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Review

Novel Pharmacological Approaches to Neurological Diseases: A Review of Recent Clinical Breakthroughs

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Abstract

Neurological diseases present significant global health challenges due to their high prevalence, substantial disability burden, and previously limited therapeutic options. Recent breakthroughs in neuropharmacology and precision medicine have dramatically advanced treatment paradigms, ushering in targeted medications that alter disease progression, alleviate symptoms, and improve patient quality of life. This review systematically examines recent pharmacological innovations across Alzheimer's disease, Parkinson's disease, and multiple sclerosis (MS). For AD, landmark disease-modifying therapies such as aducanumab and lecanemab targeting amyloid pathology, and the introduction of transdermal donepezil, have expanded therapeutic possibilities. In PD, novel formulations like opicapone and sublingual apomorphine provide enhanced control of motor fluctuations. For MS, oral sphingosine-1-phosphate receptor modulators (ozanimod, ponesimod), home-administered B-cell therapies (ofatumumab), novel fumarate formulations (monomethyl fumarate), and optimized monoclonal antibodies (ublituximab) represent significant therapeutic advancements. This review provides clinicians and researchers with comprehensive, structured insights into these novel pharmacotherapies, highlighting their clinical efficacy, dosing considerations, and safety profiles, thereby facilitating informed clinical decision-making and promoting precision medicine in neurology.

Keywords: Neurology, Pharmacotherapy, Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis

INTRODUCTION

Neurological diseases constitute a major global health challenge due to their high prevalence, disability burden, and limited therapeutic options historically available (1). Until recently, many neurological conditions lacked targeted treatments, relying heavily on supportive and symptomatic care. However, the rapid evolution of neuropharmacology and precision medicine in the recent years has transformed therapeutic approaches significantly, providing clinicians and patients with a spectrum of new medications that alter disease courses, reduce symptom burden, and enhance quality of life (2,3).

Each section provides detailed descriptions of newly approved drugs, their mechanisms of action, clinical efficacy based on pivotal trials, recommended dosing regimens, routes of administration, and critical safety considerations. Organized tables accompany the text to facilitate concise comparisons and practical application. Furthermore, the review emphasizes emerging trends in precision medicine, particularly the increased use of targeted monoclonal antibodies, antisense oligonucleotides, and transformative gene therapies.

By synthesizing comprehensive and systematically structured evidence on emerging pharmacotherapies, this narrative review, grounded in PubMed and FDA/EMA database analyses, seeks to provide neurologists, clinicians, researchers, and healthcare professionals with an up-to-date overview of current therapeutic options and their translational relevance to clinical practice.

METHODS

This narrative review was conducted through a structured literature search of the PubMed, FDA, and EMA databases covering publications and regulatory

Table 1. Key Recent Drug Approvals in Alzheimer's Disease (2020–2024)

Drug (Brand)	Year	Indication	Mechanism	Key Efficacy Results	Dosing	Major Side Effects	Clinical Importance
Aducanumab (Aduhelm)	2021	Early Alzheimer's (MCI/mild)	Anti-amyloid antibody	Modest slowing of cognitive decline (controversial)	IV every 4 weeks	ARIA (edema, bleeding), headache	First amyloid-clearing therapy
Lecanemab (Leqembi)	2023	Early Alzheimer's (MCI/mild)	Anti-amyloid antibody	~27% slower cognitive decline	IV every 2 weeks	ARIA, infusion reactions, headache	Proven clinical benefit, slows AD progression
Donepezil (Adlarity patch)	2022	Mild–severe Alzheimer's	Acetylcholinesterase inhibitor	Equivalent efficacy to oral form	Weekly transdermal patch	Skin irritation, less GI upset	Improved compliance and tolerability

approvals between January 2020 and June 2025. The search combined keywords including neurology, pharmacotherapy, Alzheimer's disease, Parkinson's disease, multiple sclerosis, novel drug approval, monoclonal antibody, and gene therapy. Priority was given to peer-reviewed clinical trials, meta-analyses, and regulatory summaries describing newly approved or late-phase pharmacological agents. Reference lists of relevant articles were also screened to identify additional studies. Data were synthesized qualitatively to highlight mechanisms of action, efficacy outcomes, dosing, and safety profiles of recent therapeutic advances in neurology.

ALZHEIMER'S DISEASE

Alzheimer's disease (AD) saw the first disease-modifying therapies reach clinical use in 2021–2023. Aducanumab was approved in 2021 for early AD (mild cognitive impairment or mild dementia stage) (4,5). It is a monoclonal antibody targeting aggregated beta-amyloid, designed to clear amyloid plaques from the brain. In clinical trials, a high dose of aducanumab modestly slowed cognitive decline in one Phase III study, though a parallel study was negative (4,5). The FDA granted approval based on the surrogate outcome of plaque reduction (6). Aducanumab is administered via intravenous infusion every four weeks. Major side effects include amyloid-related imaging abnormalities (ARIA), such as cerebral edema or microhemorrhages seen on MRI in about one-third of patients (often asymptomatic, but occasionally causing headache or confusion) (7). Despite controversy over its unclear clinical benefit, aducanumab's approval was significant as the first therapy aimed at AD's underlying pathology (4-7) (Table 1).

Lecanemab (Leqembi), approved in 2023, is another anti-amyloid monoclonal antibody for early-stage AD (8). Lecanemab binds soluble amyloid protofibrils, facilitating clearance of amyloid. In the Phase III CLARITY-AD trial, lecanemab treatment led to a statistically significant slowing of cognitive and functional decline (approximately 25–30% less decline on a clinical dementia rating scale at 18 months compared to placebo) (9). This provided the first clear evidence of clinical benefit with amyloid removal. Lecanemab is given by IV infusion every two weeks. Its safety profile also features ARIA (incidence ~12% for edema, higher in APOE4 gene carriers), plus infusion-related reactions (10). While ARIA requires monitoring, most cases are mild (10). Lecanemab's approval (first under accelerated status, then full approval) marked a milestone as a therapy that both reduces amyloid burden and demonstrates a measurable, albeit modest, clinical benefit in AD (8-10).

In addition, a new formulation of an existing AD drug was introduced during this period. Donepezil transdermal patch (Adlarity) was approved in 2022 for mild to severe AD dementia (11,12). This once-weekly patch provides continuous delivery of the acetylcholinesterase inhibitor donepezil. It offers similar cognitive symptomatic benefits as oral donepezil but with improved adherence (weekly dosing) and reduced gastrointestinal side effects (since the transdermal route avoids high peak oral dosing). The most common adverse effects of the patch are application-site reactions and mild cholinergic effects. This formulation provides an alternative option for patients who have difficulty with daily oral medications (12).

PARKINSON'S DISEASE

While no cures emerged, new therapies addressed motor fluctuations in Parkinson's disease (PD) between 2020 and 2024. Opicapone (Ongentys), approved in 2020, is an add-on therapy for PD patients experiencing "off" episodes while on levodopa (13). Opicapone is a catechol-O-methyltransferase (COMT) inhibitor that prevents peripheral breakdown of levodopa, thereby increasing levodopa's availability to the brain. In clinical trials, opicapone (25–50 mg once daily) significantly reduced daily "off" time and increased "on" time (periods of good motor control) by about 1 hour on average, comparable to the older COMT inhibitor entacapone (13). Unlike entacapone, which must be taken with each levodopa dose, opicapone's long duration allows for once-daily dosing. Its side effect profile mainly reflects enhanced levodopa effects: dyskinesias (involuntary

Table 2. Key Recent Drug Approvals in Alzheimer's Disease (2020–2024)

Drug (Brand)	Year	Indication in PD	Mechanism	Key Results	Dosing	Major Side Effects	Clinical Importance
Opicapone (**Ongentys**)	2020	Add-on for levodopa "off" episodes	COMT inhibitor	~1 hour less daily "off" time	Oral, once daily at bedtime	Dyskinesia, insomnia, constipation, hypotension	Simplifies dosing, improves levodopa effectiveness
Apomorphine sublingual film (**Kynmobi**)	2020	Acute treatment of "off" episodes	Dopamine agonist	Rapid symptom relief within ~15 min	Sublingual, as needed (up to 5× daily)	Nausea, oral irritation, hypotension, sedation	Non-injectable, rapid rescue from sudden "off" episodes

COMT: catechol-O-methyltransferase

movements) were the most common adverse effect as higher levodopa levels can cause them. Other side effects include insomnia, constipation, low blood pressure, and vivid dreams. Opicapone's once-daily dosing and potent COMT inhibition offer a convenient way to manage motor fluctuations in advanced PD (13,14).

Apomorphine sublingual film (Kynmobi) was approved in 2020 as an acute rescue therapy for intermittent "off" episodes in PD (15) (**Table 2**). Apomorphine is a fast-acting dopamine agonist that can rapidly alleviate Parkinsonian symptoms when oral medications have temporarily lost effect. Previously available as a subcutaneous injection (Apokyn), apomorphine was often underused due to injection burden (15,16). The sublingual film formulation allows patients to place a strip under the tongue at the start of an off episode. In Phase III trials, sublingual apomorphine produced a clinically meaningful improvement in motor function within 15–30 minutes, with significantly more patients converting from an "off" state to an "on" state (improved mobility) compared to placebo (17). Doses are titrated (10–30 mg) based on effect, and up to 5 doses per day may be used as needed. Side effects are notable: nausea and vomiting can be prominent (antiemetic pre-treatment is recommended, though 5-HT3 antagonist antiemetics are contraindicated due to severe hypotension risk). Other common adverse effects include dizziness, orthostatic hypotension, oral mucosal irritation or ulceration (from the film), somnolence, and potential hallucinations. In clinical studies a substantial proportion of patients discontinued due to side effects like nausea or mouth irritation. Despite these challenges, the sublingual film provides a non-invasive, rapid-onset option to rescue patients from disabling off off episodes states, improving daily functioning and independence (17).

MULTIPLE SCLEROSIS

Several innovative disease-modifying therapies for multiple sclerosis (MS) were introduced in 2020–2024, expanding treatment options for relapsing forms of MS. Ozanimod (Zeposia), approved in 2020, is an oral sphingosine-1-phosphate (S1P) receptor modulator (18) (**Table 3**). It selectively binds S1P_1 and S1P_5 receptors, trapping lymphocytes in lymph nodes and preventing them from entering the CNS to cause inflammation. In Phase III trials (SUNBEAM and RADIANCE), ozanimod significantly lowered the annualized relapse rate and reduced new brain MRI lesions compared to interferon beta-1a (19). For example, the high-dose ozanimod group had an ARR of ~0.18 per year versus ~0.35 on interferon, nearly a 50% reduction. Ozanimod is taken once daily orally. Its safety profile is similar to fingolimod but with greater selectivity: most common side effects are nasopharyngitis, headache, elevated liver

Table 3. New Multiple Sclerosis Drugs (2020–2024)

Drug (Brand)	Year	Indication	Mechanism	Key Outcomes	Dosing	Side Effects	Clinical Importance
Ozanimod (**Zeposia**)	2020	Relapsing MS	S1P receptor modulator	~45% relapse reduction, fewer MRI lesions	Oral once daily	Headache, elevated liver enzymes, bradycardia, infection risk	Oral convenience with high efficacy, improved safety over older S1P agents
Ponesimod (**Ponvory**)	2021	Relapsing MS	$S1P_1$ receptor modulator	~30–35% relapse reduction vs teriflunomide	Oral once daily (14-day titration)	Bradycardia, hypertension, infections	Short half-life allows quick reversal if therapy interrupted
Ofatumumab (**Kesimpta**)	2020	Relapsing MS	Anti-CD20 (B-cell depletion)	~50% relapse reduction, ~90% fewer new MRI lesions	Monthly subcutaneous injection	Injection reactions, flu-like symptoms, infections	First at-home injectable anti-CD20 therapy
Monomethyl fumarate (**Bafiertam**)	2020	Relapsing MS	Nrf2 pathway activator (fumarate)	Similar efficacy as dimethyl fumarate (50% relapse reduction)	Oral capsule twice daily	Flushing, GI upset, lymphopenia, rare PML risk	Potentially improved GI tolerability compared to dimethyl fumarate
Ublituximab (**Briumvi**)	2022	Relapsing MS	Anti-CD20 antibody	~60% relapse reduction, ≥90% fewer MRI lesions	IV infusion every 24 weeks	Infusion reactions, infections, rare serious infections	Short infusion duration, extended dosing interval; potent B-cell therapy

MS, Multiple Sclerosis; S1P, Sphingosine-1-phosphate; $S1P_1$, Sphingosine-1-phosphate receptor subtype 1; CD20, Cluster of Differentiation 20; Nrf2, Nuclear factor erythroid 2–related factor 2; GI, Gastrointestinal; PML, Progressive Multifocal Leukoencephalopathy; IV , Intravenous; ARR, Annualized Relapse Rate.

enzymes, and mild first-dose bradycardia (thus a dose-escalation starter pack is used). It has no required genetic testing. Ozanimod offers a convenient oral alternative for relapsing MS with efficacy comparable to injectables (19,20).

Ponesimod (Ponvory), approved in 2021, is another oral S1P_1 receptor modulator for relapsing MS (21). In the head-to-head Phase III OPTIMUM trial against teriflunomide, ponesimod showed superior efficacy: about a one-third lower relapse rate (ARR ~0.19 vs 0.29) and significant reductions in MRI lesion activity (22). Ponesimod is taken once daily, with a 14-day titration at initiation. A distinguishing feature is its relatively short half-life (~33 hours), if therapy is stopped, immune effects wear off within a week, allowing quicker lymphocyte recovery than fingolimod. This can be advantageous if therapy must be interrupted (e.g. for infection or pregnancy). Side effects of ponesimod include dose-dependent transient bradycardia (on first doses), hypertension, elevated liver enzymes, and other S1P-class effects like macular edema and respiratory slight declines (22,23). The option to rapidly eliminate the drug makes ponesimod an appealing choice for some patients concerned about reversibility of immune suppression.

Ofatumumab (Kesimpta) was approved in 2020 as the first B-cell therapy for relapsing MS that patients can self-administer at home (24,25). Ofatumumab is a fully human monoclonal antibody targeting CD20 on B-lymphocytes, similar to ocrelizumab, but delivered via subcutaneous injection rather than IV infusion. In the Phase III ASCLEPIOS I and II trials, monthly ofatumumab injections were superior to oral teriflunomide: annual relapse rates were reduced by ~50% (ARR ~0.1 vs 0.2), and ofatumumab significantly slowed disability progression and cut MRI lesion counts. Dosing is 20 mg subcutaneously; after initial loading doses at weeks 0, 1, and 2, it's given monthly (26). The safety profile showed mostly mild injection-related reactions (local redness, flu-like symptoms) and a risk of infections (e.g. upper respiratory infections) due to B-cell depletion, comparable to other anti-CD20 therapies. Unlike IV therapies, there were no infusion reactions and no requirement for premedication. Ofatumumab's key value is offering highly effective B-cell–mediated suppression of MS disease activity in a convenient at-home injection, lowering barriers to accessing potent therapy (24-26).

Monomethyl fumarate (Bafiertam) gained approval in 2020 as a novel fumarate formulation for relapsing MS. Bafiertam contains the active metabolite of dimethyl fumarate (Tecfidera) (27). It activates the Nrf2 pathway to reduce neuroinflammation and oxidative stress. Bafiertam was approved via demonstration of bioequivalence to dimethyl fumarate, and thus yields similar efficacy in reducing relapses and delaying progression. The advantage is in tolerability: Bafiertam uses a lower starting dose and may cause fewer gastrointestinal side effects (nausea, diarrhea) and vasodilatory effect-flushing, since it delivers the active metabolite directly, potentially reducing GI irritation from intermediate metabolites. The dosing is 95 mg capsules, two twice daily (after a one-week half-dose starter) (28). Side effects mirror Tecfidera overall: flushing, GI upset, decreased lymphocyte counts, and rare serious risks like PML (progressive multifocal leukoencephalopathy) in severely immunosuppressed patients. Bafiertam's introduction provided patients another oral fumarate option, with hopes of improved GI tolerability while maintaining the known benefits of this mechanism (28).

Ublituximab (Briumvi), approved in 2022, is a monoclonal antibody against CD20 for relapsing MS (29). Like ocrelizumab and ofatumumab, ublituximab depletes B-cells, but it is engineered (glycooptimized) to enhance antibody-dependent cytotoxicity (29,30). In the ULTIMATE I & II Phase III trials, ublituximab (given every 6 months IV) was superior to teriflunomide, cutting annual relapses by ~60% (ARR ~0.08 on ublituximab vs 0.19 on teriflunomide) and markedly reducing new MRI lesion formation (31). Notably, over 40% of ublituximab-treated patients had no evidence of disease activity. The dosing begins with an infusion split over day 1 and 15, then one infusion every 24 weeks. Infusion time can be as short as one hour after the first dose, making it a relatively quick administration. Adverse effects include infusion reactions (premedication is used to mitigate these), mild infections (nasopharyngitis, etc.), and laboratory abnormalities like low immunoglobulins with prolonged therapy. Overall safety and efficacy are in line with other B-cell therapies (31,32). Ublituximab's approval gives another high-efficacy option, and its shorter infusion duration and potential for flexible dosing schedules provide practical advantages in MS care.

LIMITATIONS

This comprehensive review has several limitations, including its focus on neurological medications approved specifically between 2020 and 2025, thus excluding earlier foundational treatments and therapies still under investigation. Additionally, regulatory approval status may vary across different regions (e.g., FDA versus EMA), limiting the global applicability of certain treatments. Given the rapidly evolving nature of neurological therapeutics, emerging developments after the preparation of this manuscript might not be included. Furthermore, due to the recent approval of many therapies, particularly gene therapies and biologics, long-term safety and efficacy data remain limited. Lastly, potential publication bias favoring positive trial outcomes may have influenced the overall interpretation

of clinical benefits. Readers should therefore interpret the summarized evidence in light of ongoing research and emerging clinical data.

CONCLUSION

The period from 2020 to 2025 has marked a remarkable advancement in the pharmacological management of neurological diseases, significantly expanding therapeutic options across Alzheimer's disease, Parkinson's disease, and multiple sclerosis. The introduction of novel targeted therapies, including disease-modifying antibodies, innovative small molecules, and optimized biologics, has shifted the therapeutic paradigm toward more precise, mechanism-based interventions.

While antisense oligonucleotides and gene therapies represent promising and rapidly advancing frontiers in neurotherapeutics, they remain emerging research areas and were therefore not discussed in detail in this review. As clinical experience with these modalities grows, future evidence is expected to clarify their long-term safety, efficacy, and applicability across different neurological disorders.

Ongoing research, vigilant post-marketing surveillance, and efforts to ensure equitable access to these innovative treatments will be essential to fully realize their potential and sustain the current momentum toward precision medicine in neurology.

DECLARATIONS

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