Pink Sheet
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March 2017
Pharma intelligence informa

Consumer Health Focus

Alka-Seltzer Antacid Will 'Plop, Plop Fizz, Fizz' Without Aspirin

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Original *Alka-Seltzer* pioneered offering an effervescent remedy for acid indigestion and pain and the iconic OTC brand looks to be the first in the category to reformulate without its analgesic component, aspirin, partly due to a risk of serious bleeding.

In advance of an FDA advisory panel meeting April 4 on the safety of antacid/aspirin products available under an OTC monograph, **Bayer AG**'s consumer products business announced it is bowing to winds of change and is reformulating the product marketed since 1931, along the way establishing "plop, plop, fizz, fizz" as an iconic advertising tag line.

The brand remained on the market over those decades despite competition that frequently grew and despite FDA requiring label warnings about potential liver damage from drinking alcohol while using products containing aspirin, related compounds and nonsteroidal anti-inflammatory drugs in 1998 and about the risk of serious bleeding from antacid/aspirin products in 2010.

In addition to helping prevent potential misuse of three Alka-Seltzer products that contain aspirin for pain relief and sodium bicarbonate and citric acid for acid indigestion, Bayer Consumer Health says it is reformulating the products because consumers are moving to single-indication products to remedy common conditions.

The pain relief indication will be removed from the labels with aspirin removed from the Alka-Seltzer antacid products – original, lemon-lime and extra-strength versions, which combine as the top-selling antacid/analgesic brand in the US *(see table below)*.

Alka-Seltzer's history as the first effervescent antacid/aspirin for acid indigestion and pain relief includes decades of advertising featuring "Speedy" the cartoon character and sales in pharmacies and other venues from single-dose dispensing machines.

"We see consumer purchase trends moving more and more in the direction of [products] that are focused solely on heartburn and the relief of stomach upset," said Andre Schmidt, US medical affairs vice president for **Bayer Consumer Health**, on March 23.

"Given the shift in consumer trends and consumer preferences and as well we eliminate any potential misuse that might happen with these combination products, we made the decision to reformulate certain Alka-Seltzer effervescent products," Schmidt, a physician, said in an exclusive interview about the change.

Bayer HealthCare LLC, which includes Bayer Consumer, says it is conducting stability tests of the new formulation and it has not started manufacturing. Reformulating and producing distribution inventory of an OTC monograph product should require one to two years, the firm says.

The existing antacid/aspirin Alka-Seltzer products will remain available during the reformulation, though the firm says it has advised distributors, retailers and other businesses that market or sell the brand that it will replace the current products.

Other antacid/aspirin products marketed for acid indigestion and pain include numerous private label/store brands as well as **Tower Laboratories Inc.**'s *Bromo Seltzer* and **Navarro Discount Pharmacies LLC**'s *Vida Mia Pain Relief*.

ALL BAYER ANTACIDS WILL BE SINGLE-INGREDIENT

The reformulation is limited to the three Alka-Seltzer effervescent tablet products indicated for gastric symptoms and headache or body ache from causes including overindulgence in food or alcohol.

Products in the brand's *Alka-Seltzer Plus* line of effervescent tablets and capsules for cough/cold, congestion and sinus relief do not contain aspirin and are not being reformulated. Each of those contains acetaminophen and also combinations of dextromethorphan, guaifenesin, phenylephrine, doxylamine succinate or chlorpheniramine maleate.

Formulations also will remain the same for Alka-Seltzer brand chewables for heartburn (calcium carbonate) or gas and heartburn (calcium carbonate/simethicone) relief and a gummy-format calcium supplement for heartburn.

The chewables and the gummy, Schmidt says, compete directly with other antacid brands that for three of four years ago have showed "a consistent trend" of taking the single-ingredient approach.

"We just see that the consumer asks more

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MARCH 2017

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and more for these types of products and not the combination products," he said.

Removing aspirin from the antacid effervescent tablets and the pain relief indication from their labels " is very much in line with the rest of the Alka-Seltzer family of products," Schmidt added.

BAYER ALSO REVIEWS RISK/ BENEFIT PROFILE

Schmidt acknowledged that FDA is concerned about the safety of antacid/aspirin combinations. Before scheduling an advisory panel to consider whether the formulations and other OTC nonsteroidal anti-inflammatory drugs and acetaminophen products should remain available under an OTC monograph, the agency in June 2016 published a Drug Safety Communication stating that the use of the products indicated to treat heartburn, sour stomach, acid indigestion or upset stomach is associated with internal bleeding.

Schmidt said Bayer contacted FDA, prior to the agency's advisory panel announcement, about reformulating and relabeling the three Alka-Seltzer products and the change is not in response to the meeting, but follows Bayer's own product risk-benefit review and its consumer preference tracking.

The firm is not aware what FDA's panel, in a joint meeting of the Nonprescription Drugs and Drug Safety and Risk Management advisory committees, will specifically discuss or what if anything the agency will require.

"We obviously knew that the FDA is continually looking at how to improve the monograph. That was certainly also the reason why we looked into the product, together with the change in consumer trends. We just took the decision that it's a good time point right now to make this decision," Schmidt said.

FDA's Center for Drug Evaluation and Research on March 3 said it continues to receive reports of internal bleeding potentially linked to use of antacid/aspirin products, including reports of patients requiring blood transfusions, despite requiring a warning statement about the risk of serious bleeding, including in the stomach and gastrointestinal tract, in the combination products' Drug Facts labels since 2010 and since its 2016 Drug Safety Communication. *(Also see "Safety Review For Upset Stomach, Hangover OTCs Reconsiders Science" - Pink Sheet, 7 Mar, 2017.)*

Antacid/aspirin products are among the OTCs containing acetaminophen or NSAIDs that were required to add a label warning on a risk of serious bleeding in a 2009 rule amending the OTC monograph for internal analgesics, antipyretics and antirheumatics, going beyond changes the agency proposed in a 2006 tentative final rule. The proposed guidelines included clearly highlighting the presence of acetaminophen in a drug and identifying ingredients as NSAIDs – ibuprofen, naproxen and ketoprofen in addition to aspirin. But the final rule added revised warnings against the use of multiple acetaminophen products and concurrent use of acetaminophen and the Rx anticoagulant warfarin. *(Also see "FDA Expands Acetaminophen, NSAID Labeling Beyond Tentative Final Rule" - Pink Sheet, 4 May, 2009.)*

CDER opened a docket–FDA-2017-N-0965 – for public comment on the NDAC/DSRAM joint meeting at the Tommy Douglas Conference Center in Silver Spring, Md., and will accept comments through April 3; comments received by March 21 will be provided to the committees and others will be considered the agency.

The gastrointestinal OTCs that will be discussed are for conditions such as heartburn, nausea, fullness, belching, gas, acid indigestion or sour stomach and are marketed under FDA's internal analgesic and antacid monographs and the nonprescription products indicated for hangovers on the meeting agenda are available under the overindulgence, internal analgesic and stimulant monographs. Through March 24, FDA had not published the committees' rosters, questions they will consider and other agenda details for the meeting.

FIZZING AT TOP OF ANTACID/ANALGESIC CATEGORY

While competition grows from single-ingredient antacid products, Alka-Seltzer dominates the antacid/analgesic combination category, according to market research firm IRI's sales data from sales at supermarket, drugstore and mass merchandise chains, military commissaries and some club and discount chains. Chicago-based IRI's data cover the 52 weeks ending Feb. 19.

US Antacid/Analgesic Combination Product Sales By Brand	Sales	% Change From Year Ago	Market Share	% Change From Year Ago
Total	$53.1m	(4.11)	–	–
Alka Seltzer	$45.4m	(3.58)	85.59	0.47
Private label	$7.6m	(6.62)	14.27	(0.38)
Handy Solutions	$27,311	(57.25)	0.05	(0.06)
Family Care	$20,384	(7.59)	0.04	(0.00)
Convenience Valet	$14,183	(40.24)	0.03	(0.02)
Lil Drugstore	$9,306	(5.63)	0.02	(0.00)

OTC Monograph Reform, User Fee Legislation Coming 'Any Day' – CHPA

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Legislation with proposals that drug firms were hesitant to get behind – reforming FDA's OTC drug monograph program and establishing a user fee program to support the agency's work – is close to surfacing in Congress with the industry's backing.

A separate change also requiring legislation but that the industry has backed from the start, eliminating the Affordable Care Act requirement that consumers have prescriptions to buy OTC drugs with flexible spending, health savings and other pretax accounts, took a backward step as the House cancelled a vote on legislation to repeal the act.

Consumer Healthcare Products Association President and CEO Scott Melville discussed the trade group's legislative priorities at the association's Annual Executive Conference in Amelia Island, Fla., on March 21.

Melville said CHPA expects a bill will be introduced to Congress "any day now."

"While optimistic about the prospects for it happening, we have more options to think about the innovations that can be unleashed once reforms are enacted," he said, adding that monograph reform is a "once-in-a-lifetime initiative."

FDA in 2014 launched an initiative to improve and modernize the OTC monograph system, opening a docket for comments and conducting a public hearing to solicit feedback on making the process "more agile and responsive." *(Also see "FDA Floats OTC Monograph Overhaul To Be "More Agile And Responsive"" - Pink Sheet, 24 Feb, 2014.)*

"At first we viewed reform as a potential threat," Melville said.

"However, as we prepared for the hearing, our view point began to evolve and we [started to see] monograph reform not as a threat but as an opportunity to work with FDA and Congress to develop a better regulatory framework that could preserve and improve the monograph for generations to come."

> CHPA sees "monograph reform not as a threat but as an opportunity to work with FDA and Congress to develop a better regulatory framework that could preserve and improve the monograph for generations to come." – President and CEO Scott Melville

As Center for Drug Evaluation and Research officials and industry stakeholders alike suggested in comments and during discussions on monograph reform, CHPA says it expects the legislation will allow FDA to add to or change a monograph through administrative orders rather than requiring a rulemaking for any change. Similarly, the legislation likely will authorize FDA to establish a more efficient process for making monograph drug label changes.

The agency has made few changes to OTC monographs since its initial decisions in the early 1970s as it n establishing the platform to set conditions for drugs available nonprescription to be generally recognized as safe and effective for certain indications. Products with active ingredients or indications not within a monograph must gain pre-market approval through the NDA review process.

FDA officials as well as industry stakeholders say changes are needed before any additions to the monograph are likely. *(Also see "OTC Drug Industry Could Stand To Gain With 'Pragmatist' In White House" - Pink Sheet, 11 Nov, 2016.)*

USER FEES PART OF REFORM

CDER also says no monograph progress can happen without user fees to support its work, and in 2016 the center began a separate but related initiative on looking at proposing a user fee program to support its monograph work. *(Also see "OTC Monograph User Fees Inspire Wary Support From Industry" - Pink Sheet, 13 Jun, 2016.)*

Numerous drug firms initially questioned potentially paying additional user fees, but in the second half of 2016 executives from CHPA and several OTC drug makers met regularly with CDER staff to discuss the framework for a potential user fee program and for legislation to establish the program. *(Also see "OTC Monograph User Fees: FDA-Industry Talks Move From Basics To Details" - Pink Sheet, 2 Aug, 2016.)*

According to a CDER report on a September 2016 webinar it conducted for industry stakeholders, its monograph work has included nearly 90 rulemakings, many pending simultaneous, in 26 therapeutic categories encompassing more than 100,000 OTC drug products. "Despite the scope of the responsibilities, the monograph review program is very small," the report says.

Additionally, CDER's OTC program resources "are often consumed by external mandates," including completing evaluations of sunscreen monograph ingredient proposals and publishing guidance on submitting those proposals under deadlines imposed by the Sunscreen Innovation Act or removing numerous OTC antiseptic wash ingredients under a consent decree to litigation, according to the report.

Still, CDER says, "Even without current external mandates, and even with desired monograph reforms, it would take many decades to finalize GRASE determinations for pending monographs, if resources remain at current levels."

While FDA considered monograph reform and a potential user fee program in separate initiatives with separate dockets for comments on each, CHPA expects that proposals for both will come in the same legislation.

"That is the intention, that user fees would be included in the modernization package bill," said CHPA spokesman Mike Tringale.

The industry, Tringale added in an email, is satisfied with the results of its discussions on both topics and expects a bill soon will be introduced. "CHPA feels optimistic about where everyone is regarding discussions and progress regarding OTC monograph reforms," although "there are still several things that need to fall into place," he said.

CDER's monograph work currently is funded strictly from FDA's direct appropriation, although the vast majority of OTCs are available under monographs. User fees currently touch the OTC drug space with sponsors of Rx-to-OTC switch applications subject to Prescription Drug User Fee Act costs and firms that submit abbreviated NDAs for generic equivalents of switches or other nonprescription NDA drugs subject to Generic Drug User Fee Act costs.

However, the value of a monograph user fee to the industry will differ from Rx drug user fee programs. Those programs were established to help FDA evaluate long waiting lists of applications and their value has been shown in the agency more quickly determining whether to approve new Rx ingredients or medical devices.

The agency has no monograph proposals waiting, though, since advising sponsors of eight long-pending time and extent applications to amend the sunscreen monograph that their information was insufficient for review in 2015. *(Also see "Sunscreen Group Remains Cloudy About FDA's Ingredient Evaluations" - Pink Sheet, 3 Nov, 2016.)*

DIRECT OTC PURCHASES WITH PRE-TAX ACCOUNTS

Melville discussed legislative prospects for including direct purchase of OTCs in pre-tax savings accounts again, speaking four days before House Speaker Paul Ryan, R-WI, cancelled a vote on American Health Care Act after Republicans in the far-right Freedom Caucus refused to support the bill because it would not entirely repeal the Affordable Care Act and more moderate GOP members balked at Medicaid program cuts the bill would make. *(Also see "Fate Of OTCs In Health Savings Accounts Rests In Capitol Hill Negotiations" - Pink Sheet, 11 Jan, 2010.)*

CHPA had tempered support for the AHCA, suggesting the legislation was not its preferred method to include OTCs once again in consumers' pre-tax saving accounts after lobbying for years to remove from the ACA the provision requiring a prescription for OTC drug purchases with pre-tax savings. *(Also see "It's Complicated: Health Care Act Simplifies Buying OTCs With Pre-Tax Accounts" - Pink Sheet, 10 Mar, 2017.)*

Restoring direct OTC purchases to FSAs, HSAs and similar accounts may now rest on the Restoring Access to Medication Act of 2017, S. 85 proposed by Sens. Pat Roberts, R-KS, and Heidi Heitkamp, D-ND, and H.R. 394 by Reps. Lynn Jenkins, R-KS, and Ron Kind, D-WI. The legislation, which has been introduced in every session of Congress since the ACA was passed in 2010, proposes to amend the act to again allow direct purchases of nonprescription drugs with pre-tax savings accounts. *(Also see "Direct OTC Purchases With Pre-Tax Accounts Swing On ACA Change, Not Repeal" - Pink Sheet, 27 Feb, 2017.)*

Tringale said CHPA is "optimistic that restoration of OTC eligibility in FSAs/HSAs is quite possible since bills in the House and Senate still remain, and they continue to find supporters and alternate vehicles for passage."

Melville suggested that restoring health care provisions allowing OTC purchases in pre-tax savings is critical, as consumer-driven health care plans continue to multiply moving forward, especially as long as the ACA is in place. Consumer-driven health care plans are programs roughly defined as requiring consumers to pay for routine healthcare expenses out-of-pocket while high-deductible insurance covers them for "catastrophic" events.

"These plans have exploded in popularity since the enactment of the Affordable Care Act," he said. "When consumers spend their money, they become smarter purchasers. In your industry, my industry, we're all about that."

Though he acknowledged during his speech the AHCA vote could go either way, Melville said he is sure changes are coming to health care in 2017. "I'm certain that some reform will pass Congress this year and will be signed by President Trump," he said.

Trump has stated he expects the ACA to fail but his administration will allow the law to "to go its way for a while, and see how things go." Although Ryan said health care legislation will not be considered again during the current session immediately after he pulled AHCA from a vote, Trump and some lawmakers are saying they will work on other legislation to repeal the ACA.

Singapore Eye Wash Maker Blinks At US FDA's OTC Monograph, GMPs

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Emergency eye wash products made by a Singapore firm and distributed to US workplaces are noncompliant with FDA's OTC monograph for ophthalmic drug products, the agency says in a warning letter.

The warning FDA published March 28 followed an inspection at **Opto-Pharm Pte Ltd.**'s facility in Singapore during March 2016, when agency officials also found good manufacturing practices violations including failing to establish and follow appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile, such as the purified water in the firm's eye wash products.

The letter submitted March 16 to Opto-Pharm states that that the firm's "Buffered Eye & Skin" products – distributed in the US under the *Xpect* and *First Aid Direct* brands by Cintas Corp. – are not labeled or formulated in accordance with the final ophthalmic drug products monograph.

The labeled indications state that the products are intended for flushing the eye and the product name "Buffered Eye & Skin" suggest that the products are intended for flushing the eye and skin, but flushing the skin is not a permitted indication in the final monograph for eyewash drug products.

FDA added that its not aware of sufficient evidence to show the products, as formulated and labeled, are generally recognized as safe and effective, the threshold for monograph compliance, and that the products have not been approved through applications submitted to the agency, rendering them unapproved new drugs marketed illegally in the US.

According to labeling listed in the National Library of Medicine database, Opto-Pharm makes the products for Cintas, the Mason, Ohio-based firm that supplies uniforms, facility services and first aid and other products for business workplaces around the US.

The Singapore firm also makes a product with same "sterile isotonic buffer solution" formulation as Xpect and First Aid Direct, but labeled only as an eye wash and distributed by Cintas subsidiaries **Respond Industries Inc.** and **American First Aid Co.**, the NLM database indicates.

LEAKING CONTAINERS, SUSPECT EXPIRATION DATES

FDA warnings to manufacturers in Asian countries and other international markets are not uncommon, but warnings about nonprescription drugs are much less common and a warning specifically about noncompliance with agency regulations for eye wash products is practically unheard of.

The Opto-Pharm warning says the firm received customer complaints about leaking containers after shipping batches of products manufactured during periods when "numerous leaking containers and other bottle formation defects" were documented.

In addition to failing to prevent shipments after finding "numerous critical container-closure defects" during production, Opto-Pharm was re-using production-line components that are intended for single use, FDA says.

"Repeated use and re-sterilization can compromise [the equipment's] efficacy and physical/chemical stability (e.g., particles, leachables, extractables)," the letter states.

The firm "committed to develop and execute protocols for process performance qualification and equipment qualification," and in the warning letter FDA asked it to provide validation protocols and studies that evaluate whether its equipment is reliable, including determining whether the "process reproducibly yields an integral container-closure system."

A second GMP violation turned up during the inspection was failing to establish the reliability of Opto-Pharm's container-closure supplier's analyses through appropriate validation of its test results at appropriate intervals. The firm accepted values reported on the supplier's certificate of analysis without verifying the reliability of the results.

Opto-Pharm said it would send samples from the container-closure supplier to an external laboratory for density testing and periodically evaluate the supplier, however, in the warning FDA advised the firm that it should provide justification to demonstrate its specifications are appropriate for the drug products it manufactures.

Opto-Pharma also slipped on GMP compliance by failing to ensure its products bore an expiration date supported by appropriate stability testing, specifically for buffered saline and ophthalmic solutions it made in 2014 and 2015, and by failing during the inspection to provide raw data to support test results from stability studies it conducted for other products.

The warning states that "failure to conduct stability studies and lack of data supporting expiration dates compromises" detecting quality problems with marketed ophthalmic products, and that multiple customer complaints of leaking ophthalmic containers also calls into question the firm's ability to maintain sterility of its ophthalmic products throughout their labeled expiration dates.

"Without stability data, you cannot assure the quality of your products throughout their labeled shelf lives," FDA says in the letter.

Opto-Pharm committed to stability studies on its buffered saline and other products, but did not provide raw stability data for the other products. FDA asked the firm for raw stability data, within expiry, for all its ophthalmic products manufactured for the US distribution; antimicrobial effectiveness testing that evaluates whether its products contain a suitable preservative system; and an evaluation of whether it products' preservative systems remain effective at their expiration dates.

OTC Allergy Drug Use Increases: A Symptom With Multiple Causes

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US OTC switches of three intranasal corticosteroids and an oral antihistamine ingredient since 2007 are pushing an increase in consumer use of nonprescription allergy treatments and a decrease in Rx drug use, says the Consumer Healthcare Products Association.

While the industry trade group says growing use of allergy OTCs from 2009 through 2015 is a sign of more consumers prioritizing self-care over using health care services, allergy specialists said in interviews that their patients often have to start treatment with an OTC. That's because with most allergy ingredients available OTC, insurers often require patients to try a nonprescription version of an ingredient before an Rx product is covered.

"I don't have any patients who could walk into a pharmacy right now and have their insurance cover paying for an allergy drug prescription without trying an OTC drug first," said Rajan Merchant, an allergy, asthma and immunology specialist with Dignity Health in in Sacramento, Calif.

On the other hand, consumers relying on an OTC product before consulting a doctor could be wrong about their allergy type and could choose the wrong ingredient for their symptoms, say Merchant and Julie McNairn, another specialist suggested by the American Academy of Allergy, Asthma & Immunology to offer insight on allergy treatments.

"I don't think most consumers realize what the ingredients are," said McNairn, an allergist and immunologist with Allergy and Asthma Associates in Ithaca, N.Y.

According to results of a July 2016 survey CHPA commissioned, the percentage of allergy sufferers using only OTC drug remedies for allergies has increased from 53% in 2009 to 60% in 2015. At the same time, the percentage who receive a health care provider's treatment for allergies decreased from 31% in 2009 to 28% in 2015, Nielsen Homescan data included in the survey show.

"The implication here is that allergy sufferers in some cases are increasingly self-treating their symptoms," CHPA says in its report on the survey, which also included information from IMS Health on consumers' spending on Rx drugs and health care services and from questions asked of 2,000 consumers.

TARGET MARKET GROWS, TOO

The survey also shows that the number of consumers who say they have allergies has edged up, from 26.9% in 2009 to 27.8% in 2015. CHPA says that taking into account population growth and the survey results, it projects 9.7m more consumers had allergies in 2015 than had them five years earlier.

With more consumers reporting they have allergies, the number using OTC remedies will correspondingly increase.

The survey also stated, Merchant pointed out, that almost half of the respondents said they asked a doctor and 23% said they asked a pharmacist to recommend an OTC allergy drug.

"More than half the patients still are asking for advice," said Merchant, who also is a clinician and a clinical researcher Woodland Medical Group.

And when physicians determine that a patient needs a treatment for allergies, their first step is prescribing the appropriate Rx ingredient, he added. "We haven't changed our treatment guidelines."

McNairn observed that unless their patients inform them, physicians don't know how they react to OTC allergy drugs, which, although safe, still could cause potentially harmful side effects, or whether a certain ingredient is effective.

"That's the disservice that's going on here," she said.

Although nonprescription allergy drugs have histories of safe use, one criteria for a drug to be available OTC is an indication for a self-limiting condition, Merchant said. "Allergies are not necessarily considered self-limiting," he said.

The first intranasal corticosteroid approved as an OTC, **Sanofi**'s *Nasacort Allergy 24HR*, prompted concerns about growth suppression in children and inadequate long-term use data to garner a positive recommendation from FDA's Nonprescription Drugs Advisory Committee in 2013. *(Also see "Nasacort AQ Switch Gets NDAC Nod Despite Pediatric Use Concerns" - Pink Sheet, 5 Aug, 2013.)*

An American Academy of Allergy, Asthma & Immunology task force in 2006 advocated against switching intranasal corticosteroids due to their potential for overuse, complications from adverse effects and serious associated risks including bone resorption – by which bones begin to lose substance – as well as growth suppression and ocular effects such as glaucoma and cataracts. *(Also see "Steroid Nasal Sprays Not Suitable For Rx-to-OTC Switch – Task Force" - Pink Sheet, 22 May, 2006.)*

COSTS INFLUENCE SATISFACTION

From its questions for consumers, the survey showed that among those who only take OTCs to treat allergies, 87% said they are satisfied, the highest satisfaction rate among groups that respond differently to the conditions. Respondents who take both an Rx and OTC concurrently to treat allergies expressed the lowest satisfaction with their medication options, 81%.

"This could be likely due to the level of severity of their allergies, or possibly the costs associated with managing their symptoms," CHPA suggests.

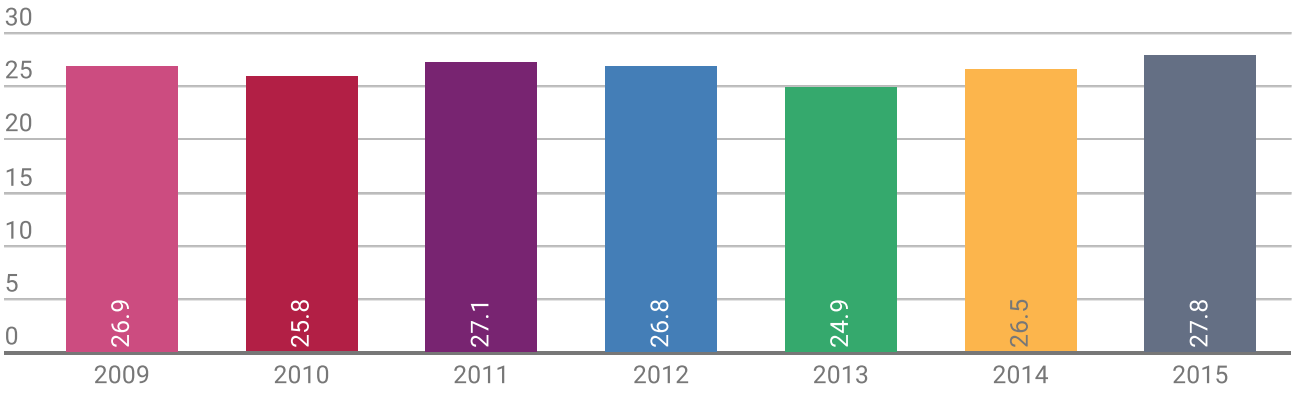
As consumers have fewer doctor visits, they also are lowering their overall spending on allergy treatments. Consumers treating with OTCs only discuss their allergies with their doctor or other health care professional an average of 1.5 times per year, spending about $37.56 in co-pays for allergy-related health care services.

Consumers opting for Rx-only allergy treatment see a doctor for the condition an average of 2.2 times per year, spending $55.09 in co-pays, and those using both Rx and OTC drugs seeks health care an average of 6 per year, accounting for $150.24 in co-pays.

Costs likely are the key influence on consumers using OTC allergy drugs without also seeking a doctor's diagnosis, McNairn observed.

"It's ultimately a cost issue and an access

Consumers' Allergy Rates And How They Respond



The Consumer Healthcare Product Association's survey conducted with Nielsen Homescan looked not only at the percentage of consumers reporting allergies during 2009-2015, but also asked how they treated the conditions, including whether they used health care services.

Source: CHPA and Nielsen Homescan survey

issue," she said. "The insurance programs are covering fewer and fewer prescription allergy drugs."

DUAL USAGE STEADY

The survey showed that of consumers with allergies, more than 90% of take some type of medication to manage their symptoms. CHPA says consumers have adjusted their behaviors as more OTC allergy drugs are available, with 66% in 2009 and 75% in 2015 purchasing an OTC either on its own or in conjunction with an Rx product.

However, with more consumers opting for OTC-only treatment, as the overall number using some type of allergy product increased, the percentage who take both an Rx and an OTC medication stayed relatively flat, 13% to 15%, over the five-year period analyzed.

The data also showed consumers' level of engagement with OTCs depends on the severity of symptoms. Households most engaged with the OTC products report moderate allergies, while the least engaged with the products have severe allergies, implying that the more severe an allergy, the more likely a prescription drug will be needed.

The survey's Nielsen Homescan component also found changes in spending on allergy OTCs, from around $33 for an average household on 2.9 trips to retail outlets in 2009 to $39 on the same number of trips in 2016.

3 CORTICOSTEROIDS, 1 ANTIHISTAMINE

The four ingredients with allergy indications moved from Rx to OTC in the US and noted in the survey report comprise three intranasal corticosteroids, each a consumer products sales driver for its marketer, and an oral antihistamine that also is a key consumer brand for its marketer.

The antihistamine is cetirizine, approved for OTC in 2007 through **Johnson & Johnson**'s switch application for its *Zyrtec* product and launched 2008, though private label versions from **Perrigo Co. PLC** reached store shelves before the brand. *(Also see "Zyrtec Launch Brings Big Boost To Johnson & Johnson, But Competition Grows" - Pink Sheet, 21 Apr, 2008.)*

The first intranasal corticosteroid ingredient available OTC was approved in 2013 through **Sanofi**'s proposal for triamcinolone acetonide, which it markets nonprescription as *Nasacortrx Allergy 24HR*. *(Also see "Sanofi's Nasacort First-In-Class Switch Receives FDA Approval" - Pink Sheet, 11 Oct, 2013.)*

GlaxoSmithKline PLC was second to the OTC intranasal corticosteroid market with fluticasone propionate, available in its *Flonase Allergy Relief* product approved in 2014. *(Also see "Flonase Allergy Relief Exclusivity Sliced Up By Label Carve-Out" - Pink Sheet, 10 Feb, 2015.)*

Under license from **AstraZeneca PLC**,J&J markets the third ingredient in the category, budesonide, available in *Rhinocort Allergy 24HR* since approval in 2015. *(Also see "Rhinocort Switch Makes Three In OTC Intranasal Corticosteroid Market" - Pink Sheet, 26 Mar, 2015.)*

OTC Allergy Drugs: Not Just For Sniffles And Headaches, Sanofi Advises

A "social experiment" Sanofi conducted featuring its newly launched OTC antihistamine, *Xyzal Allergy 24HR*, reinforces that allergies limit physical activity and diminish sleep as well as cause headaches and sniffles.

"Many allergy sufferers have gotten so used to their symptoms that they don't even realize how significantly they may be impacting their day-to-day lives, including everything from their sleep at night to their productivity during the day," says Neeta Ogden, a physician and allergist working with Sanofi Consumer Healthcare to promote managing allergies as the firm makes the ingredient levocetirizine dihydrochloride available OTC for the first time with the Xyzal Allergy 24HR launch.

The Sanofi division's US office in Bridgewater, N.J., on March 21 reported that 160 participants wore a wearable device for 30 days to track their sleep and activity. The 80 consumers with allergies participating completed a daily survey to track perceptions of their symptoms, sleep patterns and activities to provide additional context for the device data.

The firm also said tracking the participants was not a clinical trial or study, but "a first-of-its kind experiment in the allergy space" with results that "provide valuable insight into the real-life impact of allergy symptoms on people's sleep and their lives during the day."

Its conclusions include that allergy symptoms were the top sleep influence for the participants with allergies, "even more so than stress, discomfort, temperature or work." The experiment found that an allergy-burdened consumer's sleep could be disrupted – difficulty falling and staying asleep – nearly four times more than that of a person without allergies.

Additionally, the allergy-affected participants were less rested and less physically active during the day, moving an average of 3.16 miles a day while active while the other participants moved an average of 3.35 miles and burned nearly 200 more calories a day. The participants also traveled a half mile less on days they were experiencing high levels of allergy symptoms than they did on days when they felt they were experiencing a low level.

Sanofi says the difference in distances covered in daily activities equals 69 miles per year, or the distance of around two and a half marathons, and the calories are the equivalent of a glazed doughnut.

Diary information also showed the participants with allergies:

- experienced good sleep on fewer nights than people without allergies.
- felt less rested when they woke up than people without allergies.
- Felt their work was negatively impacted two out of three days when they were experiencing a high level of allergy symptoms.

FDA on Jan. 31 approved a new drug application submitted by Sanofi's Sanofi-Aventis US LLC unit to switch its Xyzal Rx allergy treatment to OTC in 5 mg levocetirizine dihydrochloride tablets indicated for children 6 and up and adults and in a 2.5 mg per 5 mL "Tutti-Frutti" flavor oral solution, indicated for children 2 and up as well as older children and adults. Launch is targeted for this spring. *(Also see "Xyzal Switch Extends Sanofi Into OTC 24-Hour Children's Antihistamine" - Pink Sheet, 2 Feb, 2017.)*

Hawaii's Proposed Oxybenzone Sunscreen Ban Fails Science Test – CHPA

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A wave of legislation in Hawaii to restrict or ban sunscreen containing oxybenzone does not flow from science and washes over more likely causes of harm to the coral reef off the state's beaches, says the Consumer Healthcare Products Association.

President and CEO Scott Melville says CHPA disputes Hawaii lawmakers' contention that degradation of the coral reef is due to sunscreen. "Most research points to other cause, like climate change and over fishing," Melville said March 21 at CHPA's Annual Executive Conference in Amelia Island, Fla.

"Unfortunately, we learned that when it comes to environmental issues at the state level, science does not always prevail," he said while discussing his association's federal and state legislative priorities for 2017.

Of 13 bills introduced in Hawaii's legislature in 2017 seeking to restrict or ban the sale of sunscreens containing oxybenzone – including legislation that would have required a prescription for oxybenzone-containing sunscreens and another bill requiring advertising disclosures on the environmental risks of the ingredient – most have died in committees within the past month. *(Also see "Hawaii Bills Seek Ban On Oxybenzone-Containing Sunscreens" - Rose Sheet, 14 Feb, 2017.)*

"We are working hard to defeat or neutralize these bills, challenge them on the scientific basis and emphasizing the public health benefits of sunscreen," Melville said. A restriction of oxybenzone in sunscreens in other states would have far-reaching implications as about 70% of sunscreens sold in the US contain the ingredient, he said.

The Personal Care Products Council has posed similar arguments, and suggested flaws in research proponents of the ban cite, including that the study's lab conditions did not reflect the complexity of the natural marine environment.

PCPC has argued that oxybenzone is one of the few active ingredients included in FDA's OTC sunscreen monograph that provides reliably effective broad-spectrum protection, and that its safety is backed by the American Academy of Dermatology.

While oxybenzone was approved as generally recognized as safe and effective and was added to the monograph, it and other sunscreen monograph ingredients could be vulnerable to removal under guidance FDA published in 2016 for evaluating the safety of additional ingredients proposed for inclusion. *(Also see "Sunscreen Industry Asks FDA For Flexibility Despite Guidances' Rigidity" - Pink Sheet, 28 Nov, 2016.)*

The agency said those standards, published within a deadline established by the industry-backed Sunscreen Innovation Act, would apply to existing monograph ingredients as well as proposed additions. *(Also see "OTC Monograph Application Reviews Get Deadlines, Not GRASE Flexibility" - Pink Sheet, 30 Nov, 2016.)*

PASSES SENATE, HOUSE SCRUTINY AHEAD

Despite CHPA and PCPC's argument, Hawaii's SB 1150, introduced on Jan. 25 by Sen. Kalani English, appears to have momentum after passing the Senate March 7 and being moved out of two House committees – Energy & Environmental Protection on March 16 and the Oceans, Marine Resources & Hawaiian Affairs on March 21.

Before moving to a full House vote, however, the bill faces tougher scrutiny in a review by the Consumer Protection & Commerce Committee, which has blocked other oxybenzone-related bills.

Still, proponents of the ban are "hopeful," said a spokesperson from the office of Sen. Will Espero, an SB 1150 co-sponsor.

The bill would prohibit the use of oxybenzone-containing sunscreens and cosmetics on any Hawaiian beach or in the ocean around the island unless the product is a prescription drug. Like other bills proposed before it, SB 1150 was prompted by a study finding that oxybenzone in sunscreens causes deformities in coral larvae and also increases the rate at which coral bleaching occurs.

Published in the February 2016 Archives of Environmental Contamination and Toxicology, the study conducted by the Haereticus Environmental Laboratory in Clifford, Va., reported vivid effects observed in coral specimens when they were exposed to oxybenzone. These included transformations of planulae "from a motile state to a deformed, sessile condition," increased rates of coral bleaching and induced ossification, "encasing the entire planula in its own skeleton."

During a meeting in September in Honolulu, the World Conservation Congress of the International Union for Conservation of Nature discussed the "threat" of oxybenzone as being "particularly acute in Hawaiian ocean waters where coral bleaching is occurring at a historic rate never before noted in recorded history," according to text of the bill.

PUSHES ZINC OXIDE, TITANIUM DIOXIDE

SB 1150 bill seeks to revise Section 187 of Hawaii law regarding conservation and resources with this amendment: "Oxybenzone: sunscreen and cosmetics restrictions. No person shall use or apply sunscreen, sunblock, or cosmetic containing any oxybenzone while on a beach in Hawaii or in the ocean, unless the sunscreen, sunblock, or cosmetic is prescription drug. For purposes of this section, 'oxybenzone' includes benzophenone-3 and 2-hydroxy-4-methoxyphenyl phenylmethanone."

The bill says its purpose is to "protect Hawaii's coral reefs by prohibiting the use of sunscreens and cosmetics containing oxybenzone at beaches or in the ocean," and urges consumers to use sunscreens containing other ingredients also part of FDA's OTC monograph.

"The legislature further finds that there are reasonable alternatives to oxybenzone-based sunscreens, such as zinc oxide and titanium oxide, that allow beach users to enjoy the outdoors without compromising sun protection," the bill states.

OCTINOXATE TARGETED IN OTHER BILLS

Espero previously sponsored a bill, SB 260, to ban sales of sun-protection products containing oxybenzone or octinoxate, which also is an OTC monograph ingredient, other than prescription products. Introduced in January, it died a month later in committee, his office says.

Similar legislation proposed on Jan. 20 by Rep. Nicole Lowen – HB 600 – would prohibit sales or distribution of oxybenzone-containing sunscreen or personal care products in the state. HB 600 acknowledged that "many factors, such as water temperature, contribute" to coral reef damage, but said that the damage "is exacerbated by the presence of chemicals that are toxic to coral" including oxybenzone and octinoxate.

Another bill, HB 818, did not propose an outright ban but would require advertisements or displays for oxybenzone-based sunscreens in Hawaii to include a conspicuous statement that "oxybenzone, when used in nearshore waters, poses serious hazards to coral and reef health."

Those and others that would limit sunscreen ingredient variety in the state stalled in committees in February.