Variation in the Coverage of Disease-Modifying Multiple Sclerosis Drugs Among US Payers

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ABSTRACT

Background: In US healthcare, individual payers create their own prescription drug coverage policies. This can lead to differences in how payers cover multiple sclerosis (MS) drugs and can thus affect patients’ access to them.

Objectives: To examine how the largest private payers cover MS drugs relative to their corresponding FDA approvals and to the evidence that payers report reviewing when formulating their policies.

Methods: We identified coverage policies for disease-modifying MS drugs issued by the 10 largest private payers that make their policies publicly accessible. We categorized each policy relative to the drug’s corresponding FDA approval as consistent, more restrictive, less restrictive, or “mixed,” ie, more restrictive than the approval in 1 way, but less restrictive in another. We then categorized the evidence that the payers reported reviewing in their policies into 6 categories: randomized controlled trials (RCTs); other clinical studies (eg, non-RCTs or observational studies); clinical reviews; health technology assessments; clinical guidelines; or cost-effectiveness analyses.

Results: Forty-six percent of coverage policies were more restrictive than the corresponding FDA approval, 38% consistent, 12% less restrictive, and 3% mixed. The payers reported reviewing an average of 1.1 RCTs, 0.4 technology assessments, 0.4 other clinical studies, 1.3 clinical reviews, and 0.8 clinical guidelines per policy. Only 1 payer reported reviewing cost-effectiveness analyses. Payers reported reviewing varying numbers of studies and reviewing differing study types in their coverage policies.

Conclusions: We found variation in how the included payers cover MS drugs and in the evidence that they report reviewing in their coverage policies.


Compared with healthcare systems in other developed countries, the healthcare system in the United States is notably fragmented, with multiple decision makers at the national and local levels.1-3 This fragmentation is apparent in the insurance market, which consists of multiple public payers (including Medicaid, Medicare, the Children’s Health Insurance Program, and the Veterans Health Administration) and private payers. As a consequence, multiple sclerosis (MS) patients across the United States receive their prescription drug insurance coverage from a variety of healthcare payers. Because payers develop their own coverage criteria to guide how their enrolled beneficiaries use drugs and biologics, different patients receiving drug coverage from different payers may have differing access to MS drugs.

We have examined how US payers cover medical technologies in a number of studies. In 1 study, we found variation in how payers cover a variety of interventions, including medications, medical devices, surgeries, and diagnostic imaging and tests.4 In another study, we found variation in how private payers cover rheumatoid arthritis treatments and in the evidence that they reported reviewing in their coverage policies.5 In a separate study, we found inconsistencies in how the largest private payers and Medicare cover medical devices.6 Other researchers have also found variation in how payers cover medical technologies, notably in regard to personalized medicine technologies.7,8

The current study builds on this body of research by examining how the largest US-based private payers cover MS drugs. Our study had 2 objectives. First, we compared how the largest private payers covered disease-modifying drugs relative to their FDA approval. Second, we examined the evidence base that the payers reported reviewing when formulating their coverage policy.

METHODS

We identified the largest US private payers in terms of market share as reported by the National Association of Insurance Commissioners.9 We then searched each payer’s website to determine whether the payer made its coverage policies publicly
We examined the coverage policies issued by 10 of the largest private payers for multiple sclerosis drugs and found variation in how the payers covered the drugs and in the evidence that the payers reported reviewing in their coverage policies.

With respect to drug coverage, payers perform their own assessments and issue their own coverage policies. This may result in differences in how payers cover drugs and may affect patients’ access to care. We compared each coverage policy with the drug’s corresponding FDA approval, accounting for the labeled indication, contraindications, and black box safety warnings. We used an approach similar to what we used to examine coverage policies for rheumatoid arthritis drugs in a previous study. First, we determined whether a drug was covered by the payer. We then categorized payer coverage for MS drugs as more restrictive than the FDA approval (the payer placed conditions on coverage beyond the FDA approval); consistent with the FDA approval; less restrictive than the FDA approval (the payer provided coverage for off-label usage not included in the FDA label); or mixed (the payer’s coverage policy was more restrictive than the FDA label in 1 way, but was less restrictive in another). An example of a mixed coverage policy was Centene’s policy for interferon beta-1a (Rebif). Centene covered interferon beta-1a (Rebif) for patients with clinically isolated syndrome (an initial episode of neurologic symptoms of duration of at least 24 hours caused by demyelination or inflammation) with MRI features consistent with MS, which was an off-label usage, but covered the drug only for patients who had first failed 2 or more alternative drugs, a condition not included in the FDA label.

For coverage policies that we found to be more restrictive than the corresponding FDA approvals, we categorized the restrictions on coverage as step-therapy restrictions (the payer restricted coverage to patients who had first failed an alternative treatment) or patient restrictions (the payer restricted coverage to patients suffering from disease of a particular type or severity).

**Evidence Base the Payers Reported Reviewing**

We reviewed each coverage policy to identify the evidence that the payers cited or discussed reviewing within it. We categorized the evidence into the following 6 categories: randomized controlled trials (RCTs), other clinical studies (eg, nonrandomized controlled trials, prospective cohort studies, and consecutive case series studies), clinical reviews (including systematic reviews of clinical evidence), clinical guidelines, health technology assessments, and cost-effective analyses. We did not account for studies that did not pertain to the drug of interest, eg, epidemiological studies, or studies that were not published in the peer-reviewed literature or promulgated by major clinical societies or health technology assessment agencies. We reported the frequency that the payers reviewed evidence in each category.

**RESULTS**

We identified 93 coverage policies for 12 disease-modifying MS drugs across the 10 payers. The payers on average issued coverage policies for 9.3 drugs. Aetna and Centene were the only payers to issue a coverage policy for all 12 MS therapies; HCSC issued coverage policies for only 2 drugs.
Each payer issued a coverage policy for alemtuzumab and natalizumab; only 2 payers, Aetna and Centene, issued a coverage policy for mitoxantrone.

Coverage Relative to the Drug’s FDA Approval: Findings

Of the 93 cover policies, 42 (45%) were more restrictive than the corresponding FDA approval, 35 (38%) were consistent, 11 (12%) were less restrictive, and 3 (3%) were mixed (FIGURE 1). On 2 occasions the payer did not cover the drug.

Thirty-six of 51 restrictions (71%) were step-therapy restrictions; 15 (29%) were patient restrictions. An example of a step-therapy restriction was in Anthem’s policy for fingolimod, in which patients were first required to fail an interferon beta, glatiramer acetate, or dimethyl fumarate before having access to fingolimod. An example of a patient restriction was in Independence Health Group’s policy for interferon beta-1b (Extavia), in which the payer did not cover the drug for patients who had experienced a first clinical episode and had MRI features consistent with MS, an FDA-approved indication. Six policies included both a step-therapy and patient restriction.

Evidence Base the Payers Reported Reviewing: Findings

Not all payers reported the evidence that they reviewed in each of their policies. Aetna and Anthem reported reviewing the most studies in their coverage policies, for an average of 15.6 and 7.7 pieces of evidence per policy, respectively. Humana and Centene reported reviewing the fewest studies, for an average of 0.3 and 0.4 studies per policy, respectively (FIGURE 2).

Nine payers reported reviewing RCTs; Anthem reviewed the most RCTs (average of 3.5 per policy), while Humana reported reviewing the fewest (average of 0.2 per policy). Six payers reported reviewing studies that fell into the “other clinical studies” category (average of 0.4 per policy); Anthem reported reviewing the most (average of 2.1 per policy), while UnitedHealthcare reported reviewing the fewest (average of 0.2 per policy). Eight payers reported reviewing clinical guidelines (average of 0.8 per policy); Aetna reviewed the most (average of 2.9 per policy), while Highmark, Humana, Blue Cross Blue Shield Michigan, and UnitedHealthcare reported reviewing the fewest (average of 0.1 per policy). Seven payers reported reviewing clinical reviews (average of 1.3 per policy); Aetna reported reviewing the most clinical reviews (average of 6.9 per policy), while Blue Cross Blue Shield Michigan and UnitedHealthcare reported reviewing the fewest (average of 0.1 per policy). Six payers reported reviewing health technology assessments (average of 0.4 per policy); Aetna reported reviewing the most (average of 2.4 per policy), while Blue Cross Blue Shield Michigan, Blue Cross Blue Shield Florida, and UnitedHealthcare reported reviewing the fewest (average of 0.1 per policy). Aetna reported reviewing 2 cost-effectiveness analyses in its coverage policies and was the only payer to report reviewing evidence of this type.

DISCUSSION

The multitude of private insurance companies in US healthcare raises the possibility of differential drug coverage. Our study is the first to examine this potential variation in the coverage of disease-modifying MS drugs among US private insurance companies.

We found that coverage policies were most often more restrictive than the corresponding FDA approval and that the most frequent reason that the coverage policy was more restrictive was due to step-therapy restrictions. These findings are consistent with previous research in which we examined private payer coverage of rheumatoid arthritis treatments.3 We found that how the payers covered the included drugs varied, and that no drug was covered the same way by each of the included payers. For example, 6 payers covered alemtuzumab in a manner that was more restrictive than the FDA approval, 3 payers’ coverage policies were consistent with the FDA approval, and 1 payer issued a coverage policy

![Figure 1. Restrictiveness of Payer Coverage of Disease-Modifying Multiple Sclerosis Drugs Relative to the Corresponding FDA Approval](image-url)
that was less restrictive than the FDA approval. Both payers that issued a coverage policy for mitoxantrone covered the drug more restrictively than the drug’s corresponding FDA approval, but their determinations differed: Aetna covered mitoxantrone for patients with RRMS but not for patients with chronic progressive disease, while Centene required patients with RRMS to first fail 2 or more alternatives before having access to the drug.

**Explanation of Study Findings**

The restrictiveness of the private payer coverage of MS drugs is broadly consistent with other research that has compared payer coverage of drugs and medical devices with their corresponding FDA approval. While the FDA is charged with ensuring that drugs are “safe and effective,” commercial payers assess whether drugs are “medically necessary” when judging coverage. Therefore, while the FDA must rely on evidence of a drug’s safety and efficacy, payers must additionally weigh other factors in their assessment, including benefit-risk trade-offs, the availability of alternatives, costs, and cost-effectiveness.

The variation among private payers’ coverage policies is also consistent with previous research. There are several potential reasons for this variation. It may be that payers use different decision-making criteria when judging drug coverage. Indeed, we found that payers report reviewing a different evidence base in their coverage policies, both in terms of the number of studies reviewed and the types of study reviewed. We found that only 1 payer (Aetna) reviewed evidence that fell into each evidence category. It is likely that some payers more thoroughly report the evidence that they review when formulating their coverage polices than do other payers.

While we found that only Aetna reported reviewing cost-effectiveness analyses in their coverage policies, it is likely that other payers consider economic factors when judging drug coverage. It is also likely that volume-based discounts obtained from product manufacturers affect how plans cover drugs; as this information is proprietary, however, we were unable to account for it in this study.

It may also be that input from customers (eg, large employers) affects drug coverage decisions and contributes to variation among payers. The identified variation could be due to payers tailoring their coverage policies to their own beneficiary populations or offering more generous drug coverage to attract enrollees.

**Implications**

Inconsistency among private payer coverage policies may affect the access patients have to MS drugs in different health plans. Differences among drug coverage policies also complicate care delivery, as physicians treating different patients enrolled in a variety of health plans must tailor treatment to the patients’ insurance. It is argued, however, that the variation in use of drugs resultant from differences among coverage policies may help accelerate our understanding of how best to use drugs.

Drug manufacturers must account for US payers’ evidence requirements when creating clinical development programs for their products. The identified differences in the evidence base that the payers report reviewing point to challenges for manufacturers when attempting to address payers’ evidentiary needs. Greater transparency in how payers use evidence in decision making would allow manufacturers to more readily meet payers’ requirements and potentially speed patients’ access to treatments.

**Limitations**

Not all payers issued publicly accessible coverage policies for each of the included drugs, a finding consistent with previous research. Further, our findings may not be generalizable to payers not included in our study. We do not account for the appeals process that is typically available to beneficiaries if coverage of their preferred drugs is denied.

Not all payers reported the evidence that they reviewed in each coverage policy. As noted above, we could account for only the evidence that payers reported reviewing in their coverage policies. It may be that payers review evidence...
that they do not report reviewing in their coverage policies. It may also be that payers perform their own analyses, eg, use their own data, which they do not report reviewing.

We did not consider symptomatic and reparative therapies in this study, eg, dalfampridine, a drug indicated to improve walking in patients with MS. We also excluded the recently approved daclizumab because it was first approved by the FDA to treat MS after we obtained the coverage policies for this analysis.17

Researchers in various countries have examined the influence of evidence and other factors in payer coverage of drugs and other medical technologies.18–22 However, in this study, the sample size was insufficient to facilitate an empirical evaluation of the relationship between coverage and the evidence the payers reported reviewing.

CONCLUSIONS
Our data illustrate variation in how payers in our sample cover disease-modifying MS drugs and suggest that patients enrolled in different health plans may have differential access to these drugs. We found that the evidence that payers reported reviewing in their coverage policies varied in terms of volume and composition. Uncertainty in payers’ evidence requirements makes it challenging for manufacturers to design clinical programs to support their products because the generated evidence may not be sufficient for all payers.

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REFERENCES