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Search For Rasi's Successor At EMA Extended

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"Agency decisions have very real, tangible and far-reaching economic implications."
– Yannis Natsis, EMA management board member

The deadline for applying to be the next executive director of the European Medicines Agency has been extended to 4 July. The agency's new boss will replace Professor Guido Rasi, whose second five-year term at the post ends in November 2020.

The original deadline of 13 June to apply for the post was extended last month, implying that not enough suitable applications were received in the first recruitment round.

The new executive director – the agency's fourth – will be appointed by the EMA management board after a long selection process. It is perhaps no surprise that the search has begun almost one-and-a-half years before Prof Rasi's term is due to end. The recruitment notice does not specify the start date but there is no indication that Rasi will serve less than the two full terms.

The EMA referred all press queries on the matter to the European Commission, which is coordinating the selection procedure. A commission spokesperson told the *Pink Sheet*: "It is not uncommon that this kind of selection procedures takes several months. The Commission is therefore taking the necessary steps to ensure continuity and a smooth transition between the current and future management of the agency."

The decision just over three years ago by the UK to leave the EU has created multiple, testing and ongoing challenges for the EMA. Not least it had to move from London to Amsterdam, losing a considerable number of staff in the process, and it had to reassign much of the work previously done by the EU – and the UK has yet to leave the union.

The recruitment notice states that the EMA in 2018 had a budget of around €338m ($382m) and 810 members of staff.

The new executive director will have the difficult job of ensuring that the EMA continues to perform its key function of evaluating and supervising medicines to protect public health, while supporting innovation. *(Also see "EMA Chief Says Brexit Has Impaired Ability To Support R&D " - Pink Sheet, 8 May, 2019.)* The notice states that candidates should have, among other things, "solid leadership skills" and an "excellent capacity to develop and implement a strategic vision… taking into account the Agency's relocation to its new headquarters [in Amsterdam]."

NEW ISSUES

In addition, there is mounting pressure on the EMA from patient representatives and advocacy groups to play a more meaningful role on issues such as pricing, improving patient access and further improving transparency of its functioning. Yannis Natsis, policy manager for universal access and affordable medicines at the European Public Health Alliance, is a new elected patients' organization representative on the EMA management board. Natsis feels that the agency has enjoyed "political carte blanche" on issues such as quality of innovation, affordability and improving patient access as no one has questioned the EMA on these topics.

"The EMA's next executive director will have to deal with these issues as the debate has changed very recently," Natsis told the *Pink Sheet*. "These issues are

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Biosimilars: Some Patient And Prescriber Groups Appear To Warm Up To Arbitrary Suffixes

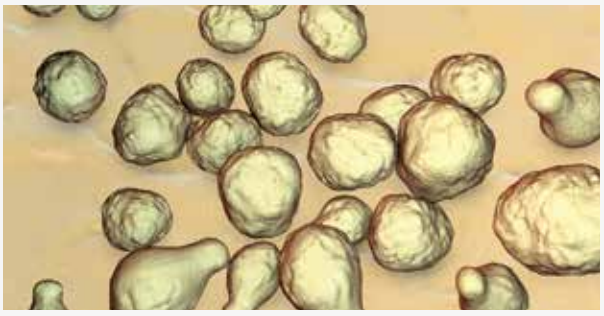
https://pink.pharmaintelligence.informa.com/PS125497

Patient and prescriber groups were largely opposed to suffixes for the nonproprietary names of biological products being devoid of meaning when the US FDA first published its nomenclature policy, although a few of these groups may be signaling less of a worry than they once had.

US Presidential Debates Begin: Pharma Is Favorite Villain – But Issues Focus Elsewhere

https://pink.pharmaintelligence.informa.com/PS125559

To no one's surprise, attacks on the drug industry are a recurring and unifying theme for the Democratic Presidential candidates as they enter the debate cycle. But rhetoric aside, the health policy proposals getting the most airtime are more threatening for other sectors.



MSF: Gilead Access Initiative 'Nothing More Than A Public Relations Stunt'

https://pink.pharmaintelligence.informa.com/PS125571

Gilead has failed to deliver on promises to make its liposomal amphotericin B (L-AmB) accessible to patients in developing countries, says Médecins Sans Frontières.

Germany Joins EU-US Inspections MRA

https://pink.pharmaintelligence.informa.com/PS125552

There is now only one country left to join the agreement between the EU and the US on recognizing the findings of inspectorates in each other's jurisdictions.

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CONTINUED FROM PAGE 1

now part of the political agenda and important for policy makers" and the EMA can no longer distance itself from them on the grounds that it is a mere scientific and technical body, he said.

The EMA's decisions, its priorities and its strategic focus send clear signals to the market on what kind of innovations society needs, said Natsis. "Its decisions have very real, tangible and far-reaching economic implications… It is a very important actor in this game," he added. Questions raised in the recent past on how the EMA can play a more supportive role in improving patient access have already helped open new channels of communications, such as with payers, health technology assessment bodies, ministries of health etc, and these must be taken further, Natsis said.

EU OMBUDSMAN INQUIRY

On the issue of transparency, Natsis expects the EMA to consider whatever recommendations come its way when the EU ombudsman concludes its inquiry into the activities conducted by the agency in the pre-marketing authorization phase. *(Also see "Ombudsman Probes Whether Industry Can Influence EMA In Pre-Submission Meetings" - Pink Sheet, 21 Jul, 2017.)* "I think it's a black box and more transparency on this front will be useful for all parties involved," Natsis said.

"The perception of independence is as important as reality itself" and it is important that the agency actively dispels any suspicions of "corporate capture" and does not dismiss these as mere conspiracy theories, Natsis added. *(Also see "EMA Argues Pre-Submission Activities Under Ombudsman's Radar Are A Legal Requirement" - Pink Sheet, 21 Sep, 2017.)*

THE RECRUITMENT PROCESS

A commission-appointed pre-selection panel will analyze all applications received for the post during which each applicant's eligibility will be verified and those with the best profile will be called for a first interview.

Following the first set of interviews, the panel will draw up a list of candidates for further interviews with the commission's Consultative Committee on Appointments (CCA). This panel will issue a further shortlist of suitable candidates to be interviewed by the commission members responsible for health and food safety. The health and food safety department at the commission (DG Santé) has responsibility for pharmaceuticals.

Following the interviews, the commission will adopt a list of candidates to be communicated to the EMA management board, who may hold further interviews before making their decision. Before the appointment, the nominated applicant will also be asked to address the relevant committee of the European Parliament and to reply to questions. The selection procedure will be carried out in English and/or French only.

THREE EXECUTIVE DIRECTORS

In November 2011, Rasi became the third executive director the EMA has had since the agency was established in 1995. Fernand Sauer was the first (1994-2000) and Thomas Lönngren the second (2001-2010).

Rasi's first term was cut short by a year. He was forced to step down in November 2014 when the EU's civil service tribunal annulled his appointment after upholding a complaint that the procedure used to select him was compromised by conflicts of interest involving candidates and members of the pre-selection panel. The EMA and the commission appealed and the EMA stressed that the grounds for the tribunal's decision were purely procedural; Rasi was re-appointed. *(Also see "Rasi Back In Office At The EMA Today" - Pink Sheet, 16 Nov, 2015.)*

Rasi's first term ran from November 2011 to November 2014 and his second term began in November 2015. From November 2014 to mid-November 2015, Rasi remained at the agency, in the role of the EMA's principal adviser in charge of strategy.

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After The Peak Of 2018's US FDA Approval Record, 2019 Looks Like A Valley

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The US Food and Drug Administration has almost 30 new molecular entity and novel biologics under review with user fee goal dates in the second half of 2019, which all but guarantees a modest annual approval count following on the record high of 2018.

The staggering approval count for 2018 was always going to be hard to match: 65 novel agents were approved last year, including the most ever for the Center for Drug Evaluation and Research (59 approvals).

At the halfway point of 2019, CDER has approved 13 novel agents and the Center for Biologics Evaluation and Research has cleared four, for a total of 17 novel agents.

The Pink Sheet's FDA Performance Tracker identified 27 novel agents remaining on the 2019 review calendar: 25 for the CDER and two for CBER.

To match last year, FDA would need to approve 48 novel agents in the second half – an impossible task. In the highly improbable scenario of FDA approving every one of the 27 known pending novel agents with 2019 user fee goal, the total would be 44.

If FDA were to maintain the 65% approval rate seen in the first half of 2019, about 18 novel agents would be cleared in the second half, and the 2019 annual would be closer to 36. *(Also see "CDER Midyear Report: Sponsors Struggle With Drop In Novel Approval Rate" - Pink Sheet, 1 Jul, 2019.)*

FDA could, of course, approve applications with 2020 user fee goals early. Eleven novel agents are currently under review with 2020 goal dates, but only four have priority review; standard review products are less likely to be approved well in advance of the user fee goal. Three of the candidates hold breakthrough therapy designations.

PREPARE FOR A NERVOUS SECOND HALF

Novel approval activity in the upcoming months will likely be dominated by agents targeting the nervous system, continuing a

trend seen since the beginning of the year. *(Also see "Hazards Ahead For New Drugs At US FDA Amid Safety Concerns, Shutdown Disruption" - Pink Sheet, 30 Jan, 2019.)*

The 10 CNS candidates on docket target a wide range of conditions across neurology, psychology, and pain, including two drugs for migraine (Allergan PLC's ubrogepant and Eli Lilly & Co.'s lasmiditan) and therapies for low back pain (Nektar Therapeutics's oxycodegol), sleep disorders (Harmony Biosciences LLC/Bioprojet 's pitolisant and Eisai Co. Ltd./'s lemborexant) and Duchenne muscular dystrophy (Sarepta Therapeutics Inc.'s exon 53-skipping golodirsen).

More of the second half drugs are believed to have priority review than standard (17 vs. 10), but the priority review count does not directly represent the number of products that FDA considers to have earned priority review. Novartis AG used a priority review voucher for brolocizumab to treat wet age-related macular degeneration, as did AbbVie Inc. to guarantee a faster assessment of upadacitinib in rheumatoid arthritis.

The two antibiotic products under review, Nabriva Therapeutics PLC's lefamulin and Merck & Co. Inc.'s combination of relebactam, cilastatin and imipenem, have qualified infectious disease product (QIDP) status, which usually confers priority review.

Four of the applications with 2019 user fee goals have earned FDA's breakthrough therapy designation. One of those, Enzyvant Sciences Ltd.'s RVT-802 tissue-based regenerative therapy for pediatric congenital athymia, could also be the first product with a regenerative medicine advance therapy (RMAT) designation to be approved.

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ANALYZE

The Pink Sheet's FDA Performance Tracker identified 27 novel agents remaining on the 2019 review calendar. For the detailed chart **The Next Noval Agents** go to https://bit.ly/2Ysqttb

Product	Sponsor	Goal Date	Indication	Type	Date Received	Regulatory History
Darolutamide	Bayer and Orion	2019-10-27 or earlier	Cancer - non-steroidal androgen receptor antagonist for treatment of non metastatic castration resistant prostate cancer (nmCRPC)	Priority review	2019-02-27 (announced)	FDA acceptance for review announced 2019-04-29; Pending
Entrectinib	Genentech (Ignyta)	2019-08-10	Cancer - Tyrosine receptor kinase inhibitor that targets TRK A/B/C and ROS1 proteins for treatment of metastatic ROS1-positive non-small cell lung cancer (NSCLC)	Priority review	2018-12	Pending

CDER MIDYEAR REPORT:

Sponsors Struggle With Drop In Novel Approval Rate

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A complete response letter (CRL) for Acer Therapeutics Inc.'s vascular Ehlers-Danlos syndrome candidate Edsivo (celiprolol) capped off a relatively difficult first half of 2019 for novel drugs and biologics under review at the US Food and Drug Administration.

The Center for Drug Evaluation and Research approved only 13 novel products in the first six months of the year, while handing out at least seven CRLs for such products. At best, industry has a novel approval rate of 65% in 2019.

This percentage is a marked decline from those in 2017 and 2018, when CDER approved, at best, 87% and 89% of novel product applications, respectively.

So far, the 2019 approval landscape is looking more like that of 2016, when the CDER doled out at least 14 CRLs to sponsors of novel drugs and biologics and only 22 approvals, which made the maximum approval rate for the year 61%. *(Also see "Novel Approvals Were Fewer But Faster At US FDA In 2016" - Pink Sheet, 2 Jan, 2017.)*

The approval rate underscores what is shaping up to be a significant slowdown in the number of overall approvals for the year.

The CRLs for both Daiichi Sankyo Co. Ltd.'s quizartinib and Alkermes PLC's ALKS 5461 (buprenorphine and samidorphan) were entirely expected, as advisory committees voted against recommending approval for each by sizeable margins *(see chart, p. 7)*.

Sanofi and Lexicon Pharmaceuticals Inc.'s Zynquista (sotagliflozin) also went to an advisory committee, although the panel offered a split 8-8 approval vote, leaving the FDA to break the tie. *(Also see "Keeping Track: Thumbs Up For Zulresso And Sunosi, Thumbs Down For Zynquista And IV Meloxicam" - Pink Sheet, 24 Mar, 2019.)*

NOVARTIS, BIG PHARMA DOMINATE SO FAR

Novartis has the podium all to itself for being the dominant sponsor in the first half of the year. The Swiss drug giant has three novel CDER approvals so far – Piqray (alpelisib), Mayzent (siponimod) and Egaten (triclabendazole) – while no other company has more than one.

Piqray is among the most interesting approvals of 2019, as it became the first novel drug approved under the FDA's Real-Time Oncology Review (RTOR) pilot program.

But Novartis also added to its dominance on the Center for Biologics Evaluation and Research side by securing the green light for its gene therapy Zolgensma (onasemnogene abeparvovec-xioi). An adeno-associated virus vector-based gene therapy, Zolgensma is indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy with bi-allelic mutations in the survival motor neuron 1 gene.

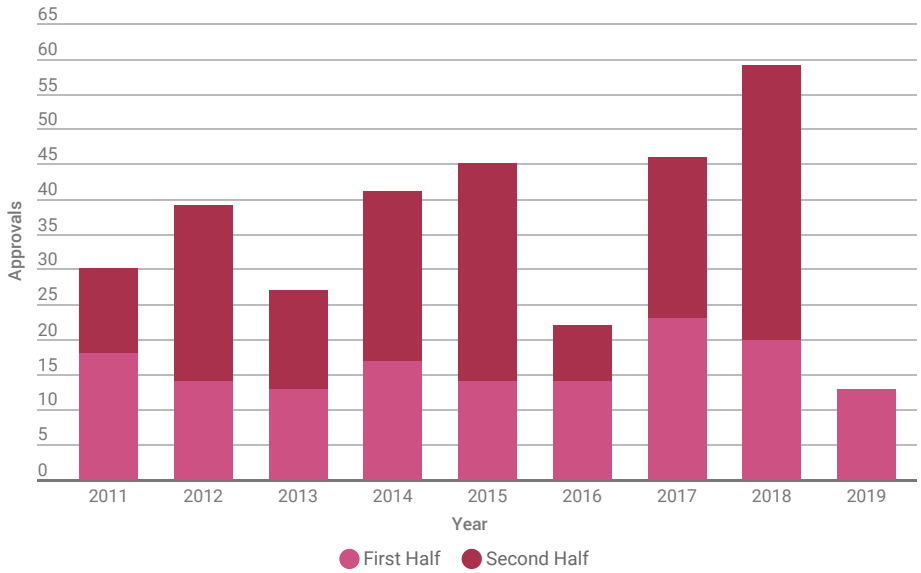
While the therapy has been lauded for its efficacy, however, the $2.1m price tag became, perhaps, an even bigger story.

More broadly, the year's first half of CDER approvals featured a predominantly big pharma presence. Nine of the 13 cleared novel CDER products are sponsored by Novartis, Sanofi, Genentech Inc., Pfizer Inc., AbbVie Inc., Janssen Pharmaceutical Cos., and Amgen Inc.

Pfizer's Vyndaqel (tafamidis meglumine) and Sanofi's Cablivi (caplacizumab-yhdp) became the first FDA-backed products, respectively, for cardiomyopathy caused by transthyretin mediated amyloidosis and acquired thrombotic thrombocytopenic purpura. *(Also see "Keeping Track: US FDA Approves Pfizer's Vyndaqel, Jacobus' Ruzurgi, But Nixes Acacia's Barhemsys Again" - Pink Sheet, 12 May, 2019.)* and *(Also see "Keeping Track: CDER Approves Its First Two Novel Agents Of 2019" - Pink Sheet, 10 Feb, 2019.)*

Meanwhile, Janssen's Balversa (erdafitinib) was described by Oncology Center of Excellence Rick Pazdur as "the first personalized treatment targeting susceptible FGFR genetic alterations for patients with metastatic bladder cancer." *(Also see "Keeping Track: NME Approvals For Evenity And Balversa; Non-NME Approvals For Dovato And Keytruda; But An RTF For Fintepla" - Pink Sheet, 14 Apr, 2019.)*

Novel CDER Approvals By Year



NOTABLE APPROVALS FROM SMALLER PHARMAS

There were two noteworthy approvals from smaller companies during the first half of 2019.

The first was Sage Therapeutics Inc. Zulresso (brexanolone) from March, which became the first FDA-approved product indicated for postpartum depression. Though a substantial clinical advance, the gamma-aminobutyric acid receptor also comes with burdensome administration, which requires a 60-hour continuous infusion with four changes in strength over the two and half days.

More recently approved was AMAG Pharmaceuticals Inc.'s Vyleesi (bremelanotide) for acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women.

Vyleesi is the second HSDD drug approved by the agency with the first being Sprout Pharmaceuticals Inc.'s Addyi (flibanserin). Although Vyleesi contains some clear labeling advantages over Addyi, including its on-demand administration, analysts remain skeptical about its market potential. *(Also see "AMAG Must Build Market For Approved Female Libido Drug To Avoid Addyi's Fate" - Scrip, 24 Jun, 2019.)*

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CDER's Novel Product CRLs: Midyear 2019

Below is the list complete response letters for CDER-regulated novel products announced by sponsors during the first half of 2019.

PRODUCT	SPONSOR	INDICATION	ISSUES	DATE ANNOUNCED	ACTIVITY
Edsivo (celiprolol)	Acer Therapeutics	**Cardiovascular, Rare Disease -** Vasodilator that promotes hemodynamic stability to make arterial wall less fragile for treatment of vascular Ehlers-Danlos syndrome (vEDS or EDS type IV), a rare hereditary disorder of collagen production, in patients with a confirmed type III collagen (COL3A1) mutation	Clinical - FDA called for an adequate and well-controlled trial to determine whether celiprolol reduces the risk of clinical events in vEDS patients	**2019-06-25**	NDA originally submitted 2018-10-25
Quizartinib	Daiichi Sankyo	**Cancer -** Selective FLT3 inhibitor for oral treatment of adults with relapsed or refractory FLT3-ITD acute myeloid leukemia (AML)	Undisclosed, but FDA raised clinical concerns at the advisory committee review including imbalance between patients in treatment and control arms who were randomized and not treated	**2019-06-21**	Breakthrough therapy designation; NDA originally submitted 2018-09-25l
Barhemsys (amisulpride, formerly APD421 and Baremsis)	Acacia Pharma	**Gastrointestinal -** I.V. formulation of the selective dopamine antagonist for management of post-operative nausea and vomiting (PONV)	Quality - FDA's second CRL cited continuing deficiencies at the contract manufacturer of the amisulpride active pharmaceutical ingredient; FDA's first CRL noted deficiencies found during a pre-approval inspection of the contract manufacturer of the active pharmaceutical ingredient; Acacia says no defects were identified that related to purity, stability, the manufacturing process or quality of the finished product	**2019-05-03** (second CRL); **2018-10-05** (first CRL)	Acacia is on track to complete the qualification of an alternative supplier of amisulpride, company said 2019-05-03; Resubmission announced 2018-11-06; Contract manufacturer submitted corrective and preventive action plan (CAPA) after receiving 'untitled letter' from FDA around 2018-10-12 noting a specific remaining deficiency; NDA originally submitted 2017-12

PRODUCT	SPONSOR	INDICATION	ISSUES	DATE ANNOUNCED	ACTIVITY
Zynquista (sotagliflozin)	Sanofi and Lexicon	**Metabolic -** Dual inhibitor of sodium glucose co-transporter types 1 and 2 (SGLT1 and SGLT2) for oral use in combination with insulin to improve glycemic control in adults with type 1 diabetes	Undisclosed	**2019-03-22**	Original NDA submission announced 2018-03-26
Iclaprim	Motif Bio	**Infectious Disease -** Dihydrofolate reductase inhibitor antibiotic for IV treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive pathogens	Clinical - FDA said additional data are needed to evaluate risk for liver toxicity	**2019-02-14**	Original NDA submission announced 2018-06-14; Qualified Infectious Disease Product (QIDP) designation
ALKS 5461 (buprenorphine and samidorphan)	Alkermes	**CNS -** Opioid system modulator fixed-dose combination of the partial mu-opioid agonist and kappa-opioid antagonist and the novel mu-opioid antagonist for adjunctive oral treatment of major depressive disorder (MDD)	Clinical - FDA requested additional clinical data to provide substantial evidence of effectiveness	**2019-02-01**	Advisory committee 2018-11-01 voted 21-2 that risk outweighed benefit; FDA acceptance for review announced 2018-04-16 after FDA Refuse to File (RTF) letter had been announced 2018-04-02; Completion of rolling NDA submission originally announced 2018-01-31
Sacituzumab govitecan (IMMU-132)	Immunomedics	**Cancer -** Antibody drug conjugate (ADC) for treatment of patients with metastatic triple-negative breast cancer (mTNBC) who previously received at least two prior therapies for metastatic disease	Quality - Letter focused on chemistry, manufacturing and controls (CMC) matters related to commercial supply of the antibody	**2019-01-17**	Breakthrough therapy designation; BLA originally submitted for accelerated approval 2018-05-18

CDER Novel Approvals: Midyear 2019

Below is a list of all CDER's novel approvals for the first half of 2019.

Key to abbreviations – **S:** Standard Review; **P:** Priority Review; **O:** Orphan Drug; **AA:** Accelerated Approval; **B:** Breakthrough Therapy; **NBE:** Novel Biologic Entity; **NME:** New Molecular Entity

SPONSOR	BRAND AND GENERIC NAME	INDICATION	APPROVAL DATE	CODES	TYPE
AMAG Pharmaceuticals	Vyleesi (bremelanotide)	**Genitourinary -** Melanocortin receptor agonist for treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD) characterized by low sexual desire that causes marked distress or interpersonal difficulty and is not due to co-existing medical or psychiatric conditions, relationship problems, or medication side effects	**6/21/2019**	S	NME

SPONSOR	BRAND AND GENERIC NAME	INDICATION	APPROVAL DATE	CODES	TYPE
Genentech (Roche)	Polivy (polatuzumab vedotin-piiq)	**Cancer -** CD79b-directed antibody–drug conjugate for use in combination with bendamustine and a rituximab product for treatment of adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least two prior therapies	**6/10/2019**	P, B, AA, O	NBE
Novartis	Piqray (alpelisib)	**Cancer -** Kinase inhibitor for use in combination with fulvestrant for treatment of postmenopausal women and men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen	**5/24/2019**	P	NME
Pfizer (FoldRx)	Vyndaqel (tafamidis meglumine) and Vyndamax (tafamidis)	**Cardiovascular, Rare Disease -** Transthyretin stabilizer formulated as 20mg oral capsules of the meglumine salt (Vyndaqel) or 61mg oral capsules of the free acid form (Vyndamax) for treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (HTTR-CM) in adults to reduce cardiovascular mortality and CV-related hospitalization	**5/3/2019**	P, O, B (Vyndaqel); S, O, B (Vyndamax)	NME
AbbVie	Skyrizi (risankizumab-rzaa)	**Immunology, Dermatology -** Interleukin-23 (IL-23) antagonist for treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy	**4/23/2019**	S	NBE
Janssen (Johnson & Johnson)	Balversa (erdafitinib)	**Cancer -** Kinase inhibitor for treatment of adults with locally advanced or metastatic urothelial carcinoma with susceptible FGFR3 or FGFR2 genetic alterations and that has progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum chemotherapy	**4/12/2019**	P, B, AA	NME
Amgen	Evenity (romosozumab-aqqg)	**Bone -** Sclerostin inhibitor for treatment of osteoporosis in postmenopausal women at high risk for fracture (history of osteoporotic fracture or multiple risk factors for fracture) or who have failed or are intolerant to other available osteoporosis therapy	**4/9/2019**	S	NBE
Novartis	Mayzent (siponimod)	**CNS -** Sphingosine 1-phosphate receptor modulator for treatment of relapsing forms of multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults	**3/26/2019**	P (Priority review voucher applied)	NME
Sage Therapeutics	Zulresso (brexanolone)	**CNS -** Neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator for treatment of postpartum depression (PPD) in adults	**3/19/2019**	P, B	NME
Jazz Pharmaceuticals	Sunosi (solriamfetol)	**CNS -** Dopamine and norepinephrine reuptake inhibitor (DNRI) to improve wakefulness in adults with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA)	**3/20/2019**	S, O (narcolepsy indication only)	NME

SPONSOR	BRAND AND GENERIC NAME	INDICATION	APPROVAL DATE	CODES	TYPE
Novartis	Egaten (triclabendazole)	**Infectious Disease -** Antihelmintic for treatment of fascioliasis (disease caused by Fasciola parasites, also known as liver flukes) in patients 6 years of age and older	**2/13/2019**	S, O	NME
Sanofi (Ablynx)	Cablivi (caplacizumab-yhdp)	**Blood Disorders -** von Willebrand Factor (vWF)-directed antibody fragment for treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP) in combination with plasma exchange and immunosuppressive therapy	**2/6/2019**	P, O	NBE
Evolus	Jeuveau (prabotulinumtoxinA-xvfs)	**Dermatology, Aesthetics -** Acetylcholine release inhibitor and neuromuscular blocking agent for temporary improvement of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adults	**2/1/2019**	S	NBE

US FDA's Integrated Review Document Would Dramatically Downsize Public Information

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The sample integrated review document posted by the US Food and Drug Administration to demonstrate its new proposed integrated review process and documentation template suggests that the agency is planning to make the review process even less transparent than under the action package streamlining that began one year ago.

"FDA believes that the format and content of the new integrated review will provide a clearer description of FDA's analysis of the scientific issues raised by the application and will thereby more effectively communicate the basis for the regulatory decision," the agency said in a 27 June 2019 Federal Register notice.

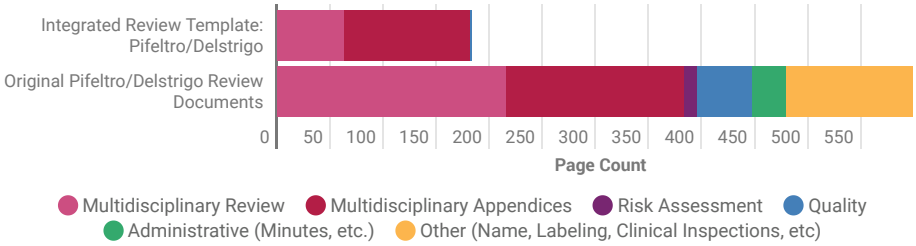
The agency also asked for comments on the clinical study report disclosure pilot program, which has only attracted one sponsor. *(Also see "US FDA May Scrap Clinical Study Report Disclosure For New Drug Approvals" - Pink Sheet, 26 Jun, 2019.)*

INTERDISCIPLINARY REPLACES MULTIDISCIPLINARY

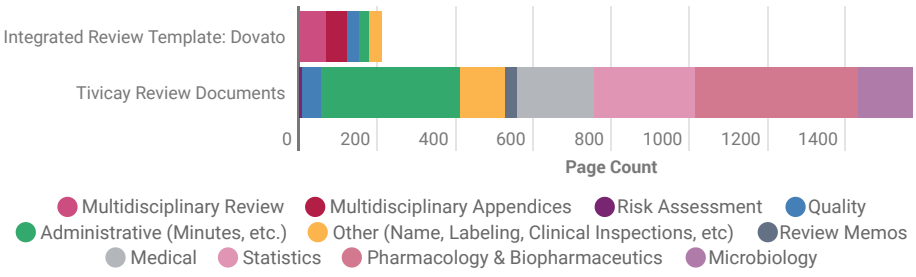
The proposed integrated review template would replace separate discipline-based

Putting Review Documents On A Diet

To illustrate its proposed integrated review document, FDA chose Merck's HIV therapy doravine, which was approved on 30 August 2018 as single-agent Pifeltro and as Delstrigo in combination with lamivudine and tenofovir disoproxil fumarate. Compared with the review documents made public following the original approval, the assessment written with the new template had a markedly lower page count.



FDA also issued review material for the 8 April 2019 approval of Viiv's HIV therapy Dovato (dolutegravir/lamivudine) using the new template, alongside some of the more traditional documents, like meeting minutes. The original approval of dolutegravir as a single agent (Tivicay) on 12 August 2013 came in a more open era before FDA's move to a multidisciplinary review format.



review documents with "a collaborative document from clinical pharmacology, biostatistics, toxicology reviewers, and other disciplines based upon the issues raised by the application," FDA said.

The change in the organization of the written review is part of the agency's program to modernize new drug regulation with a team-based focus. "The guiding principles of this initiative are the importance of conducting an issue-focused assessment, enhanced communication both within the review team and with the applicant, and stronger interdisciplinary collaboration," the FR notice said. Indeed, the agency also plans "purposeful interdisciplinary working meetings with early leadership involvement to focus on an integrated assessment of specific review issues."

The integrated review template is organized into an executive summary and an integrated assessment that "promotes succinct, integrated, focused analyses of the evidence of benefit-risk, and therapeutic individualization (e.g., special populations, drug interactions)" and "highlights key issues in an interdisciplinary manner that the review team thinks are pertinent to the decision-making process." Appendices will contain "assessments and analyses that are supportive or important to key facts/data or conclusions for the overall review."

The new initiative and template comes just a year after CDER instituted an action package streamlining effort that removed minutes from the mid-cycle and late-cycle meetings, the action package checklist, FDA information requests and correspondence. *(Also see "US FDA's Streamlined Drug Approval Packages Shine Less Light On Sponsor Interactions" - Pink Sheet, 23 Sep, 2018.)* The agency has also ceased publishing individual decision memoranda from CDER division and office leadership and condensed the remaining summary with summaries of other review disciplines in a multidisciplinary review document.

The integrated review would contain even less information than the multidisciplinary review, an imbalance illustrated by the examples FDA gave of the integrated review. The agency rewrote the review of Merck & Co. Inc.'s HIV drugs Pifeltro and Delstrigo in the new format, while leaving up the original review documents for the drugs' approval on 30 August 2018.

FDA also noted that it had issued the first review using the new format for ViiV Healthcare's Dovato (dolutegravir/lamivudine), which was approved on 8 April 2019.

The new integrated assessment produced public documents that are notably shorter than in the past *(see chart, p. 10)*.

While much of the shrinkage is due to the removal of duplicative information, the comparison shows that the new format documents reveal less about the process of the review, instead serving as a well-organized, super-size version of labeling.

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DRUG REVIEWS

PTC To Fight EMA Translarna No, Novartis Considers Revolade Next Steps

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One and possibly both of the companies who last week failed to persuade the European Medicines Agency to recommend EU approval of their respective indication extension requests will fight on and request a re-examination of their applications.

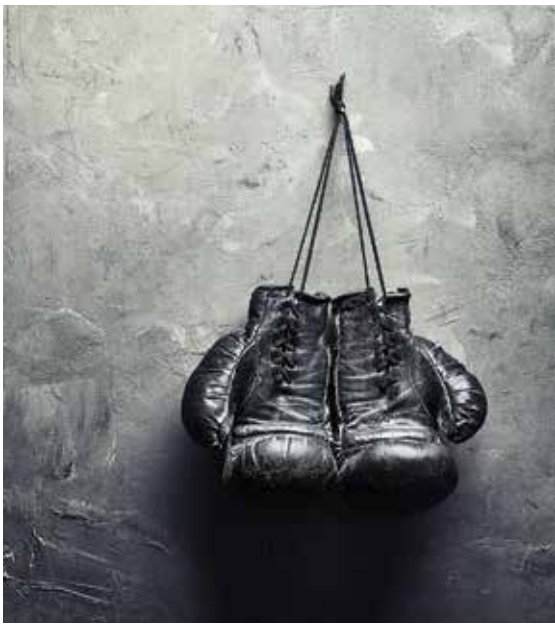
PTC Therapeutics has said it will appeal and Novartis is considering whether to do so.

Novartis had wanted the indication for Revolade (eltrombopag/eltrombopag olamine) to be extended to include first-line treatment of adult and pediatric patients aged two years and older with severe aplastic anemia (SAA). PTC had applied for the indication of Translarna (ataluren) to be extended to include non-ambulatory patients with nonsense mutation Duchenne muscular dystrophy.

The EMA's drug evaluation committee, the CHMP, considered the applications at its latest monthly meeting, which took place on 24-27 June. In both cases, the CHMP opined that the risk-benefit balance in the requested indications could not be established and so recommended refusing the changes to the original marketing authorizations.

Also in both cases it was clear that the CHMP had outstanding concerns; the two companies were slated to appear before the committee over the course of the meeting in an effort to address these concerns. *(Also see "Romosozumab Among Latest Drugs Up For CHMP Opinion" - Pink Sheet, 25 Jun, 2019.)*

Companies have 15 days from the date of the CHMP opinion in which to request a re-examination.



The first-line indication for Revolade is approved in the US and other countries. Translarna is not approved at all in the US; the Food and Drug Administration rejected PTC's marketing application for the product in late 2017. *(Also see "PTC To Appeal Translarna's Complete Response Letter From US FDA " - Pink Sheet, 25 Oct, 2017.)*

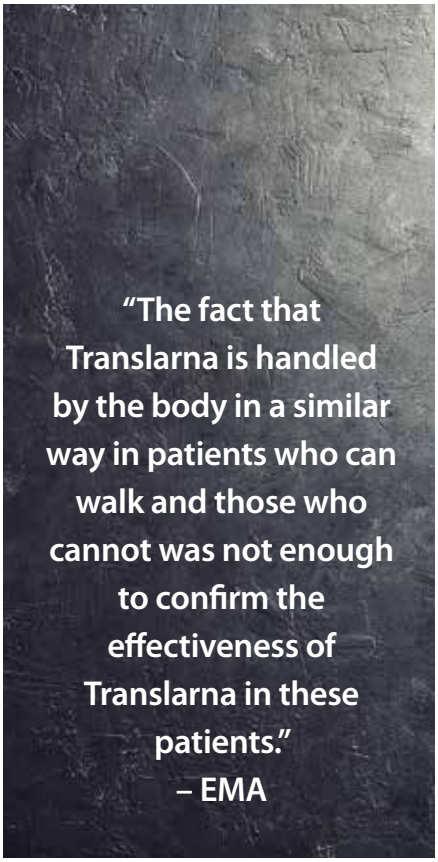
NOVARTIS

Novartis told the *Pink Sheet* that it was considering next steps and that it "may pursue" a re-examination following the CHMP's negative opinion.

The company said: "Revolade is currently approved as a second-line therapy for adult SAA patients in Europe, and we believe the data for the use as first-line therapy is compelling – a 44% complete response rate and a 79% overall response rate when added concurrently to standard immunosuppressive therapy. This compared favorably to historic controls, where the complete and overall response rates were 17% and 63% respectively. Revolade is approved for first-line therapy in the US (marketed as Promacta), Japan and a number of other countries, with additional applications pending."

Novartis provided data from a study involving 153 patients from three years of age with SAA who had not previously received immunosuppressive therapy. In the study, Revolade was combined with immunosuppressants that are used for treating aplastic anemia. The EMA noted that treatment was considered successful if the patient's white blood cell and platelet counts and hemoglobin rose to satisfactory levels.

The EMA said its main reasons for refusing the change to the marketing authorization were as follows: "The design of the study was not considered sufficiently robust to show that Revolade is effective for treating severe aplastic anaemia in previously untreated patients. The study did not make a direct comparison between Revolade combined with immunosuppressant treatment and immunosuppressant treatment alone. Instead, the comparison was with patients treated with immunosuppressants in other studies. Such comparison prevents drawing reliable conclusions on the effect of Revolade when added to immunosuppressants. Moreover, adequate amount of data were not available on the use of Revolade in children."



PTC THERAPEUTICS

PTC Therapeutics has already decided to appeal the CHMP's negative opinion on Translarna. It said in a press release: "PTC plans to request a re-examination of the procedure within the next two weeks and expects the new examination to last approximately 4 months. We remain committed to work with the CHMP to clarify the open questions and are confident we will be able to demonstrate the pulmonary benefit of Translarna in non-ambulatory patients."

In the US, the FDA rejected PTC's marketing application for Translarna in October 2017 but the product has had a conditional marketing authorization (CMA) in the EU since July 2014 for ambulatory Duchenne patients over two years of age.

According to the EMA, PTC provided data to show that the body handles ataluren in a similar way in patients who are able to walk and those who cannot. In addition, the agency said, the company presented the results of a study involving 94 patients with nonsense mutation DMD, 44 of whom were no longer able to walk. "Although the main objective of the study was to assess the long-term safety of Translarna, the study also investigated the effectiveness of treatment in patients unable to walk, measuring changes in lung function. The company then compared the results with historical data from patients with Duchenne muscular dystrophy recorded in the database of the CINRG (Cooperative International Neuromuscular Research Group)."

The EMA gave its reasoning for rejecting the extension request as follows: "The fact that Translarna is handled by the body in a similar way in patients who can walk and those who cannot was not enough to confirm the effectiveness of Translarna in these patients. This is because patients unable to walk are at a more advanced stage of the disease and have reduced muscle mass and therefore the benefits of treatment may be different. The additional data from the study could also not confirm the benefit of Translarna in patients no longer able to walk because there were problems with the way data from the CINRG database, which was used to indirectly compare the effects of Translarna, were selected and analysed."

The EMA said that Translarna patients could remain on treatment after loss of ambulation. PTC said: "While we are disappointed with the current outcome of the label expansion procedure and its impact on non-ambulatory patients with nonsense mutation Duchenne Muscular Dystrophy, we are pleased that patients on Translarna can remain on treatment after loss of ambulation."

PTC also noted that it received the annual renewal of its CMA in June 2019 for nonsense mutation DMD patients who are ambulatory and two years and over. In connection with the renewal, PTC's specific obligation for the submission of the results of Study 041, an ongoing clinical trial of ataluren, has been extended to September 2022.

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Amgen/UCB To Appeal EMA's 'Over Cautious' Evenity Rejection

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Amgen and UCB will ask the European Medicines Agency to re-examine its decision to recommend against EU-wide marketing approval of their osteoporosis drug, Evenity (romosozumab). The drug is already authorized for use in the US and several other countries.

Serious cardiovascular safety concerns prompted the EMA's drug evaluation committee, the CHMP, to recommend against EU approval of the marketing authorization application (MAA) for Evenity. The product was up for an opinion at the CHMP's latest monthly meeting, which took place on 24-27 June. *(Also see "Romosozumab Among Latest Drugs Up For CHMP Opinion" - Pink Sheet, 25 Jun, 2019.)* The MAAs for the other three medicines – La Jolla Pharmaceutical's Giapreza (angiotensin II), azacytidine from Celgene and lacosamide, also from UCB – all got the thumbs up.

Datamonitor Healthcare analyst Michael Haydock said it was "a bit harsh" of the CHMP to recommend against Evenity's approval. "The drug could have been approved with a warning to exclude patients with previous CV events or other comorbidities that put them at high CV risk," as has been done in the US, Haydock told the *Pink Sheet*.

"I think the drug is clearly efficacious… but I think the EMA are probably being over cautious because it isn't clear yet exactly which patient groups are at higher CV risk when receiving Evenity," Haydock added. The EMA said it was unclear why the medicine appeared to increase the risk of heart and circulatory problems, and there was no obvious group of patients in whom these risks were lower, due to which measures to reduce the risk could not readily be put in place.

NO JOY FOR NOVARTIS OR PTC THERAPEUTICS

There was also disappointment for Novartis and PTC Therapeutics, which failed to convince the CHMP to recommend extensions of the existing indications for their respective products, Revolade (eltrombopag) and Translarna (ataluren) (see preceding article).

Novartis had wanted the indication for Revolade to be extended to include first line treatment of adult and pediatric patients aged two years and older with severe aplastic anaemia. PTC Therapeutics had applied for the indication of Translarna to be extended to include non-ambulatory patients with Duchenne muscular dystrophy. In both cases, the EMA opined that the risk:benefit balance in the requested indications could not be established and so recommended refusing the changes.

MAA POSITIVE OPINIONS

The three MAAs that received a positive opinion from the CHMP were for:

Although Evenity is approved in several markets, including the US, Japan and South Korea, the EU regulator continues to have concerns regarding its safety.

- La Jolla Pharmaceutical's Giapreza (angiotensin II) for the treatment of refractory hypotension in adults with septic or other distributive shock. Giapreza was approved in the US in December 2017 following a priority review.
- Azacitidine Celgene, for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukemia and acute myeloid leukemia. Celgene submitted its marketing authorization application (MAA) for the product via an informed consent application. An informed consent application is one which makes use of data from the dossier of a previously authorized medicine, with the marketing authorization holder of that medicine giving consent for the use of their data in the application.
- Lacosamide UCB, for the treatment of partial-onset seizures with or without secondary generalisation. This was also submitted as an informed consent application by UCB.

NEW T2D PEDIATRIC INDICATION FOR VICTOZA

The CHMP also recommended extensions of indication for 12 products, including for Novo Nordisk's Victoza (liraglutide), in this case to include the treatment of children and adolescents aged ten years or older with type 2 diabetes.

The recommendation comes hot on the heels of the US approval earlier this month of Victoza for the treatment of type 2 diabetes in children aged 10 -17. *(Also see "US FDA Approval Of Novo Nordisk's Victoza For Young T2D Patients A Treatment Milestone" - Scrip, 18 Jun, 2019.)* Novo Nordisk said of the European development: "As the first GLP-1 receptor agonist approved for

children and adolescents with type 2 diabetes, Victoza provides this population with a new treatment option, with the last new treatment approved back in 2000."

The CHMP's recommendations are forwarded to the European Commission for the final say; the commission usually takes 67 days to issue a legally binding decision.

EVENITY NOT SAFE ENOUGH FOR EU?

Although Evenity is approved in several markets, including the US, Japan and South Korea, the EU regulator continues to have concerns regarding the safety of the drug. Amgen and UCB had been scheduled to give an oral explanation regarding their MAA at the CHMP's meeting in May, indicating that the committee still had concerns at this late stage of the evaluation process. *(Also see "Companies Keep The Faith As New Products Await EMA Verdict" - Pink Sheet, 28 May, 2019.)*

At its latest meeting, the CHMP concluded that Evenity posed an increased risk of serious effects on the heart or circulatory system, such as heart attacks or strokes. Overall data showed that there were more deaths in patients aged over 75 years who were given the medicine.

The CHMP found that the drug was effective in reducing the risk of fracture in patients with severe osteoporosis, but it said that the benefit was "not so convincing in patients with less severe disease." It concluded that Evenity's benefits did not outweigh its risks as an osteoporosis treatment in women who have been through the menopause and men at increased risk of bone fractures.

Cardiovascular concerns regarding EVENITY are well known. In the US, for example, the product's label contains a boxed warning stating that the drug may increase the risk of heart attack, stroke and cardiovascular death, and should not be used in patients who have had a heart attack or stroke in the previous year.

Haydock explained the black-box warning in the US means physicians are likely to only prescribe it to patients who they consider have low CV risk. Also, the US Food and Drug Administration has asked for a post-marketing CV study to explore further the drug's CV safety, he added.

Haydock says the drug is "clearly efficacious" and causes relatively rapid increases in bone mass density - over 12 months compared to 24 months with Eli Lilly's Forteo (Teriparatide).

Amgen and UCB are planning to ask the CHMP to re-examine its negative opinion. They said the re-examination process would give them "the opportunity to clarify our position on the submitted data with the goal of making EVENITY available to postmenopausal women at high risk of fracture in the EU." The companies maintained the body of evidence it had submitted supported a positive benefit-risk profile for the drug.

While Amgen and UCB co-developed Evenity, Amgen filed for and received approval in the US and UCB filed for approval in the EU.

AMGEN WITHDRAWS INFLIXIMAB MAA

Also of note at the CHMP meeting, Amgen has withdrawn its MAA for infliximab (ABP 710), citing a change in strategy for the product.

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Generic Industry Wants US FDA To Consider Allowing Foreign Reference Products For ANDAs

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Generic industry sponsors want the US Food and Drug Administration to consider researching whether foreign reference products could be used to show bioequivalence in the US.

Not only would such a move likely streamline generic drug approvals in the US, but also could help alleviate ongoing problems with sponsors obtaining reference product samples, they argue.

Kiran Krishnan, Apotex Inc. senior VP of global regulatory affairs, who represented the Association for Accessible Medicines, recommended FDA research to establish criteria for showing sameness between US and foreign small molecule generic reference products. He suggested solid oral immediate- and modified-release dosage forms, as well as those with complex active pharmaceutical ingredients, formulations, routes of delivery and dosage forms may be prime candidates, according to presentation slides.

Krishnan framed the potential benefit as time- and cost-saving.

"We don't want to be doing the studies again and again for the same product," Krishnan said during the FDA's recent public hearing on fiscal year 2020 generic drug research priorities. "Obviously when you try to do one study you cut down on the timelines that are needed for development."

He also indicated that the policy could create a new pathway for sponsors to more easily gain products for bioequivalence testing.

Krishnan said companies usually can find the one to two bottles

of a medicine sufficient for bridging and characterization studies, but five times that amount are needed for bioequivalence studies.

"Sometimes, and the agency is very aware of it, it's very difficult to source some of the innovator products in the US because obviously there's restricted distribution," he said. "In those instances we find that products are more easily sourced in other geographies by the same innovator products."

Indeed, the generic industry's complaints about brand sponsors denying access to samples is all too familiar. Companies have been accused of using Risk Evaluation and Mitigation Strategies, as well as other restricted distribution systems, to justify not selling samples to a generic company.

The FDA tried to curb the practice by sending letters to brand companies stating that selling samples would not violate a REMS or other regulations. *(Also see "REMS Abuse Website: Celgene, Actelion Top List Of Suspected 'Gamers'" - Pink Sheet, 18 May, 2018.)* However, even public release of the recipients of the letters has not appeared to eliminate the problem. *(Also see "REMS Abuse Website: Has It Changed The Behavior Of Innovators? " - Pink Sheet, 11 Feb, 2019.)*

AAM and other stakeholders also support the CREATES Act, which would allow generic companies to file suit against companies that deny access to samples unfairly. The bill has support in Congress, but has met several obstacles that have prevented enactment. *(Also see "Pay-for-Delay Bill Aimed At Blocking Brand/Generic Deals Gets Lower-Than-Expected Savings Estimate" - Pink Sheet, 14 May, 2019.)*

Using foreign reference products could be one way around the problem without waiting for Congress to pass the CREATES Act, which has been pending for several years.

FDA HAS LEGAL AND OTHER CONCERNS

Krishnan said Canadian and Australian regulators already allow the foreign reference products to be used when they are registered in a country with a comparable regulatory system and marketed in the country of origin by the same company marketing in their country. Canada and Australia also do not allow it for drugs with narrow therapeutic indexes or that require careful patient monitoring.

However, FDA and others were skeptical. One panel member worried about product drift, where subtle changes over time result in a product substantially different from the original.

Krishnan countered that in most cases the reference product used in the other country is made by the same manufacturer in the same facility.

But Dale Conner, director of the Office of Bioequivalence in the FDA's Office of Generic Drugs, said laws may have to change in some countries for the idea to be feasible.

"The word generic doesn't mean the same thing in a lot of countries as we have here in the US," he said. "Even though they are superficially similar there are sometimes very little things that kind of are differences and they may be not insurmountable differences, but difficult differences to overcome."

Conner also said the FDA has seen instances where the same products are co-produced in the same facility with the same name and drug substance, but by sponsor admission were different.

"We discovered that only much later," he said. "How do you deal with those kinds of things, where you're assuming same company, same brand name, same drug substance, manufactured in roughly the same place? How do you provide assurance if you're a generic sponsor and you don't access to any of their secret proprietary information, how do you go about assuring regulatory agencies that you're really using the same reference?"

Krishnan said those questions are the reason AAM wants the agency to research the idea.

> Allowing foreign reference products to be used for ANDAs could serve as another step toward global harmonization of the generic drug approval process.

"The expectation is these tests would be able to highlight the differences, if any," he said.

Interestingly, the FDA already allows biosimilar sponsors to use non-US-licensed reference products in some studies necessary for their applications, if a bridge between the US and foreign reference, as well as the biosimilar, is established. *(Also see "Biosimilar Sponsors Say Pharmacokinetic Bridging Studies Should Be The Exception, Not The Norm " - Pink Sheet, 26 Feb, 2019.)*

The FDA will consider the foreign reference standard and other proposals in creating its FY 2020 generic drug regulatory science research plan. Generic drug user fee dollars are allocated to research projects each year. *(Also see "US FDA's Generic Research Projects Appear To Be Opening Way For ANDAs " - Pink Sheet, 6 Jun, 2018.)*

ANOTHER STEP FOR GLOBAL HARMONIZATION

Allowing foreign reference products to be used for ANDAs could serve as another step toward global harmonization of the generic drug approval process.

The FDA is working through the International Conference on Harmonization to set common generic drug standards around the world, without lowering its own. *(Also see "ICH Generic Drug Harmonization May Be Another Cost-Lowering Opportunity" - Pink Sheet, 7 Feb, 2019.)*

Global convergence also could help lower the cost of medicines, another effort involving generics in the US. The Trump Administration and FDA have pushed for more generic competition to increase pricing pressure on expensive products.

The agency has responded with record generic drug approvals, but many of those products have not reached the market. *(Also see "Is Bloom Gone From Rosy ANDA Approvals Figures?" - Pink Sheet, 12 Nov, 2018.)*

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'No-Deal Brexit' Pharmacy Substitution Rules Take Effect In UK

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Under new legislation that took effect on 1 July, pharmacists in the UK can now override a doctor's prescription by dispensing another product, even one that contains a different active substance, if there is a "serious shortage" of the prescribed drug.

"Serious Shortage Protocols" will allow pharmacists to give the patient either the same product in a different form or strength, a generic or a biosimilar version, or a therapeutically equivalent drug, without consulting the prescribing physician – but only under very specific circumstances.

SSPs are part of the "Human Medicines (Amendment etc.) (EU Exit) Regulations 2019," which amend the UK Human Medicines Regulations 2012 and were first published at the beginning of this year as part of preparations for the UK's scheduled departure from the EU on 29 March (now extended to 31 October). Additional legislation that came into effect on 1 July extends the use of SSPs from just prescription-only medicines to any drug or appliance.

The Department of Health and Social Care has said the protocols are intended for use during any serious national shortage, not just for potential supply shortages in a no-deal Brexit scenario. Similarly, the Pharmaceutical Services Negotiating Committee, which represents the interests of community pharmacies in England, said that while SSPs were "linked to planning for any no-deal Brexit, they are not dependent on it."

But the introduction of SSPs is clearly driven by fears of major drug supply interruptions in the event of the UK leaving the EU without a deal. The government recently published details of other plans for dealing with supply disruptions caused by possible hold-ups of imports of medicines, particularly at the UK channel ports. *(Also see "UK Pharma Decries Govt's Latest No-Deal Brexit Planning" - Pink Sheet, 27 Jun, 2019.)*

> "Serious Shortage Protocols" permit substitution – in very specific circumstances – with the same product in a different form or strength, a generic or a biosimilar version, or a therapeutically equivalent drug.

Industry bodies had expressed concern over the SSP move after it was announced. The UK pharmaceutical industry association, the APBI, had initially cautioned that switching a patient's medicine was "not a simple thing to do," but subsequently welcomed the government's clarification that SSPs would be used "only in exceptional circumstances." *(Also see " Pharmacists To Get New Substitution Powers To Tackle Brexit Shortage Risk " - Pink Sheet, 21 Jan, 2019.)*

The British Generic Manufacturers Association (BGMA) told the *Pink Sheet*'s sister publication *Generics Bulletin* in January that the "flexibilities put forward should only be capable of being applied in limited circumstances. This would be the case of a 'no-deal' Brexit where government and industry have exhausted all other options to supply medicines to the UK market and there is an imminent and real risk of serious patient need not being met."

Moreover, a legal challenge to the SPP legislation had been mounted by the Good Law Project in February on the grounds that the Secretary of State for Health and Social Care did not have the power to make this change, and even if he did the process to do so had been "rushed and inadequate." However, in May the GLP conceded defeat after the Court of Appeal dismissed its attempt to overturn a March ruling that the legislation "plainly an important legislative measure designed to enable the Secretary of State effectively

to address serious drug shortages, including any potential drug shortages that may occur in the event of a no-deal Brexit."

WHEN SSPS WOULD BE USED

As their name suggests, SSPs are intended to be used only for "serious shortages." While the PSCN notes that this term is not defined in the legislation, it says it "arguably denotes more than a simple shortage that may be resolved by other measures."

In a briefing document published in June, the PSNC said: "If, in the Secretary of State for Health and Social Care's opinion, there is, or may be, a serious shortage of a medicine or appliance then he or she may consult, for instance with medical experts, and decide to issue an SSP."

The protocol will specify an alternative product or quantity that may be supplied by community pharmacists. This could be an alternative strength or formulation, a generic or therapeutic alternative, or a reduced quantity of the product.

"Community pharmacy contractors must consider the SSP and, if, in the supervising pharmacist's opinion – exercising his or her professional skill and judgment – the alternative product or quantity is reasonable and appropriate for the patient, they may supply the alternative product or quantity (only as specified in the SSP and subject to any conditions in the SSP), provided that the patient consents/agrees to the alternative SSP supply," the PSNC said.

> Substitution is not considered suitable for medicines for certain patient groups, such as those with epilepsy.

The product that is dispensed must be labelled to show that it has been supplied in accordance with the SSP. "The SSP must be identified, usually by its number, and the prescriber of the original product (ie, the one that has not been dispensed) may need to be notified," according to the committee. "For example, if a product with a different active substance is supplied, the pharmacist "must notify the patient's general practice of the alternative SSP supply." Patient consent agreement is required for supply of an alternative product or quantity in accordance with an SSP.

NOT ALWAYS SUITABLE

The PSNC warns that changes to certain medicines, even when in short supply, will not be suitable for some patient groups, such as those with epilepsy. "SSPs will only specify changes to specific medicines that medical experts believe to be appropriate; and pharmacists will always have the professional discretion not to supply an alternative to any individual patient."

SSPs are technically an exemption from the requirement that prescription-only medicines must only be supplied in accordance with a prescription issued by a practitioner such as a family doctor. Like the similar existing exemption, Patient Group Directions, SSPs will contain various sections providing certain types of information, such as the name of the prescribed medicine, details of the product dispensed, the period of validity of the SSP, any advice to refer the patient back to the prescriber, and any special considerations regarding certain patient groups.

According to the Royal Pharmaceutical Society, the government has said that operational guidance for SSPs is under preparation and the intention is that it will be made available on the website of the National Health Service Business Services Authority (NHS BSA) before or when the first SSP is issued. Any SSPs issued will also be available on the NHS BSA website.

Published online 2 July 2019

Recent And Upcoming FDA Advisory Committee Meetings

TOPICS	ADVISORY COMMITTEE	DATE
Boehringer Ingelheim's Ofev (nintedanib) for systemic sclerosis-associated interstitial lung disease	Arthritis	July 25
Intra-Cellular Therapies' lumateperone tosylate capsules for schizophrenia	Psychopharmacologic Drugs	July 31
Gilead's Descovy (emtricitabine/tenofovir alafenamide) for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection among individuals who are HIV-negative and at risk for HIV	Antimicrobial Drugs	August 7
Aimmune Therapeutics' peanut [*Arachis hypogaea*] allergen powder to reduce the risk of anaphylaxis after accidental exposure to peanut in patients ages 4-17 years with a confirmed peanut allergy diagnosis	Allergenic Products	Sept. 13

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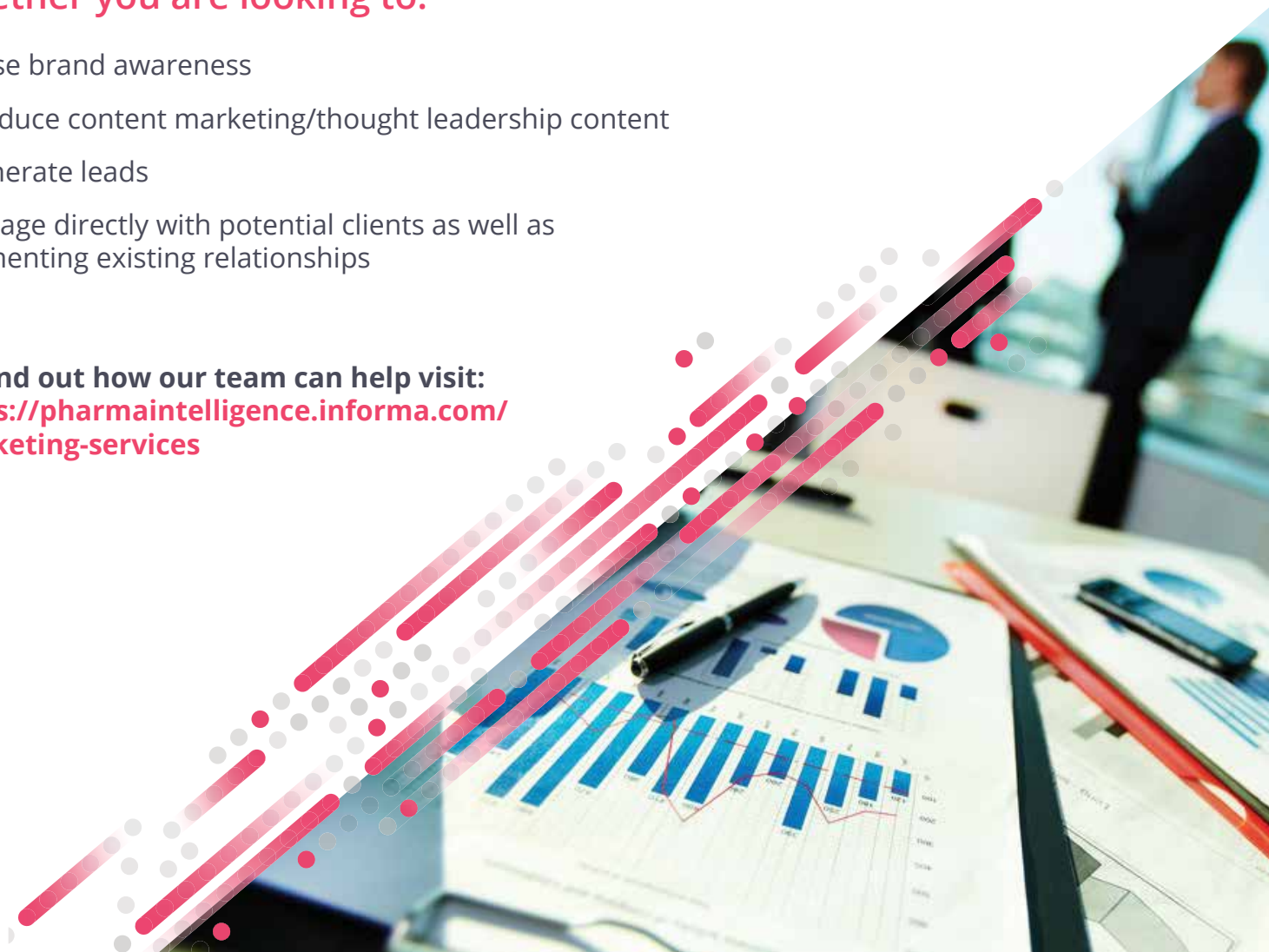

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