary artery bypass graft (CABG) surgery. 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. NSAIDs are contraindicated in the setting of CABG.

References

1. Cambia® Prescribing Information. Newark, CA: Depomed, Inc.; March 2017. Available at: www.Cambia®rx.com. Accessed, January 21, 2021
2. Pennsaid® Prescribing Information. Lake Forest, IL: Horizon Pharma USA Inc.; March 2020. Available at: www.Pennsaid®.com ,January 21, 2021
3. Solaraze® Prescribing Information. Melville, NY: PharmaDerm; May 2016. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021005s016lbl.pdf. Accessed, January 21, 2021
4. Zipsor® Prescribing Information. Newark, CA: Depomed, Inc.; May 2016. Available at: www.Zipsor®.com. Accessed ,January 21, 2021
5. Zorvolex® Prescribing Information. Philadelphia, PA: Iroko Pharmaceuticals, LLC; September 2019. Available at: www.Zorvolex®.com. Accessed ,January 21, 2021
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed ,January 21, 2021
7. Treatment of actinic keratosis. Last updated November 04, 2020. In: UpToDate® Post, TW (Ed), UpToDate, Waltham, Ma, 2020. Accessed with subscription at: https://www.uptodate.com/. Accessed on 01/29/2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Updated references	04/2020	05/20/2020
Updated Criteria II, A, i to: Currently receiving medication that has been authorized by Rxadvance, or documentation supports that member is currently receiving Cabometyx or Cometriq for a covered indication and has received this medication for at least 30	05/08/2020	05/20/2020

days;		
Policy was reviewed: 1) Dosing Information and Therapeutic Alternatives all abbreviations PO,QD,BID,TID changed to full forms. 2) Dosing Information Zorvolex OA dose added separately. 3) Dosage Forms Zipsor added Liquid Filled & Pennsaid added w/w 4) Continuation therapy criteria II.A.1. rephrased to "Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy. 5) Initial Approval Criteria Other diagnoses/indications deleted 6) Therapeutic Alternatives verbiage changed. 7) References were updatedAdded trial and failure, quantity criteria under initial approval criteria for Actinic keratosis (Section D)	01/21/2020	03/09/2021