

From: David Bedich

Sent: Wednesday, September 15, 2021

To: Pharmacy Drug Information

Subject: Request to speak during public comment section and review of Drug Class Update with New Drug Evaluation: Topical Antiparasitics by Oregon P&T

To whom it may concern,

I formally request a live audience with the Oregon P&T committee, to expound upon the clinical and pharmacologic gap in the published Drug Class Update with New Drug Evaluation: Topical Antiparasitics (DCU/NDE/TA) recently presented to the Committee for consideration. This updated recommendation lacks significant evidence-based clinical research regarding resistance to head lice treatments rendering them **completely ineffective in the State of Oregon**. Absent from the published recommendation to the committee, are the 20-year clinical resistance studies completed by Dr. John M. Clark (PhD. Entomology (concentration on insecticide toxicology), UMass, toxicology and environmental chemistry) whose research was funded by the National Institute of Health (NIH). Dr. Clark's clinical research has been published in multiple peer-reviewed journals and accepted as strong clinical evidence due to a lack of bias, stringent measurement criteria and depth/scope of prevalence measures which included the state of Oregon.

Upon review of the recent Antiparasitic Pharmacologic drug class submission to Oregon's P&T, the conclusions and recommendations are in conflict with the fiduciary responsibility of the P&T committee for the children in Oregon and appears to breach the P&T committee's Review Standard which clearly states the committee will act based on "*sound evidence-based research and processes widely accepted by the medical profession.*" With the lack of complete evidentiary, scientific evidence regarding resistance, the recommendations submitted for the Antiparasitic drug class is not only incomplete, it is clinically flawed.

Based on the evidence standards required for said Drug Class recommendations, the research conducted by Dr. Clark and Associates utilized three different scientific validation tests to conclude that head lice in the areas of Portland, Lake Oswego and Tigard, Oregon has become 100% resistant to permethrin/pyrethrin. Additionally, permethrin/pyrethrin resistance tallied between 77%-85% in head lice collected from the smaller Wilsonville Oregon, and well on the way to becoming 100% resistant at the time of the last report and publication in 2016.

Based on the NIH funded evidence-based research demonstrating significant head lice resistant to permethrin/pyrethrin in the state of Oregon, we respectfully ask the P&T committee to enable pediatricians to follow the science of the American Academy of Pediatrics (AAP). The AAP states the following, "In areas with known resistance to an over-the-counter pediculicide, parents should involve their pediatrician for treatment with a prescription medication such as spinosad or topical ivermectin." (ref. <https://bit.ly/3nsFBWB>)

Natroba (spinosad) Topical Suspension 0.9%* does meet the criteria outlined by the AAP. It is the ONLY head lice medication with no known resistance to the active compound, spinosad, in head lice. In addition, Amanzougaghene et Al. Human Lice, the current state of knowledge, *Frontiers in Cellular and Infection Microbiology*, published that Natroba is the only head lice medication currently available in the US market, proven to be ovicidal and pediculicidal activity.

A spinosad based product like Natroba is now dispensed in 2 out of every 3 head lice prescriptions in the US market (IQVIA audit 12 month ending 9/2021).

To conclude, I would respectfully request that the State of Oregon P&T committee strongly consider the addition of Natroba (spinosad) Topical Suspension 0.9% to the Oregon Antiparasitic PDL Drug Class update without restrictions. Adding Natroba would place the State of Oregon in alignment with their fellow State members of the purchasing consortium, SSDC and as well as aligns with the AAP's and CDC's recommendations.

Thank you for your consideration.

*full prescribing visit www.natroba.com

Supplemental Table 1. Head Louse Collection Summary and Quantitative Sequencing Results

State/ Collection Site	Human Pop.	Pop. Size	Sub.	Total Lice	Lice for QS	Stage	RAF MI	SD	RAF TI	SD	RAF LF	SD
Oregon												
Lake Oswego	36,619	M	1	14	14	2nd Instar	0.99	0	1.01	0	0.99	0
Portland	3,831,074	H	5	57	10	F	0.99	0	1.01	0	0.99	0
Tigard	48,035	M	1	64	16	3rd Instar	0.99	0	1.01	0	0.99	0
Wilsonville	19,509	M	1	98	13	2nd Instar	0.77	0.01	0.85	0	0.82	0

Supplemental Table link <https://bit.ly/390sF1S>

TABLE 2 | Main Therapeutic options for pediculosis treatment.

Pediculicide	Class	Mechanism of action	Adulticide/ovicidal activities	Documented adverse health effect	Documented resistance in lice	References
PEDICULICIDE WITH A NEUROTOXIC MODE OF ACTION						
DDT, dichlorodiphenyltrichloroethane	Organochloride	Opening of sodium ion channels in neurons	Yes/yes	Toxic	Yes	Durand et al., 2012; Bonilla et al., 2013
Lindane	Organochloride	Inhibition of α -aminobutyric acid-gated chloride channel	Yes/yes	Toxic	Yes	Durand et al., 2012; Bonilla et al., 2013
Natural pyrethrins	Chrysanthemum extract	Delayed repolarization of voltage-gated	Yes/no	Minor	Yes	Bonilla et al., 2013
Permethrin, synthetic pyrethrin	(+)-3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropan carboxylate	The same as natural pyrethrins	Yes/no	Minor	Yes	Durand et al., 2012; Bonilla et al., 2013; Clark et al., 2013
Malathion	Organophosphate	Irreversible inhibition of acetylcholinesterase	Yes/no	Minor	Yes	Durand et al., 2012; Bonilla et al., 2013; Kwon et al., 2014
Carbaryl	Carbamate	Irreversible inhibition of acetylcholinesterase	Yes/no	Moderate to very toxic	Yes	Durand et al., 2012; Bonilla et al., 2013
Ivermectin*	Macrocyclic lactone	Binding to glutamate-gated chloride ion channels	Yes/no	None to minimal	Yes	Chosidow et al., 2010; Clark et al., 2013; Diatta et al., 2016
Spinosad	Macrocyclic lactone	Overstimulates nerve cells by acting like acetylcholine	Yes/yes	Minor	No	Aditya and Rattan, 2012; Feldmeier, 2014

Natroba ONLY medication documented NOT to have resistance and both Ovicidal and Pediculicidal

Ref. www.frontiersin.org Where Are We With Human Lice? A Review of the Current State of Knowledge Nadia Amanzougaghene^{1,2*}, Florence Fenollar^{2,3}, Didier Raoult^{1,2} and Oleg Mediannikov^{1,2*} ¹Aix Marseille Univ, IRD, AP-HM, Frontiers in Cellular and Infection Microbiology

Gratefully,

David Bedich

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2021 OR PDL - Antiparasitics

PDL contains No AAP Recommend options

Table 121-0030-1 Oregon Fee-for-Service Enforceable Physical Health Preferred Drug List

Effective: July 1, 2021

System	Class	Preferred	
Dermatologicals	Antiparasitics, Topical	permethrin	COMBO. PKG
		permethrin	CREAM (G)
		permethrin	LIQUID
		piperonyl butox/pyrethr/permet	KIT
		piperonyl butoxide/pyrethrins	GEL (GRAM)
		piperonyl butoxide/pyrethrins	GEL (ML)
		piperonyl butoxide/pyrethrins	KIT
		piperonyl butoxide/pyrethrins	LIQUID
		piperonyl butoxide/pyrethrins	SHAMPOO

American Academy
of Pediatrics



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“...with known resistance to an over-the-counter pediculicide ... parents should involve their pediatrician for treatment with a prescription medication such as **spinosad** or topical ivermectin.”

In Vitro Assessment of Natroba on Head Lice



Knockdown resistant human head lice to either the pyrethrins or pyrethroid insecticides – after administration of **Natroba**^{TM*}

Permethrin-resistant Lice – non-application of a compound



Permethrin-resistant Lice – after application with Permethrin¹⁴



Permethrin-resistant Lice – after application with Natroba¹⁴



Phase 3 clinical trials of NatrobaTM **did not** examine the frequency or occurrence of knockdown resistance in the population studied.

*Source: Videos created in collaboration with J. Marshall Clark, et al, and the Departments of Veterinary and Animal Sciences, Molecular Pharmacology, Microbiology, and Biochemistry and Molecular Biology at the University of Massachusetts, Amherst

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Where Are We With Human Lice? A Review of the Current State of Knowledge Nadia Amanzougaghene^{1,2*}, Florence Fenollar^{2,3}, Didier Raoult^{1,2} and Oleg Mediannikov^{1,2*} ¹Aix Marseille Univ, IRD, AP-HM, Frontiers in Cellular and Infection Microbiology | www.frontiersin.org 21 January 2020.

American Academy of Pediatrics



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*“...with known resistance to an over-the-counter pediculicide ... parents should involve their pediatrician for treatment with a prescription medication such as **spinosad** or topical ivermectin.”*

Source – AAP website

<https://www.aap.org/en-us/about-the-aap/aap-press-room/pages/AAP-Updates-Treatments-for-Head-Lice.aspx?nfstatus=401&nftoken=00000000-0000-0000-0000-000000000000&nfstatusdescription=ERROR:+No+local+token>

AAP Updates Treatments for Head Lice

4/27/2015

It's probably making you squirm just thinking about it – your child comes home from school scratching his head. He has lice. It's every parent's nightmare, but it is important to remember that head lice is a nuisance, not a serious disease or a sign of poor hygiene.

An updated clinical report by the American Academy of Pediatrics (AAP) "Head Lice," in the May 2015 issue of Pediatrics (published online April 27), provides information to pediatricians and other health practitioners on safe and effective methods for treating head lice, including new products and medications.

Most cases of head lice are acquired outside of school. In the report, the AAP continues to recommend that a healthy child should not be restricted from attending school because of head lice or nits (eggs). Pediatricians are encouraged to educate schools and communities that no-nit policies are unjust and should be abandoned. Children can finish the school day, be treated, and return to school.

Unless resistance has been seen in the community, pediatricians and parents should consider using over-the-counter medications containing 1 percent permethrin or pyrethrins as a first choice of treatment for active lice infestations. The best way to interrupt a chronic lice problem is with regular checks by parents and early treatment with a safe, affordable, over-the-counter pediculicide. After applying the product according to the manufacturer's instructions, parents should follow with nit removal and wet combing. The treatment should be reapplied at day 9, and if needed, at day 18.

In areas with known resistance to an over-the-counter pediculicide, or when parents' efforts on their own do not work, parents should involve their pediatrician for **treatment with a prescription medication such as spinosad or topical ivermectin**. These are new medications that were introduced since the last time the AAP published recommendations on head lice in 2010.

Once a family member is identified with head lice, all household members should be checked. The AAP does not recommend excessive environmental cleaning, such as home pesticides. However, washing pillow cases and treating natural bristle hair care items that may have been in contact with the hair of anyone found to have head lice are reasonable measures.

While it is unlikely to prevent all cases of head lice, children should be taught not to share personal items such as combs, brushes, and hats. Regular observation by parents can also be an effective way to detect and quickly treat head lice infestations.

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The American Academy of Pediatrics is an organization of 62,000 primary care pediatricians, pediatric medical subspecialists and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents and young adults.

State Provided Access is key to curing Head Lice

National Spinosad MS is 66%

Permethrin/Pyrethrin National share is ~22%

Topical Ivermectin is 3% based on the same factors

Oregon's Permethrin/Pyrethrin MS 69%

Spinosad TRx in OR is 9% due to lack of access

Topical Ivermectin is 3% based on the same factors

Market	Product Name	TRX
✓ Market Name: 1	SPINOSAD	206,443
✓ Product Name: 8	PERMETHRIN 1%	60,350
Product Detail ID: 28	MALATHION	19,495
Product Detail Name: 28	PIP/PYRE	10,284
	IVERMECTIN	9,515
	VANALICE	3,048
	LINDANE SHAMPOO	2,619
	ULESFIA	10
	Grand Total	311,764

Market	OR
✓ Market Name: 1	TRX
✓ Product Name: 6	
Product Detail ID: 18	
Product Detail Name: 18	
	PERMETHRIN 1%: 1,075
	MALATHION: 294
	SPINOSAD: 158
	PIP/PYRE: 116
	IVERMECTIN: 57
	LINDANE SHAMPOO: 33
	Grand Total: 1,733

MS – Market Share

Note: The purpose of this document is to provide the clinical and/or pharmacoeconomic information regarding ZEPOSIA™ (ozanimod) as requested; it is not intended to be used for any other purpose. This document contains relevant information for ZEPOSIA, which may or may not be included in the U.S. Prescribing Information (USPI). BMS does not suggest or recommend the use of ZEPOSIA in any manner other than as described in the USPI.

ZEPOSIA® (ozanimod) capsules, for oral use

Indications: Treatment of adults with 1) moderately to severely active ulcerative colitis (UC) or 2) relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease.¹

Recommended Dosage and Administration:

Assessments Prior to First Dose of ZEPOSIA: Complete Blood Count: Obtain a recent (i.e., within the last 6 months or after discontinuation of prior MS or UC therapy) complete blood count (CBC), including lymphocyte count.

Cardiac Evaluation: Obtain an electrocardiogram (ECG) to determine whether pre-existing conduction abnormalities are present. In patients with certain pre-existing conditions, advice from a cardiologist should be sought.

Liver Function Tests: Obtain recent (i.e., within the last 6 months) transaminase and bilirubin levels.

Ophthalmic Assessment: In patients with a history of uveitis or macular edema, obtain an evaluation of the fundus, including the macula.

Current or Prior Medications:

- If patients are taking anti-neoplastic, immunosuppressive, or immune-modulating therapies, or if there is a history of prior use of these drugs, consider possible unintended additive immunosuppressive effects before initiating treatment with ZEPOSIA.
- Determine if patients are taking drugs that could slow heart rate (HR) or atrioventricular (AV) conduction.

Vaccinations: Test patients for antibodies to varicella zoster virus (VZV) before initiating ZEPOSIA; VZV vaccination of antibody-negative patients is recommended prior to commencing treatment with ZEPOSIA. If live *attenuated* vaccine immunizations are required, administer at least 1 month prior to initiation of ZEPOSIA.

Dosing Information:

Treatment Initiation: Initiate ZEPOSIA with a 7-day titration, as shown in Table below.

Maintenance Dosage: After initial titration, the recommended maintenance dosage of ZEPOSIA is 0.92 mg taken orally once daily starting on Day 8. ZEPOSIA capsules should be swallowed whole, with or without food.

Dose Titration Regimen

Days 1-4	0.23 mg once daily
Days 5-7	0.46 mg once daily
Day 8 and thereafter	0.92 mg once daily

Re-initiation of ZEPOSIA After Treatment Interruption: If a dose of ZEPOSIA is missed during the first 2 weeks (wks) of treatment, reinitiate treatment using the titration regimen. If a dose of ZEPOSIA is missed after the first 2 wks of treatment, continue with the treatment as planned.

How Supplied: Capsules: 0.23 mg, 0.46 mg, 0.92 mg

Mechanism of Action: Ozanimod is a sphingosine 1-phosphate (S1P) receptor modulator that binds with high affinity to S1P receptors 1 and 5. Ozanimod blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. Ozanimod has minimal or no activity on S1P₂, S1P₃, and S1P₄. The mechanism by which ozanimod exerts therapeutic effects in MS and UC is unknown but may involve the reduction of lymphocyte migration into the central nervous system and intestine.

UC Studies:

Registrational Phase 2 and 3 Studies

TOUCHSTONE (a Phase 2, double-blind, placebo-controlled trial) evaluated the efficacy and safety of ozanimod in adult patients with moderately to severely active UC. During an 8-wk induction, 197 patients were randomized 1:1:1 to receive once daily ozanimod 0.92 mg (n = 67), ozanimod 0.46 mg (n = 65), or placebo (n = 65); after 8 wks, patients with clinical response¹ continued their regimen for 24 wks (maintenance; n = 42, n = 36, and n = 25, respectively). Non-responders were eligible to enter an optional open-label period.²

- Clinical remissionⁱⁱ rate at Wk 8 (primary endpoint) was statistically significantly greater with ozanimod 0.92 mg (16% [11/67]; $P = .048$) and 0.46 mg (14% [9/65]; $P = .14$) vs placebo 6% (4/65); clinical remission was maintained at Wk 32 in 5/11, 7/9 and 2/4 patients, respectively. Because there was no statistically significant difference in Wk 8 clinical remission for ozanimod 0.46 mg vs placebo group, all subsequent analyses were considered to be exploratory and the results not significant. At Wk 32, clinical remission rate was nominally significantly greater with both ozanimod 0.92 mg (21% [14/67]; $P = .01$) and ozanimod 0.46 mg (26% [17/65]; $P = .002$) vs placebo (6% [4/65]).
- At Wks 8 and 32:
 - Clinical response rate was nominally significantly greater with ozanimod 0.92 mg (Wk 8: 57% [38/67], $P = .02$; Wk 32: 51% [34/67], $P < .001$) vs placebo (Wk 8: 37%, [24/65]; Wk 32: 20% [13/65]); there was no significant difference with ozanimod 0.46 mg (Wk 8: 54% [35/65], $P = .06$; Wk 32: 35% [23/65], $P = .06$) vs placebo.
 - Mean reduction from baseline in the Mayo Clinic score (SD) was nominally significantly greater with ozanimod 0.92 mg (Wk 8: -3.4 [2.79], $P = .0042$; Wk 32: -3.4 [2.93], $P = .0004$) vs placebo (Wk 8: -2.0 [2.52]; Wk 32: -1.6 [2.72]); there was no significant difference with ozanimod 0.46 mg (Wk 8: -2.6 [2.92], $P = .1415$; Wk 32: -2.2 [3.07], $P = .1932$) vs placebo.
 - The proportion of patients who achieved mucosal healingⁱⁱⁱ was nominally significantly greater with both ozanimod 0.92 mg (Wk 8: 34% [23/67], $P = .002$; Wk 32: 33% [22/67], $P = .005$) and ozanimod 0.46 mg (Wk 8: 28% [18/65], $P = .03$; Wk 32: 32% [21/65], $P = .006$) vs placebo (Wks 8 and 32: 12% [8/65]).
- At Wk 8, the proportion of patients who achieved histologic remission^{iv} was not significantly different with ozanimod 0.92 mg (22% [15/67]; $P = .07$) and ozanimod 0.46 mg (14% [9/65]; $P = .63$) vs placebo (11% [7/65]) but was nominally significantly greater at Wk 32 for both ozanimod 0.92 mg (31% [21/67], $P < .001$) and ozanimod 0.46 mg (23% [15/65], $P = .02$) vs placebo (8% [5/65]).

¹ Clinical response = decrease in Mayo Clinic score of ≥ 3 points and $\geq 30\%$ and decrease in rectal bleeding subscore of ≥ 1 point or a subscore of ≤ 1

ⁱⁱ Clinical remission = Mayo Clinic score of ≤ 2 with no subscore > 1

ⁱⁱⁱ Mucosal healing = endoscopy subscore ≤ 1

^{iv} Histologic remission = Geboes score < 2 on a scale from 0 to 5, with higher scores indicating more severe histologic inflammation

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Safety

- In the ozanimod 0.92 mg, ozanimod 0.46 mg and placebo groups, respectively: Treatment-emergent adverse events (TEAEs) were reported in 39% (26/67), 40% (26/65), and 40% (26/65) patients; serious TEAEs were reported in 3 (4%), 1 (2%), and 6 (9%) patients; and adverse events (AEs) led to discontinuation in 1 (1%), 3 (5%), and 4 (6%) patients.
- Cardiac AEs were reported in no patients treated with ozanimod 0.92 mg, 1 (2%) with ozanimod 0.46 mg, and 2 (3%) with placebo. Asymptomatic, transient 1st-degree atrioventricular block and sinus bradycardia developed in 1 patient in the ozanimod 0.46 mg group on day 8; the event resolved without intervention, after which the patient discontinued treatment.
- Increase in alanine aminotransferase (ALT) > 3x upper limit of normal occurred in 4 patients (3 on ozanimod 0.92 mg, 1 on ozanimod 0.46 mg).
- Squamous-cell carcinoma of the skin occurred in 1 patient on ozanimod 0.92 mg; the patient was previously treated with mercaptopurine for > 2 years.

True North was a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of ozanimod in patients with moderately to severely active UC. During a 10-wk induction period, patients were randomized 2:1 into the blinded cohort 1 (n = 645) to receive once daily ozanimod 0.92 mg (n = 429) or placebo (n = 216) or assigned to an open-label cohort 2 to receive once daily ozanimod 0.92 mg (n = 367). At Wk 10, ozanimod-treated clinical responders from cohort 1 and cohort 2 were re-randomized 1:1 to ozanimod 0.92 mg (n = 230) or placebo (n = 227) and placebo responders continued placebo (n = 69) for a 42-wk double-blind maintenance period. Induction non-responders could enter a separate open-label extension trial.^{3,4}

- Clinical remission^v rate (primary endpoint) was statistically significantly greater with ozanimod vs placebo at both Wk 10 (end of induction; 18.4% vs 6.0%, $P < .0001$) and Wk 52 (end of maintenance; 37.0% vs 18.5%, $P < .0001$).
- All key secondary endpoints were achieved by a statistically significantly greater proportion of patients treated with ozanimod vs placebo at Wk 10 (all $P < .001$) and Wk 52 (all $P < .005$):
 - Clinical response^{vi}: Wk 10 (47.8% vs 25.9%); Wk 52 (60.0% vs 41.0%); Endoscopic improvement^{vii}: Wk 10 (27.3% vs 11.6%); Wk 52 (45.7% vs 26.4%); Mucosal healing^{viii}: Wk 10 (12.6% vs 3.7%); Wk 52 (29.6% vs 14.1%); Maintenance of remission^{ix}: Wk 52 (51.9% vs 29.3%); Corticosteroid-free remission^x: Wk 52 (31.7% vs 16.7%); Durable remission^{xi}: Wk 52 (17.8% vs 9.7%)
- Histologic remission^{xii} was achieved by a significantly greater proportions of patients on ozanimod vs placebo at both Wk 10 (18.2% vs 7.4%) and Wk 52 (33.5% vs 16.3%), (both $P < .001$).
- In a subgroup analysis of tumor necrosis factor inhibitor (TNFi)-naïve patients, the proportion of patients who achieved primary/select key secondary endpoints^{xiii} was significantly improved with ozanimod vs placebo ($P < .02$) at both Wks 10 and 52. In patients with prior TNFi use, ozanimod vs placebo showed a nominally statistically significant improvement in clinical response at Wk 10 ($P = .008$) and the proportion of patients achieving primary/select secondary endpoints^{xiii} were significantly increased at Wk 52 ($P < .04$).
- In a post hoc analysis, symptom improvement with ozanimod vs placebo was observed as early as Wk 2 (i.e., 1 wk after completing the required 7-day dosage titration). Nominally significant improvements with ozanimod vs placebo, respectively, were seen in rectal bleeding subscore (RBS) starting at Wk 2 (difference: -0.16 [95% CI, $-0.298, -0.023$]) and stool frequency subscore (SFS) beginning at Wk 5 (difference: -0.19 [95% CI, $-0.336, -0.047$]). At Wk 10, a nominally significantly greater proportion of patients on ozanimod vs placebo patients achieved an RBS = 0 (52% vs 30.1%; $P < .0001$), SFS ≤ 1 ^{xiv} (41.7% vs 27.3%; $P = .0017$) or both RBS = 0 and SFS^{xiv} ≤ 1 (34.5 vs 18.5, $P = .0001$).⁵

Safety: Among patients treated with ozanimod vs placebo, respectively:

- TEAEs were reported in 40.1% (172/429) vs 38.0% (82/216) of patients during induction and 49.1% (113/230) vs 36.6% (83/227) during maintenance.
- Serious TEAEs occurred in 17 (4.0%) vs 7 (3.2%) patients during induction and 12 (5.2%) vs 18 (7.9%) during maintenance; the most common serious TEAE was UC flare during both induction [6 (1.4%) vs 4 (1.9%) patients] and maintenance [1 (0.4%) vs 9 (4.0%) patients]. TEAEs led to treatment discontinuation in 14 (3.3%) vs 7 (3.2%) patients during induction and in 3 (1.3%) vs 6 (2.6%) patients during maintenance.
- Most common TEAEs during induction were anemia [18 (4.2%) vs 12 (5.6%) patients], nasopharyngitis [15 (3.5%) vs 3 (1.4%) patients], and headache [14 (3.3%) vs 4 (1.9%) patients]; and during maintenance were increases in ALT [11 (4.8%) vs 1 (0.4%)] and headache [8 (3.5%) vs 1 (0.4%)].

Please refer to the Important Safety Information included in the cover letter & accompanying full Prescribing Information and Medication Guide.

References: 1) Zeposia. Prescribing Information. Celgene Corporation; 2020. 2) Sandborn WJ, et al. *N Engl J Med*. 2016;374:1754-62. 3) Sandborn WJ, et al. Presented at AIBD; Dec 10-12, 2020; Virtual Meeting. Poster 88. 4) Danese S, et al. Presented at AIBD; Dec 10-12,2020; Virtual Meeting. Poster 104. 5) Osterman MT, et al. Presented at DDW; May 21-23,2021; Virtual Meeting.

^v Clinical remission = 3-component Mayo score results: rectal bleeding score = 0, stool frequency score ≤ 1 and decrease from baseline ≥ 1 , and mucosal endoscopy score (MES) ≤ 1 without friability

^{vi} Clinical response = reduction in 3-component Mayo Clinic score of ≥ 2 points and $\geq 35\%$, and decrease in RBS of ≥ 1 point or absolute RBS ≤ 1 point

^{vii} Endoscopic improvement = MES ≤ 1 without friability

^{viii} Mucosal healing = endoscopic improvement plus histological remission (Geboes < 2.0 ; no neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue) in the same patient

^{ix} Maintenance of remission = clinical remission at 52 wks in the subset of patients who were in remission at Wk 10

^x Corticosteroid-free remission = clinical remission at 52 wks without corticosteroids for ≥ 12 wks

^{xi} Durable remission = remission at Wks 10 and 52 in all patients who entered the maintenance phase

^{xii} Histologic remission = Geboes index score < 2.0 and absence of neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue in the same patient

^{xiii} Secondary endpoints reported for Wk 10 were clinical response, endoscopic improvement, and mucosal healing. Select secondary endpoints reported for Wk 52 were clinical response, endoscopic improvement, mucosal healing, and corticosteroid-free remission

^{xiv} Including a decrease of ≥ 1 point from baseline SFS

To: Dr. Sara Fletcher, PharmD, MPH, BCPS
osupharm.di@oregonstate.edu

Subject: Draft Dossier for the Drug Class Update with New Drug Evaluation: Topical Antiparasitics

Date: 08-19-2021

My contact information: John Marshall Clark, Ph.D., Professor of Environmental Toxicology and Chemistry and Director of the Massachusetts Pesticide Analysis Laboratory, Department of Veterinary & Animal Sciences, University of Massachusetts, Amherst, MA 01003. Office phone: 413-545-1052, Mobile phone: 413-335-0056, Fax: 413-577-4267, Email: jclark@vasci.umass.edu, Office location: N443 Morrill I Science Center

Professional disclaimer: As a principal investigator, I have conducted NIH-supported research regarding human head lice (*Pediculus humanus capitis*) resistance to permethrin and pyrethrin insecticides over the past 20 years. Following the peer-reviewed publication of this research, I have consulted on behalf of ParaPRO, LLC., to discuss and explain the protocols, findings and outcomes of my research to further assist healthcare organizations and State Medicaid Review Boards in their decision making for the category of Pediculicides and Scabicides.

Dr. Fletcher,

I just completed a review of your recently authored dossier, "Drug Class Update with New Drug Evaluation: Topical Antiparasitics." In doing so, I understand that it was published as a draft document and therefore open to comments for your consideration prior to the deadline of 8/31/2021. I respectfully submit the following information for your review and where appropriate, ask that you incorporate my research findings into the Topical Antiparasitics dossier prior to your final submission to the Oregon P&T Committee for the October meeting. My goal is to assist you in an understanding of my two decade long NIH-sponsored research specifically addressing the level and prevalence of pediculicide-resistant human head lice and the direct correlation our data has on your current recommendation to the P&T Committee. If you conclude that a change is warranted to your initial recommendation, this will allow you adequate time to address any omissions in your dossier prior the P&T Committee's October meeting. I look forward to meeting you and hope to provide public comment at the P&T Committee meeting in October. Please find attached my DUR/Pharmacy & Therapeutics Committee Public Comment/Testimony Declaration.

The following information outlined below should assist you and the State of Oregon in its complete assessment of the antiparasitic category based on the states' updated rule published earlier this year pertaining to peer reviewed, outcomes-based research.¹

1. Permethrin/Pyrethrin-resistant head lice (PRHL) have been detected in 132 of 137 locations in all 48 US States sampled with an overall mean resistance allele frequency of 0.983 (98.3%).²
 - a. Resistance to permethrin or pyrethrins in insects is caused by multiple mechanisms, one of which is target site insensitivity at the neuronal voltage-sensitive sodium channel, which is known as *knockdown resistance* or *kdr*.
 - b. In our research study, we sampled four locations in Oregon: three locations had a mean percent *kdr* resistance allele frequency of 100% and the fourth location was 80.9%.³
2. The American Academy of Pediatrics (AAP) states that, "In areas with known resistance to an over-the-counter pediculicide..., parents should involve their pediatrician for treatment with a prescription medication such as spinosad or topical ivermectin."⁴

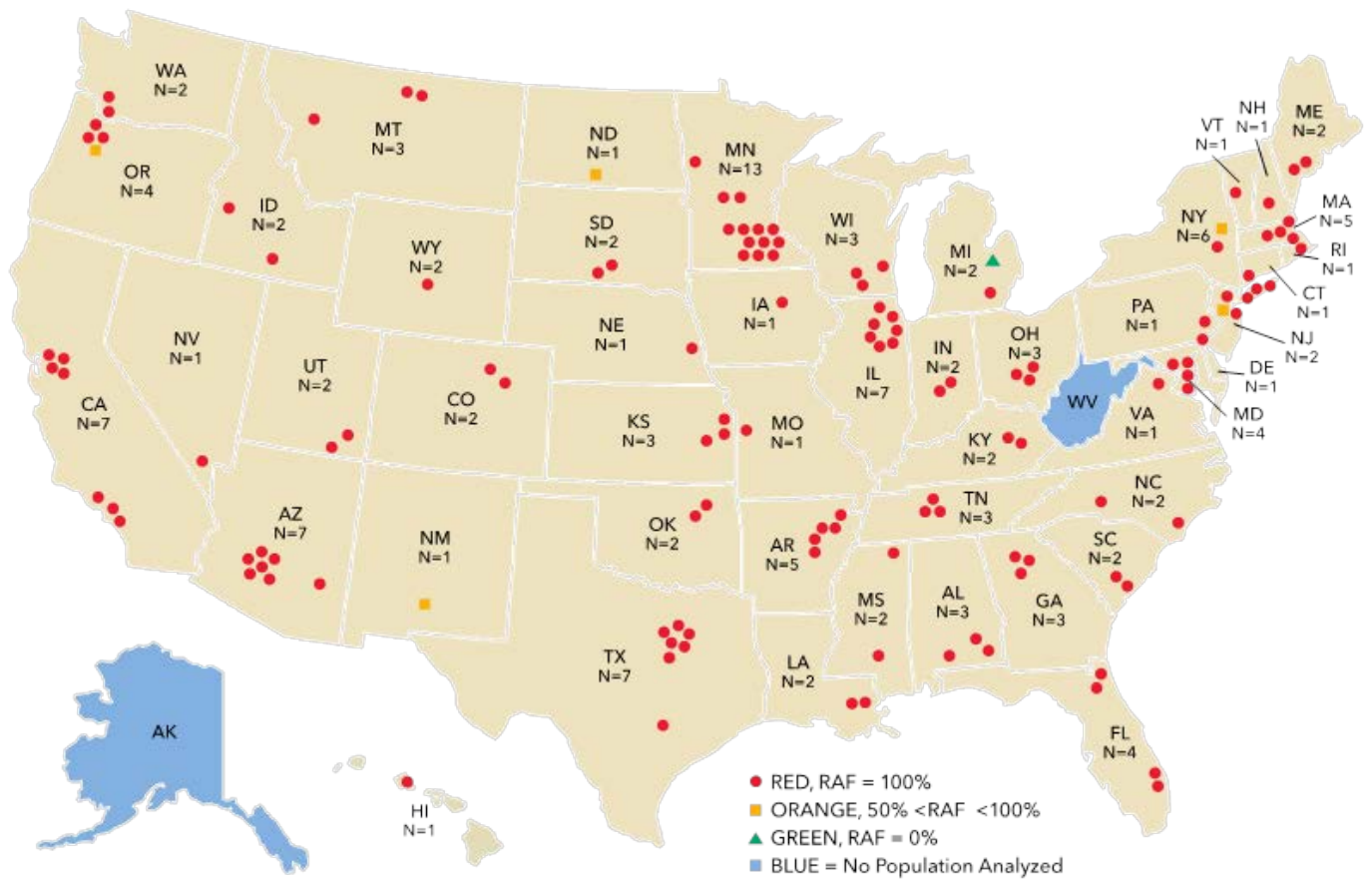
I appreciate the State of Oregon's willingness to consider additional evidence-based research during this draft review period and am hopeful that you found this supplemental information beneficial.

Warm regards,
John Marshall Clark, Ph.D.
Professor and Director, MPAL

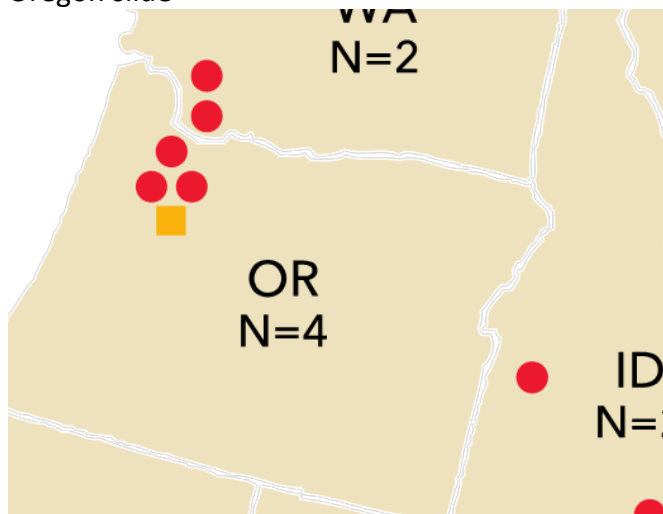
References

1. "Review Standards and Methods for Quality Assessment of Evidence" REVIEW STANDARDS AND PREFERRED SOURCES OF EVIDENCE 1. The P&T Committee and department staff will evaluate drug and drug class reviews based on sound evidence-based research and processes widely accepted by the medical profession. These evidence summaries inform the recommendations for management of the preferred drug list (PDL) and clinical prior authorization (PA) criteria. These methods support the principles of evidence-based medicine and will continue to evolve to best fit the needs of the Committee and stay current with best practices. (complete document found here [OREGON HEALTH AUTHORITY \(orpd.org\)](https://www.oregonhealthauthority.org/pdl))
2. [Expansion of the Knockdown Resistance Frequency Map for Human Head Lice \(Phthiraptera: Pediculidae\) in the United States Using Quantitative Sequencing | Journal of Medical Entomology | Oxford Academic \(oup.com\)](https://doi.org/10.1093/jme/tjz011) (see slide below for more detail)
3. <https://bit.ly/3k5L56r> (see slide below for more detail)
4. <https://bit.ly/3suN1Jv>

US kdr Resistance slide (see complete reference 2)



Oregon slide





Oregon State Medicaid
OSU Drug Use Research & Management Program
500 Summer Street NE
E35
Salem, OR 97301-1079

September 22, 2021

Dear Oregon State Medicaid,

Thank you for your request about Zeposia® (ozanimod) which has been forwarded to Medical Information by Wendy Bibeau. You have requested information regarding a written testimony request for Zeposia (ozanimod) for ulcerative colitis for the Oregon Medicaid P&T committee meeting.

Please note that Bristol Myers Squibb does not recommend the use of ZEPOSIA in any manner inconsistent with that described in the Full Prescribing Information. Please review the end of this letter for full indications and boxed warnings, and consult the attached Full Prescribing Information for ZEPOSIA. For information concerning ongoing clinical trials, please visit www.ClinicalTrials.gov.

Zeposia® - Medicaid Summary

Summary

Thank you for your unsolicited request regarding the Medicaid Summary for Zeposia® (ozanimod).

As requested, please find the following attached:

– Oregon Medicaid Summary

Important Safety Information

Contraindications:

- Patients who in the last 6 months, experienced myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure or have the presence of Mobitz type II second-degree or third degree atrioventricular (AV) block, sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker
- Patients with severe untreated sleep apnea
- Patients taking a monoamine oxidase (MAO) inhibitor

Infections: ZEPOSIA may increase the susceptibility to infections. Life-threatening and rare fatal infections have occurred in patients receiving ZEPOSIA. Obtain a recent (i.e., within 6 months or after discontinuation of prior MS or UC therapy) complete blood count (CBC) including lymphocyte count before initiation of ZEPOSIA. Delay initiation of ZEPOSIA in patients with an active infection until the infection is resolved. Consider interruption of treatment with ZEPOSIA if a patient develops a serious infection. Continue monitoring for infections up to 3 months after discontinuing ZEPOSIA

- Herpes zoster was reported as an adverse reaction in ZEPOSIA-treated patients. Herpes simplex encephalitis and varicella zoster meningitis have been reported with sphingosine 1-phosphate (S1P) receptor modulators. Patients without a healthcare professional-confirmed history of varicella (chickenpox), or without documentation of a full course of vaccination against varicella zoster virus (VZV), should be tested for antibodies to VZV before initiating ZEPOSIA. A full course of vaccination for antibody-negative patients with varicella vaccine is recommended prior to commencing treatment with ZEPOSIA
- Cases of fatal cryptococcal meningitis (CM) were reported in patients treated with another S1P receptor modulator. If CM is suspected, ZEPOSIA should be suspended until cryptococcal infection has been excluded. If CM is diagnosed, appropriate treatment should be initiated
- Progressive Multifocal Leukoencephalopathy (PML) is an opportunistic viral infection of the brain that typically occurs in patients who are immunocompromised, and that usually leads to death or severe disability. No cases of PML were identified in active-controlled MS clinical trials with ZEPOSIA. PML has been reported in patients treated with S1P receptor modulators and other MS and UC therapies and has been associated with some risk factors. If PML is suspected, withhold ZEPOSIA and perform an appropriate diagnostic evaluation. If confirmed, treatment with ZEPOSIA should be discontinued
- In the MS and UC clinical studies, patients who received ZEPOSIA were not to receive concomitant treatment with antineoplastic, non-corticosteroid immunosuppressive, or immune-modulating therapies used for treatment of MS and UC. Concomitant use of ZEPOSIA with any of these therapies would be expected to increase the risk of immunosuppression. When switching to ZEPOSIA from

immunosuppressive medications, consider the duration of their effects and their mode of action to avoid unintended additive immunosuppressive effects

- Use of live attenuated vaccines should be avoided during and for 3 months after treatment with ZEPOSIA. If live attenuated vaccine immunizations are required, administer at least 1 month prior to initiation of ZEPOSIA

Bradyarrhythmia and Atrioventricular Conduction Delays: Since initiation of ZEPOSIA may result in a transient decrease in heart rate and atrioventricular conduction delays, dose titration is recommended to help reduce cardiac effects. Initiation of ZEPOSIA without dose escalation may result in greater decreases in heart rate. If treatment with ZEPOSIA is considered, advice from a cardiologist should be sought for those individuals:

- with significant QT prolongation
- with arrhythmias requiring treatment with Class 1a or III anti-arrhythmic drugs
- with ischemic heart disease, heart failure, history of cardiac arrest or myocardial infarction, cerebrovascular disease, and uncontrolled hypertension
- with a history of Mobitz type II second-degree or higher AV block, sick sinus syndrome, or sino-atrial heart block

Liver Injury: Elevations of aminotransferases may occur in patients receiving ZEPOSIA. Obtain liver function tests, if not recently available (i.e., within 6 months), before initiation of ZEPOSIA. Patients who develop symptoms suggestive of hepatic dysfunction should have hepatic enzymes checked and ZEPOSIA should be discontinued if significant liver injury is confirmed. Caution should be exercised when using ZEPOSIA in patients with history of significant liver disease

Fetal Risk: There are no adequate and well-controlled studies in pregnant women. Based on animal studies, ZEPOSIA may cause fetal harm. Women of childbearing potential should use effective contraception to avoid pregnancy during treatment and for 3 months after stopping ZEPOSIA

Increased Blood Pressure: Increase in systolic pressure was observed after about 3 months of treatment and persisted throughout treatment. Blood pressure should be monitored during treatment and managed appropriately. Certain foods that may contain very high amounts of tyramine could cause severe hypertension in patients taking ZEPOSIA. Patients should be advised to avoid foods containing a very large amount of tyramine while taking ZEPOSIA

Respiratory Effects: ZEPOSIA may cause a decline in pulmonary function. Spirometric evaluation of respiratory function should be performed during therapy, if clinically indicated

Macular edema: S1P modulators have been associated with an increased risk of macular edema. Patients with a history of uveitis or diabetes mellitus are at increased risk. Patients with a history of these conditions should have an ophthalmic evaluation of the fundus, including the macula, prior to treatment initiation and regular follow-up examinations. An ophthalmic evaluation is recommended in all patients at any time if there is a change in vision. Continued use of ZEPOSIA in patients with macular edema has not been evaluated; potential benefits and risks for the individual patient should be considered if deciding whether ZEPOSIA should be discontinued

Posterior Reversible Encephalopathy Syndrome (PRES): Rare cases of PRES have been reported in patients receiving a S1P receptor modulator. If a ZEPOSIA-treated patient develops unexpected neurological or psychiatric symptoms or any symptom/sign suggestive of an increase in intracranial pressure, a complete physical and neurological examination should be conducted. Symptoms of PRES are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. Delay in diagnosis and treatment may lead to permanent

neurological sequelae. If PRES is suspected, treatment with ZEPOSIA should be discontinued

Unintended Additive Immunosuppressive Effects From Prior Immunosuppressive or Immune-Modulating Drugs: When switching from drugs with prolonged immune effects, the half-life and mode of action of these drugs must be considered to avoid unintended additive immunosuppressive effects while at the same time minimizing risk of disease reactivation. Initiating treatment with ZEPOSIA after treatment with alemtuzumab is not recommended

Severe Increase in Disability After Stopping ZEPOSIA: Severe exacerbation of disease, including disease rebound, has been rarely reported after discontinuation of a S1P receptor modulator. The possibility of severe exacerbation of disease should be considered after stopping ZEPOSIA treatment so patients should be monitored upon discontinuation

Immune System Effects After Stopping ZEPOSIA: After discontinuing ZEPOSIA, the median time for lymphocyte counts to return to the normal range was 30 days with approximately 90% of patients in the normal range within 3 months. Use of immunosuppressants within this period may lead to an additive effect on the immune system, therefore caution should be applied when initiating other drugs 4 weeks after the last dose of ZEPOSIA

Most Common Adverse Reactions that occurred in the MS clinical trials of ZEPOSIA-treated patients ($\geq 4\%$): upper respiratory infection, hepatic transaminase elevation, orthostatic hypotension, urinary tract infection, back pain, and hypertension

In the UC clinical trials, the most common adverse reactions that occurred in $\geq 4\%$ of ZEPOSIA-treated patients and greater than in patients who received placebo were upper respiratory infection, liver test increased, and headache

For additional safety information, please see the full Prescribing Information and Medication Guide

Product Indication: Zeposia® (ozanimod):

ZEPOSIA is a sphingosine 1-phosphate receptor modulator indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.
- Moderately to severely active ulcerative colitis (UC) in adults.

Please refer to the end of this information packet for the following:

- Reporting adverse event cases or product quality complaints, or to provide information on exposure to a BMS product during pregnancy or lactation.

With the aim to continuously improve the quality of our service we would like to request you complete a brief satisfaction survey. It will only take you 3 minutes to complete. The survey can be accessed at the below link:

[Click here](#)

We trust that you will find this information helpful. If you have further questions or require additional information, please contact BMS Medical Information Department at 1-800-321-1335.

Sincerely,
BMS Medical Information

For Your Consideration:

Adverse Event / Pregnancy

If you become aware of a patient who has experienced an adverse event with a BMS product, has received treatment with a BMS product during pregnancy or lactation, or has become pregnant while her partner received treatment with a BMS product, please contact us at 1-800-721-5072.



Date: 8/30/2021

To: *Members of the Oregon Health Authority Pharmacy & Therapeutics Committee*

OHSU Health

Division of Addiction Medicine

3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098
tel 503 887 4388
seaman@ohsu.edu

From: Andrew Seaman, MD

Assistant Professor of Medicine, Oregon Health & Sciences University

Medical Director of Hepatitis and HIV Services, Central City Concern

Director Oregon HCV Elimination ECHO

Re: Direct Acting Antiviral Authorization Considerations, 10/7/2021

Thank you for the opportunity to offer community feedback on considerations for Direct Acting Antiviral (DAA) therapy for hepatitis C virus (HCV) infections. I would like to address two main points, 1) removal of “Chronic Hepatitis C” from PA criteria in favor of “positive hepatitis C RNA,” and 2) removal of all prior authorization criteria for direct acting antivirals.

Allowing Treatment of Acute Hepatitis C

The national and international guidelines now suggest removing all mention of HCV chronicity from treatment determinations with DAAs. Both the [American Association for the Study of Liver Diseases / Infectious Diseases Society of America joint guidelines](#) and the [European Association for the Study of the Liver](#) recommend treating hepatitis C without waiting for repeat testing to confirm chronicity. This is for several reasons. First, from the public health perspective, individuals with recent acute infection have clearly demonstrated their current risk behaviors and are at a far higher risk of transmitting the virus than individuals who have chronic infection. Treatment of individuals with acute infection is also more cost effective than deferring treatment until confirming chronic infection.¹ This is in part because early access to treatment leads to a reduction in HCV viremia prevalence and new infections.² Mathematical modeling suggests treatment of acute hepatitis C among people who inject drugs can reduce further transmission.³

There is also a moral obligation to treat individuals for a potentially lethal viral illness when we have an opportunity to do so. As the medical director of Oregon’s largest HCV elimination program at Central City Concern, I have first-hand experience of treating over a thousand highly vulnerable individuals with hepatitis C infection. This population often comes in and out of care. We have done everything we can at CCC to limit internal systemic barriers to treatment, including developing new screening and work up algorithms that allow us to initiate treatment almost immediately following screening and confirmation of HCV viremia.⁴ These systems allow us to treat the majority of individuals with HCV we encounter (75-80%). However, when payers require us to delay treatment 6 months to

confirm chronicity, we too often lose people. Some of them will be treated down the line, some will infect others, and some will never be treated and possibly develop complications. As I have presented to this committee before, hepatitis C is about far more than just liver disease. HCV increases the risk of diabetes and worsens pre-existing metabolic syndrome. It is associated with chronic kidney disease, myocardial infarctions, hematologic malignancies, and severe and persistent mental illness. The idea of HCV itself is also a reminder of past stigmatized behaviors and successful treatment is associated with higher engagement with substance use treatment and harm reduction services.⁵

This one is simple: cut out “chronic,” approve treatment for all with HCV viremia. None of this would be necessary to discuss, however, if we would follow states taking a lead in this epidemic and remove all requirement for prior authorization for direct acting antiviral therapy.

We should remove ALL prior authorization requirements for DAAs

There are now 8 states that have completely removed prior authorization requirements for HCV treatment with direct acting antivirals: Washington, Louisiana, New York, California, Indiana, Wisconsin, Michigan, and most recently, Rhode Island. Oregon should be next.

Hepatitis C treatment has transformed from an extremely complex algorithm with complex decision making around medication selection and duration, to the current reality, where the vast majority of HCV viremic patients could be given one of two pangenotypic agents with virtually no clinically required pre-treatment evaluation besides an HCV RNA test. Even as we develop lower barrier HCV testing modalities like the Dried Blood Spot HCV RNA test our group helped bring to the market in the United States for the first time, we are struggling to translate these advances into clinical progress. There are individuals who want treatment but simply cannot undergo the extensive phlebotomy-based testing required by payers to initiate treatment. In addition, prior authorization requirements—lenient or not—add a time buffer between diagnosis and treatment initiation without any clinical benefits to the beneficiaries of the Oregon Health Program. These barriers lead to loss to follow up, sustained community HCV transmission, and greater long-term cost to state taxpayers.

Removing prior authorization requirements will not lead to widespread misuse of these medications. Medical providers have a duty to practice medicine to the extent of their capacity and training; removing prior authorization restrictions will not change this. As the director of the Oregon Hepatitis C Elimination ECHO and the lead clinician on a current expansion of telemedicine treatment of hepatitis C in rural Oregon, I can attest that community providers remain reticent to prescribe DAAs until they feel expert in the subject matter. In fact, we often must gently nudge providers to start prescribing well after they likely could have begun. Removing the prior authorization is about taking payer barriers out of the equation so we can truly focus our innovations on patient level barriers to treatment and move toward HCV elimination in Oregon.

Once again, I am asking you to do the right thing: end all prior authorization restrictions for direct acting antivirals in Oregon.

A handwritten signature in black ink, appearing to read "Andrew Seaman". The signature is fluid and cursive, with a long horizontal stroke at the end.

Andrew Seaman, MD

References:

- 1) Bethea ED, Chen Q, Hur C, Chung RT, Chhatwal J. Should we treat acute hepatitis C? A decision and cost-effectiveness analysis. *Hepatology*. 2018 Mar;67(3):837-846. doi: 10.1002/hep.29611. Epub 2018 Jan 24. PMID: 29059461; PMCID: PMC5826841.
- 2) Boerekamps A, van den Berk GE, Lauw FN, Leyten EM, van Kasteren ME, van Eeden A, Posthouwer D, Claassen MA, Dofferhoff AS, Verhagen DWM, Bierman WF, Lettinga KD, Kroon FP, Delsing CE, Groeneveld PH, Soetekouw R, Peters EJ, Hullegie SJ, Popping S, van de Vijver DAMC, Boucher CA, Arends JE, Rijnders BJ. Declining Hepatitis C Virus (HCV) Incidence in Dutch Human Immunodeficiency Virus-Positive Men Who Have Sex With Men After Unrestricted Access to HCV Therapy. *Clin Infect Dis*. 2018 Apr 17;66(9):1360-1365. doi: 10.1093/cid/cix1007. PMID: 29186320.
- 3) Martin NK, Thornton A, Hickman M, Sabin C, Nelson M, Cooke GS, Martin TCS, Delpech V, Ruf M, Price H, Azad Y, Thomson EC, Vickerman P. Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? *Epidemiological and Modeling Insights*. *Clin Infect Dis*. 2016 May 1;62(9):1072-1080. doi: 10.1093/cid/ciw075. Epub 2016 Feb 16. PMID: 26908813; PMCID: PMC4826456.
- 4) Seaman A, King CA, Kaser T, Geduldig A, Ronan W, Cook R, Chan B, Levander XA, Priest KC, Korthuis PT. A hepatitis C elimination model in healthcare for the homeless organization: A novel reflexive laboratory algorithm and equity assessment. *Int J Drug Policy*. 2021 Jul 26:103359. doi: 10.1016/j.drugpo.2021.103359. Epub ahead of print. PMID: 34325969.
- 5) E Williams B, Nelons D, Seaman A, Witkowska M, Ronan W, Wheelock H, Zaman A, Garcia J. Life projects: the transformative potential of direct-acting antiviral treatment for hepatitis C among people who inject drugs. *Int J Drug Policy*. 2019 Oct;72:138-145. doi: 10.1016/j.drugpo.2019.03.015. Epub 2019 Apr 15. PMID: 30995968.



Permethrin *Resistance Mechanisms* & *Monitoring...*

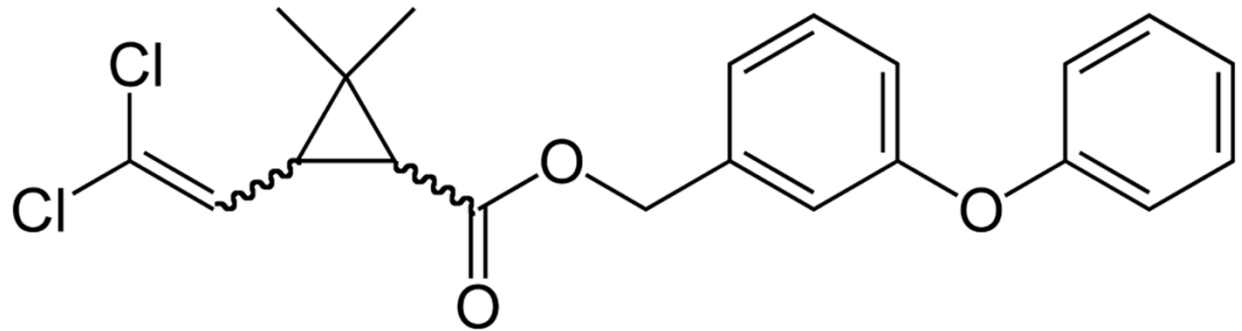
and how it pertains to the selection of effective new pediculicides

Permethrin

(a Pyrethroid Insecticide)

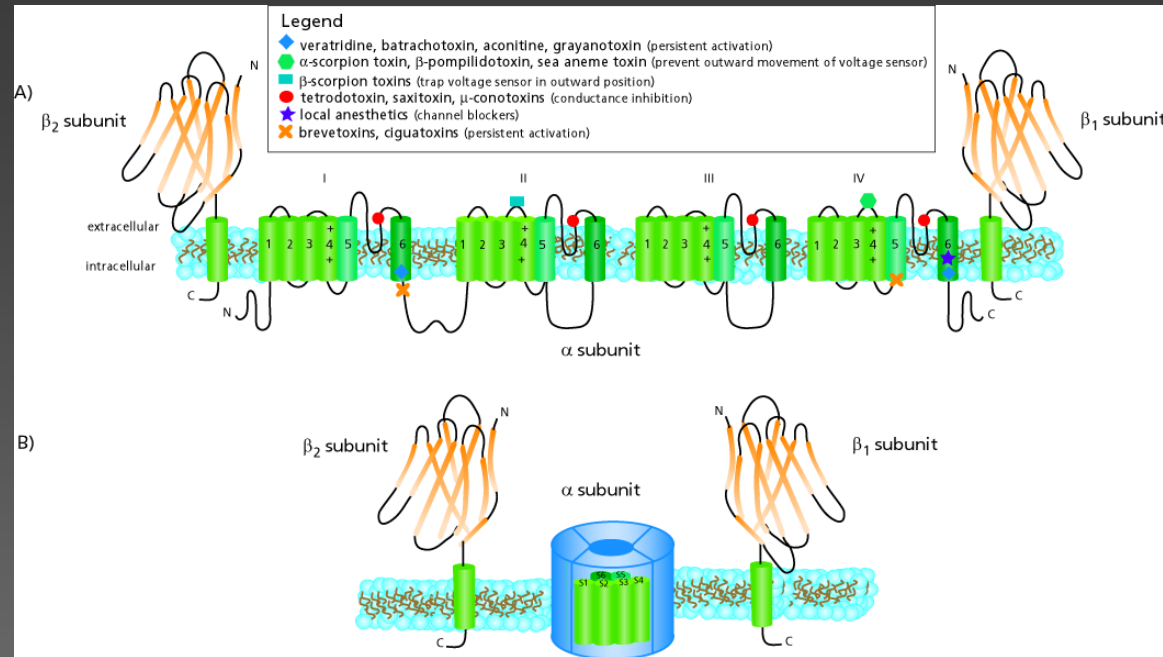


First-line therapy



Q: So why is Nix no longer killing head lice?

Permethrin resistant lice elicit a knockdown resistance phenotype (*kdr*)



Kdr is due to point mutations within the α -subunit gene of VSSC leading to target site insensitivity

NOTE: *Kdr* results in cross-resistance to DDT and the natural pyrethrins (e.g., RID[®])

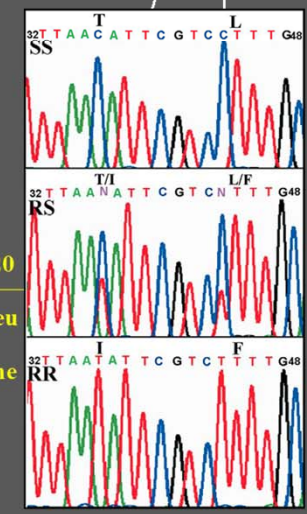
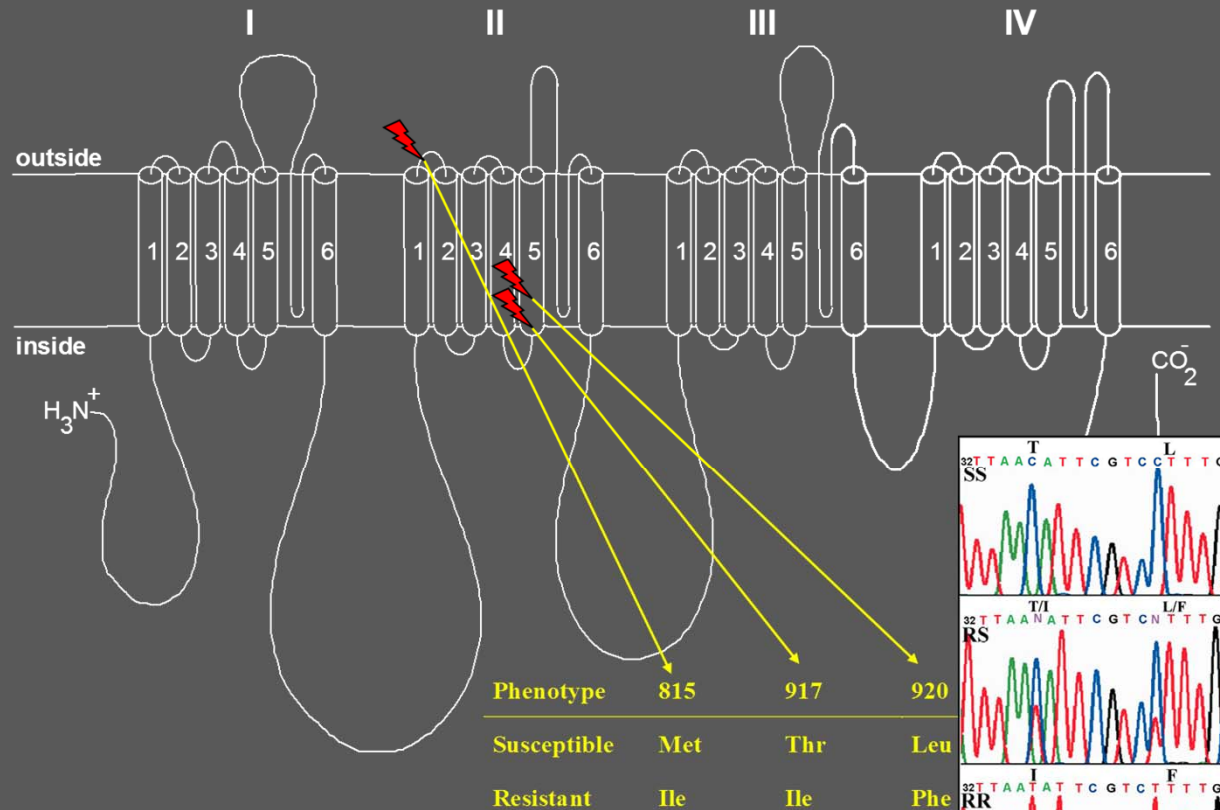


Permethrin resistance is due to 3 *kdr*-type mutations (MI, TI, LF) in the **VSSC** causing target site insensitivity

M815I (MI)

T917I (TI)

L920F (LF)



Lee et al. 2000. Pestic. Biochem. Physiol. 66:130-143

Yoon et a., 2008. Insect Biochem.& Mol. Biol. 38:296-306

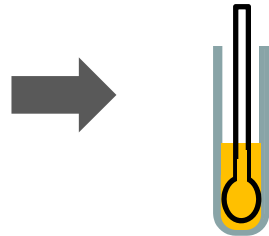
Quantitative Sequencing (QS) Procedures

Population genotyping method



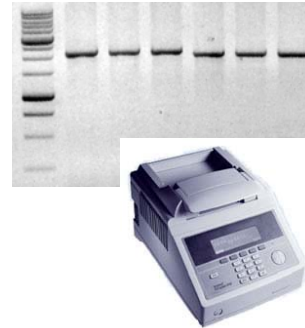
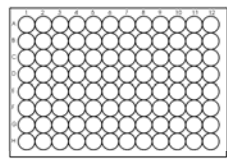
Lice collection:

14-28 lice
per site X
~90 sites

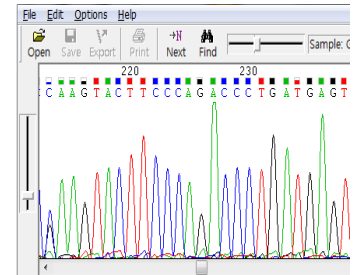


**Genomic DNA
Extraction:**

In a 96-well format ~90 samples



PCR:



QS:

**Two sequencing
reaction = one
lice population**



1 day

3 hrs

5 hrs

Kwon et al. J. Med. Ent. 45:912-920, 2008.

Expansion of the knockdown resistance frequency map for human head lice (*Phthiraptera: Pediculidae*) in the United States using quantitative sequencing.

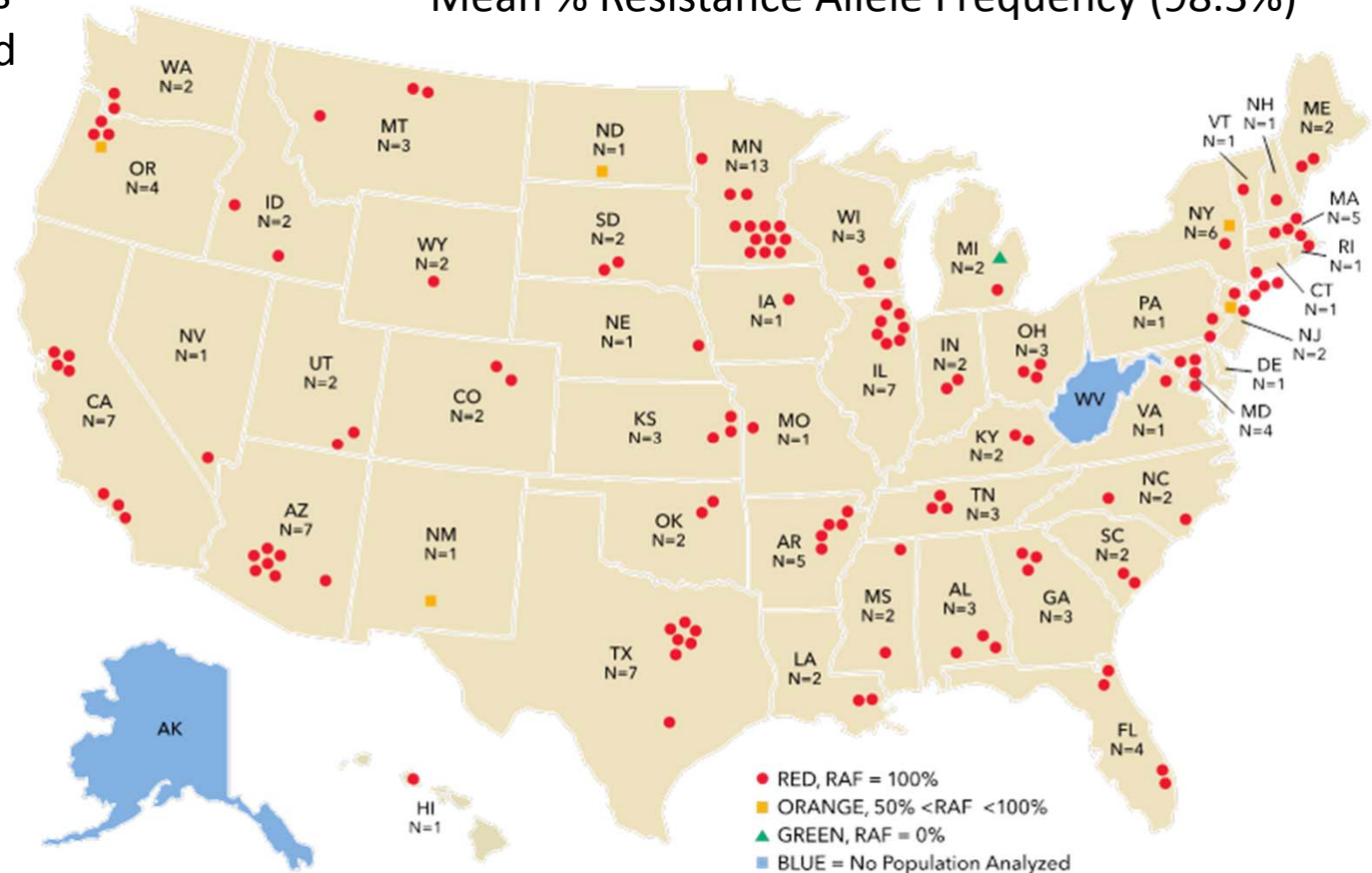
(Gellatly et al. J. Med. Entomol. 2016)

METHODS

- 48 US states sampled
- 138 sites
- 479 human subjects
- 14,281 lice collected
- Kdr detected by QS

RESULTS

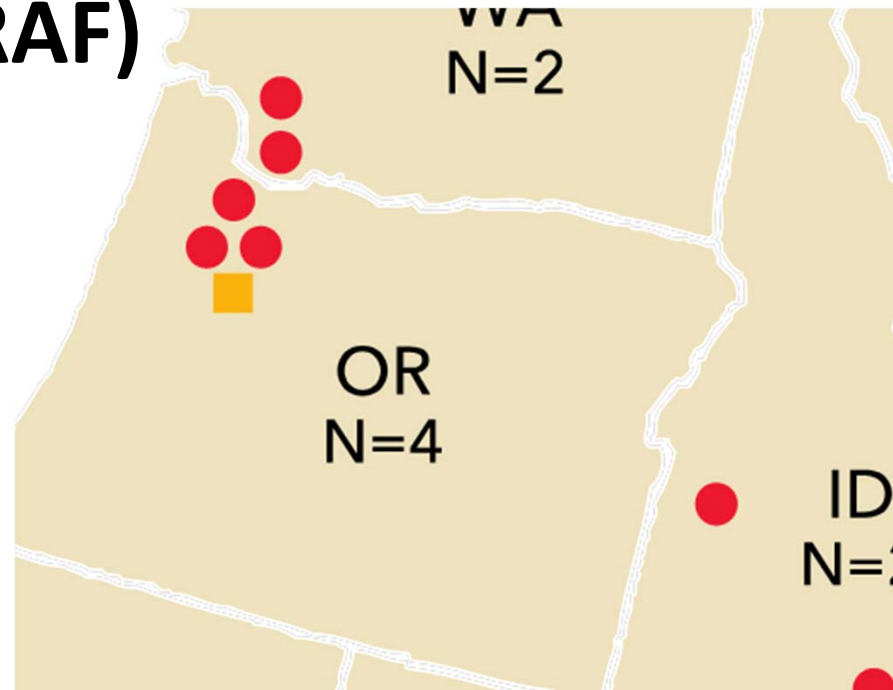
- 48/48 states had kdr
- 132/138 sites has 100% kdr
- Mean % Resistance Allele Frequency (98.3%)



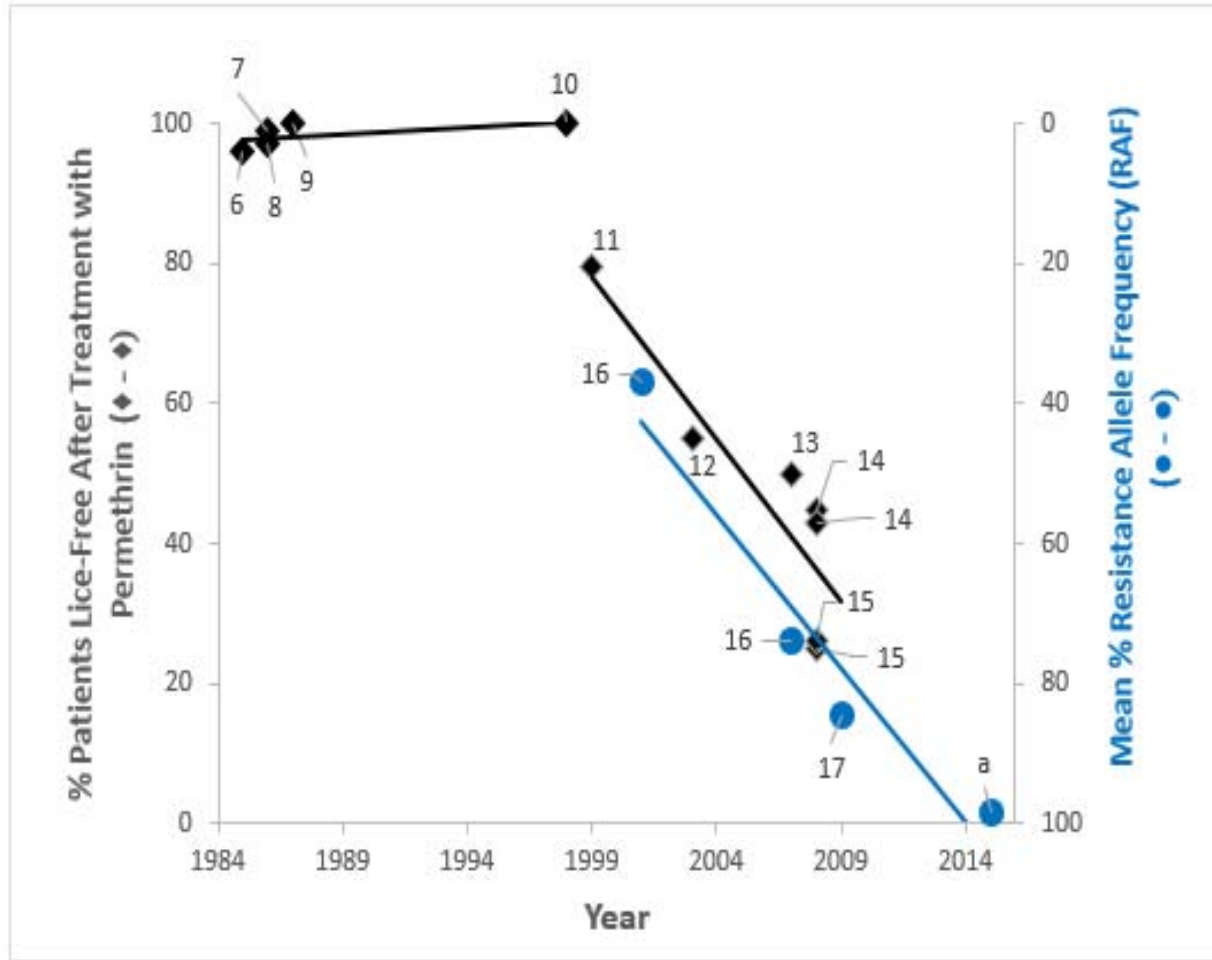
Oregon

Location (Mean % RAF)

- Lake Oswego (100%)
- Portland (100%)
- Tigard (100%)
- Wilsonville (80.9%)



Clinical
Studies



QS

^aGellatly et al. 2015 data from this paper

Note: Clinical studies included wet combing so efficacy due to permethrin is lower than reported

Gellatly et al. 2016. J. Med. Entomol. 53: 653-659

Caring Ambassadors Program, Inc.

Empowering people to be ambassadors for their own health since 1997.

Caring Ambassadors Program
Lorren Sandt, Executive Director
P.O. Box 1748
Oregon City, OR 97045

Public Comment HCV Direct-Acting Antivirals Class Update and Treatment Guidelines

OSU Drug Use Research and Management Program
Oregon Drug Use Review / Pharmacy & Therapeutics Committee
October 7, 2021

The Caring Ambassadors Program is a national, nonprofit advocacy organization based in Oregon City, Oregon. We respectfully submit our written comment on the current criteria and suggest an update to the current Hepatitis C PDL class to treat Chronic Hepatitis C Virus (HCV). We would like to recognize and thank you for the previous changes that have allowed us to increase access to care and cure for Oregonians living with hepatitis C. Many people are cured, but we still have barriers that limit the opportunities to eliminate this virus and save healthcare dollars and, more importantly, lives.

Thank you for the proposed update to the guidelines for treating children. This is unfortunately a growing population. Thankfully with the new DAA's, children can be cured prior to developing any complications from living decades with the virus.

We ask that Oregon's Medicaid program allow full access to FDA-approved hepatitis C direct-acting agents by removing the prior authorization criteria for using these therapies as 8 other states have already done. Additionally, we advocate for providing treatment for all people living with hepatitis C at the time of diagnosis, regardless of acute versus chronic infection.

AASLD guidelines;

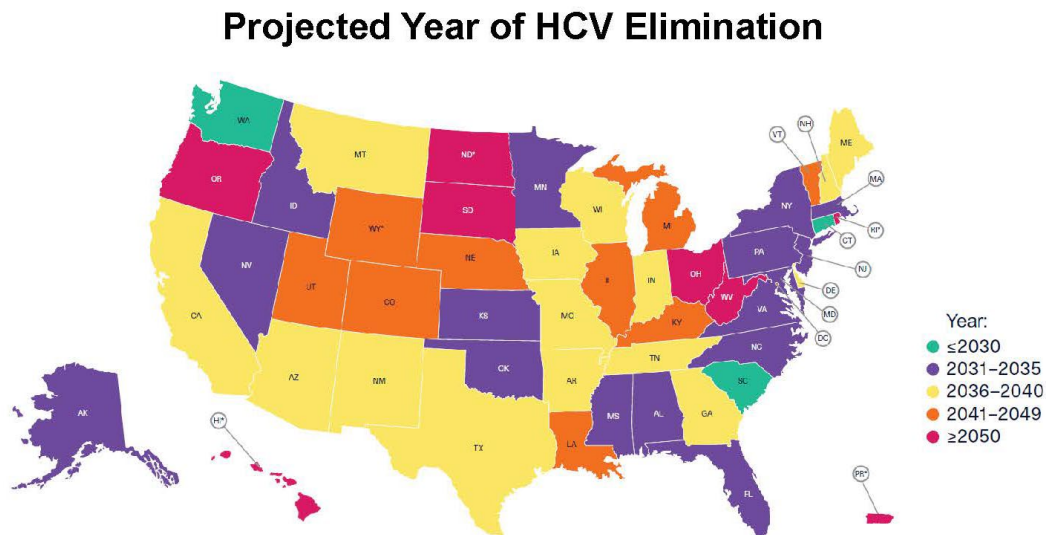
“Access to HCV treatment for people at high risk of onward transmission, including those with acute and recent HCV infection, should be a priority... Because Acute hepatitis C virus infection is a chronic problem.

HCV screening is recommended because of the known benefits of care and treatment in reducing the risk of decompensated cirrhosis, hepatocellular carcinoma, and all-cause mortality, and the potential public health benefit of reducing transmission through early treatment, viral clearance, and reduced risk behaviors ([Chou, 2020](#)); ([Owens, 2020](#)); ([Schillie, 2020](#)); ([Smith, 2012](#)).

Patients with acute HCV infection should be treated upon initial diagnosis without awaiting spontaneous resolution, using a “test and treat” strategy and according to the simplified approach, if eligible. Real-world data have demonstrated a reduction in HCV viremia prevalence and incidence with unrestricted access to HCV therapy ([Boerekamps, 2018](#)). In addition, mathematical modeling suggests that DAA treatment scale-up, especially among those at highest risk of transmission, can reduce HCV incidence and prevalence ([Martin, 2013](#)); ([Martin, 2016](#)). Moreover, delay introduced by waiting for spontaneous clearance may be associated with loss to follow up.”

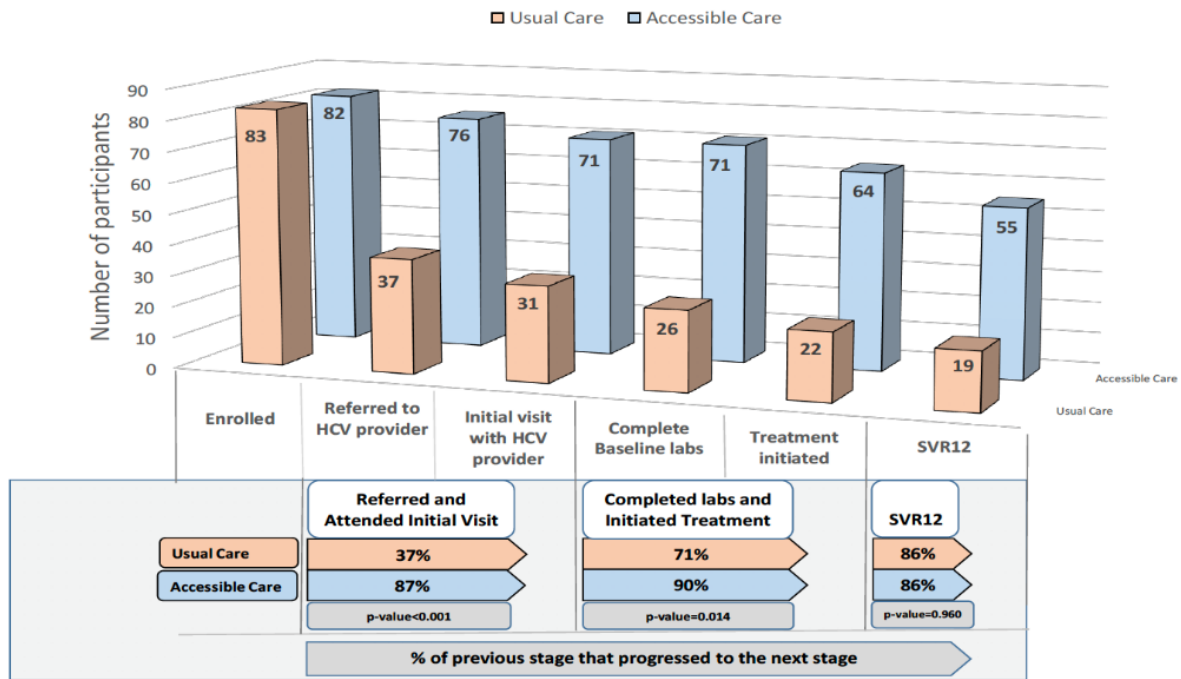
Treating acute hepatitis C treatment in Oregon is also a health equity issue. Native Americans and Black Oregonians are disproportionately affected by acute and chronic HCV and have the highest mortality rate in our state. ([Thomas2020](#))

Oregon is not on target for elimination.



But we could be. Data from Central City Concern, the Oregon Hope Study, and the Accessible Care Study all show how reducing barriers to care result in higher numbers of people being cured. ([Seaman2021](#)) ([Korthius2021](#))([Eckhardt 2018](#))

Hepatitis C virus (HCV) infection treatment cascade comparing the Accessible Care arm with Usual Care.



Hepatitis C treatment saves lives and is cost saving to the health care system. ([Milliman 2021](#))
 Please consider removing some of the final state-controlled barriers to the elimination of hepatitis C.
 Thank you for all your work, your time, and consideration.

Respectfully,

Lorren Sandt
 Executive Director
 Caring Ambassadors Program