0110-science

FDA approves new antibody to slow Alzheimer’s disease, even as safety concerns linger

自译：FDA批准新抗体降低阿兹海默病，~~提高安全观察~~

# 微软：FDA批准减缓阿尔茨海默病新抗体，即使安全问题仍然存在

Agency warns about brain swelling and bleeding on drug’s label, but imposes *few* restrictions on lecaneamb’s use.

自译：机构宣布脑肿胀和药物充血，并强制少数实验室应用限制。

**微软：该机构警告药物标签上的脑肿胀和出血，但对lecaneamb的使用几乎没有限制。**

The U.S. Food and Drug Administration (FDA) today approved a controversial Alzheimer’s disease treatment for broad use—with caveats. The drug, an antibody called lecanemab, is the first to clearly slow cognitive decline in patients with early-stage disease, fueling excitement in the Alzheimer’s field ***and*** hope for patients and families. But its benefits appear modest, and it *comes with* potentially serious side effects②, including brain swelling and bleeding. At least three people taking lecanemab in a clinical trial died① after brain bleeds or swelling *and* some others had serious brain injuries③. The drug’s makers, Eisai and Biogen, say lecanemab wasn’t necessarily at fault.

自译：FDA现在批准了一个具有争议性的阿兹海默病治疗药物，它伴随着争议性被广泛的使用。一个叫lecanemab的抗体，是第一个在早期病人中明确显现出降低认知下降、提升大脑阿兹海默病区的兴奋的作用，这给了病人和家庭希望。但是它对明显温和的、潜在的秘密性效果，包括脑水肿和脑充血。在临床试验中，至少三人服用lecanemab死亡，均在脑充血、脑水肿以及其他大脑损伤之后。药物生产者，Eisai and Biogen，说lecanemab在功能障碍中并非必要。

**微软：美国食品和药物管理局（FDA）今天批准了一种有争议的阿尔茨海默病治疗方法的广泛使用 - 但有警告。这种名为lecanemab的抗体是第一个明显减缓早期疾病患者认知能力下降的药物，激发了阿尔茨海默氏症领域的兴奋以及患者和家庭的希望。但它的好处似乎不大，并且伴随着潜在的严重副作用，包括脑肿胀和出血。在临床试验中，至少有三名服用lecanemab的人在脑出血或肿胀后死亡，其他一些人患有严重的脑损伤。该药物的制造商Eisai和Biogen表示，lecanemab不一定有错。**

In a nod to safety concerns, the drug’s **label** will include a warning about developing a type of brain swelling or bleeding called ARIA, which ***stands for*** amyloid-related④imaging abnormalities, and recommend that anyone taking lecanemab have three MRIs in roughly the first 6 months of treatment to watch for those side effects. The label also suggests “**additional caution**⑤” ***be exercised in？*** giving **blood thinners**⑥ to patients on lecanemab, which may heighten the risk of brain bleeds. Two of the trial **participants** who died had also been given such drugs.

自译：出于对安全性的首肯，药物实验将警告包括提高脑充血和脑血肿几率的大类药，叫ARIA，支持淀粉样蛋白信息素异常，推荐任何人使用lecanemab在三种情况下，有大约6个月治疗期去观察副作用。实验同样显示出“额外注意事项”，被锻炼在病人脑血供量不足的区域使用，可能会增加脑出血的风险。两个实验参与者死亡均被给过药。

**微软：为了对安全问题的认可，该药物的标签将包括关于发展一种称为ARIA的脑肿胀或出血的警告，它代表淀粉样蛋白相关的成像异常，并建议任何服用lecanemab的人在大约前6个月内进行三次MRI治疗以观察这些副作用。该标签还建议在给服用lecanemab的患者服用血液稀释剂时要“格外小心”，这可能会增加脑出血的风险。死亡的试验参与者中有两名也服用了此类药物。**

Today’s announcement is unlikely to heal deep ***divisions①*** over whether lecanemab is a breakthrough for Alzheimer’s patients and their families, or a risky drug with limited benefits. The approval ***comes*** ***under②*** FDA’s “accelerated approval⑥” pathway for conditions with unmet medical needs. The companies had applied last summerbased on early evidence of benefit from the antibody. Since then, the firms have reported and published results from a pivotal **trial** of lecamenab in nearly 1800 people, and Eisai has announced plans to file for traditional, full FDA approval by the end of March.

自译：今天的报告中，lecanemab治愈深度组织的可能性很小，它对阿兹海默病患者及家庭是一个突破，还是一个有有限的益处的风险药物。药物批准申请已经到FDA“加速审批”通道，它审批条件未满足医药需求。~~在此之前~~，公司完成报道和公开发表成果——对关键的lecanemab1800人实验和Eisai在三月末宣布的FDA申请计划。

**微软：今天的公告不太可能弥合关于lecanemab是否是阿尔茨海默氏症患者及其家人的突破，或者是一种益处有限的风险药物的深刻分歧。该批准是根据FDA的“加速批准”途径进行的，适用于医疗需求未得到满足的疾病。这些公司去年夏天根据抗体益处的早期证据提出申请。从那时起，两家公司已经报告并公布了在近1800人中进行的lecamenab关键试验的结果，**Eisai**宣布计划在3月底之前申请传统、全面的FDA批准。**

窗体顶端

窗体底端

A looming question is whether and when the Centers for Medicare & Medicaid Services (CMS), the federal agency that ***pays for*** many treatments for older Americans, will reimburse for lecanemab—key to its uptake among potential recipients in the United States. In April 2022, CMS announced it would ***decline to*** reimburse for another Alzheimer’s antibody, aducanumab, also made by Biogen and Eisai, except in the context of certain clinical trials⑥. Both drugs help ***clear away*** or prevent the creation of amyloid plaques（先行词）,（which is） a buildup in the brain of a protein ***widely*** ***thought*** to ***drive*** the **cognitive decline** and other **symptoms** of Alzheimer’s disease. But the evidence of clinical benefit is weaker for aducanumab. CMS also said it would only consider ***covering drugs*** in this class after **full FDA approval**.

自译：一个迫在眉睫的问题是，是否和何时联邦机构CMS花费很多治疗给年龄大的美国人，会~~偿还~~lecanemab，在美国是吸收潜在受益人的关键。在2022年4月，CMS宣布将会降低其他阿兹海默病抗体的偿还，aducanumab也是Biogen and Eisa生产研发的，除了在临床试验中。这两种药都能明显地防止淀粉样斑块的发展，防止脑内蛋白通过广泛的控制认知下降和其他阿兹海默病症状。但是临床有益证据和aducanumab差太多。CMS同样声称它只能在完整的FDA审批后确认。

**微软：一个迫在眉睫的问题是，为美国老年人支付许多治疗费用的联邦机构医疗保险和医疗补助服务中心（CMS）是否以及何时将报销lecanemab - 这是其在美国潜在接受者中接受的关键。2022 年 4 月，CMS 宣布将拒绝报销同样由渤健和卫材生产的另一种阿尔茨海默氏症抗体 aducanumab，但某些临床试验除外。这两种药物都有助于清除或防止淀粉样斑块的产生，（淀粉样斑块）是大脑中被广泛认为会导致认知能力下降和阿尔茨海默病其他症状的蛋白质积聚。但aducanumab的临床获益证据较弱。CMS还表示，只有在FDA完全批准后，才会考虑涵盖此类药物。**

At an Alzheimer’s meeting in San Francisco last month, Maria Carrillo, a neuroscientist and chief science officer of the Alzheimer’s Association, argued that CMS ought to ***back*** lecanemab and all drugs given FDA’s blessing. “Any drug that receives accelerated approval should be covered by CMS,” she said.

自译：在加利福尼亚阿兹海默病会议上，神经学家、阿兹海默病协会首席科学顾问Maria Carrillo，提出CMS必须回到lecanemab，同时，所有的药品必须送FDA审，她说，“任何接受正规批准的药品都应被CMS覆盖。”

**微软：上个月在旧金山举行的阿尔茨海默氏症会议上，阿尔茨海默氏症协会的神经科学家兼首席科学官Maria Carrillo认为，CMS应该支持lecanemab和所有得到FDA祝福的药物。“任何获得加速批准的药物都应该由CMS覆盖，”她说。**

Lecanemab is “a win for all of us,” Carrillo said at last month’s meeting. There, the mood was **celebratory** *even as* reservations about lecanemab simmered. Last month, a letter describing lecanemab as a “foundational advance”⑧ began collecting signatures from researchers and medical practitioners; *to date*, nearly 230 people have signed it. “Every day of delay in patient **access** to this **therapy** may ***result in*** treatable patients **progressing**,” the letter reads. (Many, but not all, signers are recent consultants or grant recipients⑨ of Eisai or Biogen.)

自译：lecanemab 是“所有人的胜利”， Carrillo表示在上个月的会议中，对lecanemab的情绪仍然有所保留。上个月，一封描述lecanemab “建设性成果”开始收集从研究者和医药公司的成果，大概230个人标记它“每一天在患者中的延迟访问也许是治疗病人的成果”，信件中写到。（很多但不是全部，签名人是过去Eisai or Biogen的顾问或赠款接收者）

**微软：Lecanemab是“我们所有人的胜利，”卡里略在上个月的会议上说。在那里，气氛是庆祝的，即使对lecanemab的保留意见正在酝酿。上个月，一封将lecanemab描述为“基础进步”的信开始收集研究人员和医生的签名; 迄今为止，已有近230人签名。“患者获得这种疗法的每一天延迟都可能导致可治疗的患者进展，”信中写道。（许多（但不是全部）签名者是卫材或Biogen最近的顾问或赠款接受者。**

“I’m ***of the side*** that it’s not perfect, but it’s a step in the right **direction,**” says Joy Snider, a neurologist and head of the Knight Alzheimer’s Disease Research Center Clinical Trials Unit at Washington University School of Medicine in St. Louis. Snider was one of the researchers on the recently published phase 3 lecamenab study and a cosigner of the letter.

自译：“我很遗憾的它并不完美，但这是一个正确方向的进展。” Joy Snider说。他是神经学家，同时也是圣路易斯华盛顿大学医学院阿尔茨海默病研究中心临床试验部门学科带头人。Snider是最近发表过3项lecanemab研究和信件联合签名者。

**微软：“我的观点是它并不完美，但这是朝着正确方向迈出的一步，”圣路易斯华盛顿大学医学院奈特阿尔茨海默病研究中心临床试验部门的神经学家兼负责人乔伊·斯奈德说。Snider是最近发表的3期lecamenab研究的研究人员之一，也是这封信的共同签署人。**

But although Snider is excited about the drug, she also stresses that it should be “only the beginning,” and she hopes other, better therapies will follow. Among other ***concerns***, Snider worries about lecanemab’s potentially high cost. After the FDA approval, Eisai suggested it would have an annual cost of more than $25,000 for an average person, with additional costs for its infusions and monitoring. The antibody must be given intravenously every 2 weeks and the repeated MRI scans recommended by FDA will be expensive.

自译：但是尽管Snider对此药很乐观（兴奋/振奋），她依旧认为她应当“仅仅作为开始”，同时希望另一方面，会有更好的疗法跟进。在其他关注者中，Snider担心lecanemab潜在开支高。在FDI审批后，Eisai认为它年均个人消费高于$25,000元，和输液及监测的额外支出。抗体必须每两周重复给药一次，并通过FDA在MRI的监测下将会变得昂贵。

**微软：但是，尽管斯奈德对这种药物感到兴奋，但她也强调，这应该“只是一个开始”，她希望其他更好的治疗方法能够随之而来。在其他担忧中，Snider担心lecanemab的潜在高成本。在FDA批准后，卫材表示，对于普通人来说，每年的成本将超过25，000美元，输液和监测费用将增加。抗体必须每 2 周静脉注射一次，FDA 推荐的重复 MRI 扫描费用昂贵。**

Among lecanemab’s opponents is neurologist Alberto Espay of the University of Cincinnati. He believes the benefits of lecanemab across ***a population*** are minimal and its risks significant, and recently co-authored a preprint with 11 other academics expressing such concerns. “I think this drug should not be approved,” said Espay in an interview the day before FDA’s announcement. But **agency official**s, he added, “**are victims of an artificially low *bar***”10 they ***set in*** 2021 by greenlighting aducanumab. FDA’s own advisory committee had voted against that approval but was overruled. Just last week, a congressional report described FDA’s approval process for aducanumab as “rife with irregularities11.”

自译：lecanemab的对手是辛辛那提大学神经科阿尔贝托·埃斯佩。他坚信lecanemab的益处很小，危害很大，在最近的联合作者中，和11位专家提前发表了想法和担忧，“我认为这种药不应当被批准。” Espay在FDA宣告之前的采访中。但是机构官员，他增补到，“是人为低标准受害者”他们成立于2021年？FDA旗下咨询委员会投票反对批准但是被推翻了。仅仅在上周，国会报道描述FDA aducanumab的申请项目是“充斥着违规行为”。

**微软：lecanemab的反对者包括辛辛那提大学的神经学家Alberto Espay。他认为lecanemab对人群的益处很小，其风险很大，最近与其他11位学者共同撰写了预印本，表达了这种担忧。“我认为这种药物不应该被批准，”Espay在FDA宣布前一天接受采访时说。但他补充说，该机构官员 “是他们在 2021 年通过绿灯 aducanumab 设定的人为低标准的受害者”。FDA自己的咨询委员会投票反对该批准，但被否决。上周，一份国会报告将FDA对aducanumab的批准程序描述为“充斥着违规行为”。**

When it ***came to*** lecanemab, FDA did not ***turn to*** its **advisory committee** for guidance despite calls from some scientists and the drug **watchdog** Public Citizen to do so.

自译：当它？？FDA没有通过咨询委员会的指导，除了一些科学家和药物观察的机构的来电。

**微软：当涉及到lecanemab时，FDA没有向其咨询委员会寻求指导，尽管一些科学家和药物监管机构Public Citizen呼吁这样做。**

**Clinical trials** showed lecanemab was remarkably **efficient**—more so than aducanumab—in mopping up amyloid plaques. But the drug’s effects on cognition were modest: On a commonly used 18-point cognition scale, ***derived from*** the experience of patients and their caregivers, those getting the drug on average declined 0.45 points less than those getting **placebo** after 18 months. Neurologists disagree ***over whether and to*** what extent patients and caregivers would perceive this lesser decline. Snider believes it would likely be noticeable. For example, on the part of the scale that **assesses orientation**, she says, an individual who scores 0.5 “can still drive” and get around independently. “If you go to a one, you’re going to start getting lost.”

自译：临床实验显示lecanemab明显比aducanumab在清除淀粉样斑块上有效。但是药效在认知上比较温和：在普遍应用的18点认知量表——来源于患者和他们照顾者的经验，在18个月后，相对服用安慰剂，服药人群平均降低了0.45个百分点。神经学家不认为这个程度的患者和照顾者能够接受这一点点下降。Snider坚信它很可能被重视。比如说，在部分规模的评估方向上，她说，个体0.5分“仍然能导致”并接近于独立自主。“如果你去一个，你能够开始丧失。”

**微软：临床试验表明，Lecanemab在清除淀粉样蛋白斑块方面非常有效 - 比aducanumab更有效。但这种药物对认知的影响是适度的：在常用的18分认知量表上，根据患者及其护理人员的经验得出，那些服用这种药物的人在18个月后平均比服用安慰剂的人少0.45分。神经学家对于患者和护理人员是否以及在多大程度上会感知这种较小的下降存在分歧。斯奈德认为这可能会引起注意。例如，在评估方向的量表部分，她说，得分为0.5的人“仍然可以开车”并独立出行。“如果你去一个，你会开始迷路。**

The most serious hazard for those on lecanemab appears to be ARIA, which has been seen with other antiamyloid drugs tested in clinical trials. Although Eisai has ***stressed*** that the numbers of deaths were similar in the placebo and lecanemab-treated groups in the antibody’s latest trial, some scientists have linked the drug to the catastrophic brain bleeds and swelling, including in three people who died after receiving the drug during an extension of the **phase 3 trial**. *STAT* reported one, involving a man in his 80s, in October 2022 and *Science* described the deaths of a 79-year-old Florida woman and a 65-year-old woman who were in the early stages of Alzheimer’s disease. The case of the 65-year-old was also chronicled this week in *The New England Journal of Medicine*.

自译：lecanemab最严重的危险在ARIA显现，即药物在临床实验测试中抗淀粉样蛋白的能力。尽管Eisai~~指出~~大量的死亡在安慰剂组和ecanemab-treated治疗组在抗淀粉样蛋白中最后的实验中有着一定的相似性，一些科学家将药物和脑水肿及脑充血联系起来，包括在延长3期临床试验中3例接受药物治疗后死亡的案例。在2022年10月*STAT* 报导一例80多岁的男性，和科学杂志报道的一位79岁的佛罗伦亚女性，和65岁并在早期阿兹海默病阶段的女性。这个65岁的案例也记录在新英格兰杂志上。

**微软：对于使用lecanemab的人来说，最严重的危害似乎是ARIA的，这已经在临床试验中测试的其他抗淀粉样蛋白药物中观察到。尽管卫材强调，在抗体的最新试验中，安慰剂组和lecanemab治疗组的死亡人数相似，但一些科学家将该药物与灾难性的脑出血和肿胀联系起来，包括三人在延长3期试验期间接受该药物后死亡。STAT于2022年10月报道了一项涉及一名80多岁男子的事件，《科学》描述了一名79岁的佛罗里达州妇女和一名65岁妇女的死亡，他们处于阿尔茨海默病的早期阶段。这位65岁的病例本周也被记录在《新英格兰医学杂志》上。**

Espay worries, too, about patients who may ***develop*** less severe ARIA while taking lecamenab. For at least some of them, “I cannot imagine it’s irrelevant or inconsequential,” he says.

自译：Espay同样担忧，关于患者在服药期间接受很少的严重ARIA。在至少他们“我不能想象到这是**不相关或无关紧要的**。”

**微软：Espay也担心那些在服用lecamenab时可能会出现不太严重的ARIA的患者。至少对其中一些人来说，“我无法想象这是无关紧要或无关紧要的，”他说。**

Snider would like to see a new ***national*** database to track ARIA and any other side effects of lecanemab usage and help doctors and researchers understand who is at greatest **risk**. (The drug’s label suggests physicians can contribute reports on side effects to an existing, voluntary Alzheimer’s drug registry called ALZ-NET.) People with two copies of the *APOE4* gene, which predisposes to Alzheimer’s, may be at higher risk of ARIA. In lecanemab’s large clinical trial, 9.2% of people with two copies of the gene variant had symptomatic brain swelling, compared with 1.4% of people with no copies. Alzheimer’s patients aren’t **routinely** tested for *APOE4* because it hasn’t traditionally **affected diagnosis** or treatment.

自译：Snider想要看到一个新的民族数据去跟踪ARIA和其他lecanemab副作用，并帮助医生和研究者理解更有效的治疗。（药物实验室结论支持神经学家贡献出有价值的副作用报道）。人们携带两类可导致阿兹海默病的 *APOE4* 基因，也许对ARIA有很高的伤害。在广泛的lecanemab临床试验中，9.2%携带两种基因变体患有有症状的脑肿胀，和1.4%的无携带者。阿兹海默病患者不能够完全测出*APOE4* ，因为它没有传统的影响诊断或治疗。

**微软：Snider希望看到一个新的国家数据库来跟踪ARIA和lecanemab使用的任何其他副作用，并帮助医生和研究人员了解谁的风险最大。（该药物的标签表明，医生可以向现有的自愿阿尔茨海默氏症药物登记处ALZ-NET提供有关副作用的报告。具有两个拷贝的APOE4基因的人，易患阿尔茨海默氏症，可能患ARIA的风险更高。在lecanemab的大型临床试验中，9.2%的基因变异有两个拷贝的人有症状性脑肿胀，而没有携带的人只有1.4%。阿尔茨海默氏症患者没有常规进行APOE4检测，因为它传统上不会影响诊断或治疗。**

Although some scientists had hoped FDA would ***rule*** against giving lecanemab to people with two copies of *APOE4*, the agency ***declined*** to do so, suggesting only that people “consider testing” for *APOE4* ***status*** “to **inform** the risk of developing ARIA when deciding to **initiate** treatment.”

自译：尽管一些科学家希望FDA规范反对给携带两种*APOE4*的人群给lecanemab，机构减少支持仅仅“考虑到检测” *APOE4* 变种“去避免ARIA的风险”？

**微软：尽管一些科学家曾希望FDA能够裁定 不给拥有两份APOE4拷贝的人服用lecanemab，但该机构拒绝这样做，只是建议人们“考虑测试”APOE4状态，“以告知在决定开始治疗时发生ARIA的风险”。**

For **provider**s, the road ahead remains uncertain. “Those of us in AD [Alzheimer’s disease] research and **patient care** will continue working on how best to offer this new medication to our patients,” Snider says.

**微软：对于供应商来说，前方的道路仍然不确定。“我们这些从事AD[阿尔茨海默病]研究和患者护理的人将继续致力于如何最好地为我们的患者提供这种新药，”Snider说。**