Evaluating the Real-World Use of Topical Diclofenac Sodium Gel 1% Using US Longitudinal Electronic Health Records Database: A study supporting OTC switch

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Appendices

Table S1. Days of follow-up time per EOI cohort and deaths during follow-up per EOI cohort

Days of follow-up time	Total	No EOI	Hepatic EOI	CV EOI	HTN EOI	GI EOI	Renal EOI	Skin reaction EOI	Misuse/ abuse EOI	Death
Mean (SD) follow-up time, d	348.4 (562.4)	187.8 (338.7)	1,153.5 (861.2)	878.5 (814.7)	984.5 (835.7)	1,119.0 (845.0)	1,032.2 (839.2)	1,024.0 (825.1)	1,015.8 (865.2)	551.3 (649.2)
Median (IQR, Q1-Q3) follow-up, d	60 (60–368)	60 (55–127)	1,040 (374–1,846)	629 (140–1,433)	788 (232-1,603)	972 (366–1,793)	858 (285–1,657)	863 (290–1,635)	845 (176–1,679)	282 (50–834)
Range follow-up time, d	1–3,182	1–3,156	6–3,163	2–3,163	1–3,169	1–3,152	3–3,163	10–3,182	19–3,147	1–3,058
Death during patient follow-up, n (%)	2,210 (0.4)	0 (0)	325 (1.7)	1,510 (2.4)	223 (0.9)	160 (1.5)	767 (4.5)	368 (0.6)	43 (0.8)	2,210 (100)

CV cardiovascular, EOI event of interest, GI gastrointestinal, HTN hypertension, IQR interquartile range

Table S2. Days to first EOI since index date

Treatment patterns	All
Days from index DSG prescription to 1st outcome event*	
Mean (SD)	244.0 (368.6)
0 days, n (%)	13,752 (10)
1–30 days, n (%)	28,676 (21)
31–90 days, n (%)	26,310 (20)
91–180 days, n (%)	17,296 (13)
181–365 days, n (%)	19,084 (14)
>365 days, n (%)	29,298 (22)

DSG 1% diclofenac sodium topical gel 1%, EOI event of interest

**Time to first outcome event is time from the index date to the first occurrence of any 1 of the outcomes of interest, for only those patients with at least 1 outcome of interest (n=134,416)*

Table S3 Healthcare **utilization by overall population, stratified by EOI cohort**

Healthcare utilization	All	Hepatic EOI	CV EOI	HTN EOI	GI EOI	Renal EOI	Skin reaction EOI	Misuse/ abuse EOI	Death
All patients, n (%)	521,593 (100)	19,124 (3.7)	63,512 (12.1)	23,618 (4.5)	11,010 (2.1)	17,158 (3.3)	59,133 (11.3)	5,399 (1.0)	2,210 (0.4)
Inpatient resources,									
Patients with ≥1 hospital stays, n (%)	59,981 (11.5)	9,606 (50.2)	31,816 (50.1)	8,584 (36.4)	5,986 (54.4)	12,427 (72.4)	19,866 (33.6)	2,590 (48.0)	1,371 (62.0)
Length of stay (d),									
mean	9.8	10.2	11.1	10.9	10.3	12.2	10.6	10.5	12.6
(SD)	(23.5)	(19.0)	(27.4)	(19.5)	(17.4)	(20.5)	(31.2)	(17.4)	(17.0)
median	4	4	5	5	5	5	4	5	6
Outpatient resources									
Number of office visits, mean	12.3	54.0	40.2	37.0	53.5	51.2	44.0	55.4	23.7
(SD)	(25.6)	(55.6)	(48.2)	(46.6)	(55.4)	(55.0)	(48.5)	(61.6)	(40.7)
Number of ER visits,	0.9	5.2	4.0	3.2	5.6	5.8	3.3	7.4	3.5
mean (SD)	(3.5)	(10.3)	(7.8)	(7.2)	(10.7)	(9.4)	(7.4)	(15.7)	(5.7)

CV cardiovascular, DSG 1% diclofenac sodium topical gel 1%, EOI event of interest, ER emergency room, GI gastrointestinal, HTN hypertension

Table S4. Specialties prescribing DSG 1%

	All*
All index fills	521,593 (100)
Index fills with identifiable provider specialty	390,123 (100)
Provider specialties, n (%)	
Family practice	104,258 (26.7)
Internal medicine	83,240 (21.3)
Physician assistant	50,762 (13.0)
Surgery	44,256 (11.3)
Nurse practitioner	32,311 (8.3)
Podiatry	24,101 (6.2)
General practice	14,859 (3.8)
Physical medicine	8,694 (2.2)
Anesthesiology	6,864 (1.8)
Psychiatry & neurology	4,902 (1.3)

Pain medicine	4,546 (1.2)

DSG 1% diclofenac sodium topical gel 1%

**Provider specialties prescribing DSG 1% at rates >1% are shown in this table*

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Response Y/N
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Y
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Y
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Y
Objectives	3	State specific objectives, including any prespecified hypotheses	Y
Methods			
Study design	4	Present key elements of study design early in the paper	Y
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Y
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Y
		(b) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Y
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Y
Bias	9	Describe any efforts to address potential sources of bias	Y
Study size	10	Explain how the study size was arrived at	Y
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Y
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Y
		(b) Describe any methods used to examine subgroups and interactions	NA
		(c) Explain how missing data were addressed	NA
		(d) If applicable, explain how loss to follow-up was addressed	NA
		(e) Describe any sensitivity analyses	NA

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Y
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Y
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	Y
Outcome data	15*	Report numbers of outcome events or summary measures over time	Y
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	NA
		(b) Report category boundaries when continuous variables were categorized	Y
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Y
Discussion			
Key results	18	Summarise key results with reference to study objectives	Y
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Y
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Y
Generalisability	21	Discuss the generalisability (external validity) of the study results	Y
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Y

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web

sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.