Treatment Patterns and Antipsychotic Medication Adherence Among Commercially Insured Patients With Schizoaffective Disorder in the United States

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Abstract: This study assessed real-world treatment patterns and antipsychotic (AP) medication adherence among commercially insured US patients with schizoaffective disorder (SCA). Continuously insured adults aged 18 years or older with a diagnosis of SCA from January 1, 2009, to December 31, 2012, were identified from the Clininformatics Data Mart database. Patients were categorized into 2 cohorts: incident or prevalent SCA. Demographics and clinical characteristics were evaluated during the baseline period. Use of psychiatric medications and adherence to AP medications were evaluated during a 12-month follow-up period after index diagnosis of SCA. Of the overall study population (N = 2713; mean age, 40.2 y; 52.7% female), 1961 patients (72.3%) (mean age, 38.7 y; 51.3% female) had incident SCA, and 752 patients (27.7%) (mean age, 43.9 y; 56.5% female) had prevalent SCA. Antipsychotics were used by 74.8% of patients in the overall study population during the follow-up period. The most commonly prescribed oral AP was risperidone (23.9%), followed by quetiapine (21.4%) and aripiprazole (20.4%). Use of any long-acting injectable APs in the overall study population during the follow-up period was less than 3%. A total of 49.0% and 38.0% of the overall study population had medication possession ratios and proportion of days covered for APs of 80% or greater, respectively. Overall use of long-acting injectable APs for the treatment of SCA is low, and adherence to AP medications, measured by both medication possession ratio and proportion of days covered, is suboptimal among patients with SCA in the real-world setting.

Key Words: schizoaffective disorder, treatment patterns, antipsychotic medication adherence

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Schizoaffective disorder is a chronic mental disorder with symptoms of both schizophrenia (hallucinations, delusions, distorted thinking) and major mood disorder (depression, mania) and has an estimated lifetime prevalence of 0.3%. The diagnostic criteria for schizoaffective disorder have strengthened over time, particularly in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Patients with schizoaffective disorder have alternating periods of full or partial remission and frequent relapses of psychotic, manic, and depressive symptoms. In addition, they have a high risk for hospitalization, rehospitalization, suicide, and substance abuse. The long-term prognosis of patients with schizoaffective disorder is thought to be similar to or better than that of patients with schizophrenia but similar to or worse than that of those with mood disorders.

The recurring nature of schizoaffective disorder suggests the necessity of long-term treatment. Because no widely accepted guidelines exist, treatment is aimed at reducing or eliminating symptoms and delaying relapse. Consequently, patients often need to maintain complex pharmacological regimens as clinicians attempt to manage symptoms with antipsychotics (APs), either alone or in combination with a mood stabilizer and/or antidepressant. Antipsychotics are considered to be the cornerstone of treatment. However, only extended-release oral paliperidone and once-monthly injectable paliperidone palmitate (PP1M) have been studied in randomized, placebo-controlled trials specifically in patients with schizoaffective disorder. In the two 6-week clinical trials, extended-release paliperidone daily as monotherapy or adjunctive therapy versus placebo significantly improved the Positive and Negative Syndrome Scale total score (primary end point) among patients with schizoaffective disorder. In the 15-month clinical trial, which evaluated the efficacy and safety of PP1M as a monotherapy or an adjunctive therapy versus placebo for the treatment of schizoaffective disorder, PP1M therapy versus placebo was associated with a significant delay in psychotic, depressive, or manic relapses and better functioning.

The complex symptomatology of schizoaffective disorder makes it highly likely that patients will receive substandard management. Polypharmacy is frequent among patients with schizoaffective disorder and increases the potential for discontinuation of medications, drug-drug interactions, side effects, and costs of therapy. A study by Olfson et al of Medicaid-insured patients with schizoaffective disorder (N = 16 570) or schizophrenia (N = 38 760) observed that patients with schizoaffective disorder were significantly more likely to be prescribed with mood stabilizers, anxiolytics, and antidepressants than patients with schizophrenia. There is little other existing literature available regarding the treatment patterns of patients with schizoaffective disorder, especially in the real-world setting. To address this need, this study evaluated real-world treatment patterns among patients diagnosed with schizoaffective disorder who are commercially insured in the United States.

MATERIALS AND METHODS

Study Population

Patients aged 18 years or older with schizoaffective disorder were selected from the Optum Clininformatics Data Mart database if they had 1 or more inpatient diagnoses or 2 or more outpatient diagnoses on 2 separate dates that were 30 days or more apart containing an International Classification of Diseases, Ninth Revision, Clinical Modification code of 295.70, 295.71, 295.72, 295.73, 295.74, or 295.75 between January 1, 2009, and December 31, 2012. Patients with an additional schizophrenia
diagnosis were not excluded from the analysis. Patients were required to have 12 months of continuous medical and prescription benefit coverage prior to (ie, the baseline period) and after (ie, the follow-up period) the date of the diagnosis of schizoaffective disorder (ie, the index event) (Fig. 1). The Clininformatics Data Mart database includes physician- and patient-level transactions for patients with commercial insurance in the United States. In addition to patient demographics, payer type, enrollment information, and medical claims information, the database also includes detailed pharmacy claims data. Furthermore, data are included only for patients with both medical and prescription drug coverage, allowing users to evaluate the complete health care experience of study patients. In compliance with the Health Insurance Portability and Accountability Act of 1996, the database consists of fully de-identified data sets, with synthetic identifiers applied to patient- and provider-level data to protect the identities of the patients and the data contributors. This study is thus exempt from institutional review board approval.

The overall study population of patients with schizoaffective disorder was further stratified into 2 cohorts, one comprising patients with incident schizoaffective disorder and the other comprising patients with prevalent schizoaffective disorder. The index event for both study cohorts was the first diagnosis of schizoaffective disorder during the index identification period. Patients were considered to have incident schizoaffective disorder based on the absence of any diagnoses of schizoaffective disorder during the baseline period, defined as the 12-month period prior to the index event date. Patients were considered to have prevalent schizoaffective disorder based on having a diagnosis of schizoaffective disorder during the baseline period.

Demographics and Clinical Characteristics Evaluated During the Baseline Period

For the overall study population, as well as the incident and prevalent study cohorts, baseline patient demographics and clinical characteristics were determined. These included age, sex, US geographic region of residence, health plan type, Charlson Comorbidity Index (CCI) score, and disease-related comorbidities.

Psychiatric Medication Use Evaluated During the Baseline Period

During the 12-month baseline period, the proportions of patients treated with psychiatric medications were determined. The proportions of patients using the following drug classes were determined: APs, anxiolytics, mood stabilizers/antiepileptics, and antidepressants. Medication usage, which was not mutually exclusive, was also categorized as either long-acting injectable (LAI) or non-LAI, with further breakdown by specific AP medications. The LAIs were PP1M, risperidone, haloperidol decanoate, and fluphenazine decanoate, and the non-LAIs were perphenazine, fluphenazine, paliperidone, olanzapine, risperidone, aripiprazole, clozapine, quetiapine, and haloperidol. In addition, the degree of polypharmacy was determined for psychiatric medications. Polypharmacy was defined by the use of the following combinations of psychiatric medications: APs and mood stabilizers/antiepileptics, APs and antidepressants, APs and anxiolytics, antidepressants and mood stabilizers/antiepileptics, anxiolytics and mood stabilizers/antiepileptics, antidepressants and anxiolytics, and 3 or more drug classes.

Psychiatric Medication Use Evaluated During the Follow-Up Period

During the 12-month follow-up period, the proportion of patients treated with psychiatric medications and the proportion of patients adherent to AP medications were determined, measured by both medication possession ratio (MPR) and proportion of days covered (PDC). In addition, the percentages of patients with an AP MPR of 80% or greater and an AP PDC of 80% or greater were determined. Medication possession ratio was calculated as the total number of days of drug supply divided by the total number of days in the follow-up period. Days of drug supply included any AP medication prescribed during the follow-up period. Proportions of days covered were calculated as the total number of days with AP prescription coverage divided by the total number of days in the follow-up period.

Statistical Analyses

Bivariate descriptive statistics were used to compare demographics, clinical characteristics, use of psychiatric medications, and adherence to AP medications in patients with schizoaffective disorder in incident and prevalent study cohorts. Analysis of variance and χ² tests were used to detect statistically significant differences in continuous and categorical variables, respectively. A critical value of 0.05 was used to determine statistical significance. All statistical analyses were carried out using SAS 9.3 software (SAS Institute Inc, Cary, NC). No adjustment was made for multiplicity.

RESULTS

Demographics and Clinical Characteristics

Table 1 presents the patient demographics and clinical characteristics of the overall study population and of the study cohorts. The overall study population included 2713 patients with schizoaffective disorder (mean age, 40.2 y); 1961 patients (72.3%) had incident schizoaffective disorder and 752 (27.7%) had prevalent schizoaffective disorder. Patients with prevalent schizoaffective disorder versus incident schizoaffective disorder were significantly older (43.9 vs 38.7 y, respectively; P < 0.001), and a greater proportion was female (56.5% vs 51.3%, P = 0.014). Most (~60%) of the patients in the overall study population had a point-of-service type of health plan.

![FIGURE 1. Study periods.](http://www.psychopharmacology.com)
Patients with prevalent schizoaffective disorder versus incident schizoaffective disorder were less likely to have point-of-service health plans (45.2% vs 65.8%) and more likely to have a health plan from a health maintenance organization (34.6% vs 13.8%) \((P < 0.001)\). Compared with those with prevalent schizoaffective disorder, patients with incident schizoaffective disorder...
had a lower mean CCI score (0.72 vs 0.61, \( P = 0.030 \)) but were diagnosed with significantly more psychiatric conditions, including bipolar disorder (\( P = 0.010 \)), anxiety (\( P < 0.001 \)), depression (\( P < 0.001 \)), alcohol abuse (\( P < 0.001 \)), posttraumatic stress disorder (\( P = 0.001 \)), attention-deficit hyperactivity disorder (\( P < 0.001 \)), generalized anxiety disorder (\( P < 0.001 \)), major depressive disorder (\( P < 0.001 \)), and panic disorder (\( P = 0.003 \)).

### Psychiatric Medication Use During the Baseline Period

Among the overall study population, APs were used by 64.4% of the patients, mood stabilizers/antiepileptics were used by 31.6%, anxiolytics were used by 21.9%, and antidepressants were used by 15.5%. Use of LAI APs during the baseline period in the overall study population was less than 2%. The most commonly prescribed oral AP medication during the baseline period was risperidone (20.7%), followed by quetiapine (20.1%) and aripiprazole (18.6%). Less than 4% of the overall study population was treated with oral paliperidone or PP1M. Among the overall study population, the most common treatment regimen consisted of APs and mood stabilizers/antiepileptics (25.6%). Approximately 14% of the overall study population used 3 or more psychiatric medication classes.

### Psychiatric Medication Use During the Follow-Up Period

Among the overall study population, APs were used by 74.8% of the patients, mood stabilizers/antiepileptics were used by 36.8%, anxiolytics were used by 23.2%, and antidepressants by were used 17.9% (Table 2). Antipsychotics were more frequently used among patients with prevalent schizoaffective disorder versus those with incident schizoaffective disorder (80.3% vs 72.7%, \( P < 0.001 \)) (Table 2). Use of LAI APs during the follow-up period in the overall study population was less than 3% (Table 2). Although use of LAI APs was low among both study cohorts, patients with prevalent versus incident schizoaffective disorder had greater use of risperidone and fluphenazine decanoate but no use of PP1M (Table 2). The most commonly prescribed oral AP medication during the follow-up period among the overall study population was risperidone (23.9%), followed by quetiapine (21.4%) and aripiprazole (20.4%) (Table 2). Less than 5% of the overall study population was treated with oral paliperidone or PP1M (Table 2). Among the overall study population, the most common treatment regimen consisted of APs and mood stabilizers/antiepileptics (31.7%) (Table 3). Approximately 18% of the overall study population used 3 or more psychiatric medication classes. In comparison with patients with prevalent schizoaffective disorder, those with incident schizoaffective disorder were more frequently using combinations of antidepressants and mood stabilizers/antiepileptics (9.3% vs 6.8%, \( P = 0.038 \)) and anxiolytics and mood stabilizers/antiepileptics (13.2% vs 10.2%, \( P = 0.036 \)) (Table 3).

### AP Medication Adherence During the Follow-Up Period

A total of 49.0% of the overall study population with schizoaffective disorder who were treated with APs had an MPR of 80% or greater for APs, with a greater proportion of patients with an MPR of 80% or greater in the prevalent schizoaffective disorder cohort versus the incident schizoaffective disorder cohort (Table 3). In comparison with patients with prevalent schizoaffective disorder, those with incident schizoaffective disorder were more frequently using combinations of antidepressants and mood stabilizers/antiepileptics (9.3% vs 6.8%, \( P = 0.038 \)) and anxiolytics and mood stabilizers/antiepileptics (13.2% vs 10.2%, \( P = 0.036 \)) (Table 3).

### TABLE 2. Use of Psychiatric Medications by Drug Class and AP Use During the Follow-Up Period of the Overall Study Population With Schizoaffective Disorder and Study Cohorts With Incident and Prevalent Schizoaffective Disorders

| Drug class                  | All          | Incident Schizoaffective Disorder | Prevalent Schizoaffective Disorder |
|-----------------------------|--------------|-----------------------------------|-----------------------------------|
|                             | \( N = 2713 \) | \( n = 1961 \)                     | \( n = 752 \)                     |
| APs                         | 2030 (74.8)  | 1426 (72.7)                       | 604 (80.3)                       |
| Anxiolytics                 | 629 (23.2)   | 483 (24.6)                        | 146 (19.4)                       |
| Mood stabilizers/antiepileptics | 998 (36.8) | 741 (37.8)                        | 257 (34.2)                       |
| Antidepressants             | 485 (17.9)   | 356 (18.2)                        | 129 (17.2)                       |
| LAI AP                      |              |                                   |                                   |
| Paliperidone palmate        | 11 (0.4)     | 11 (0.6)                          | 0 (0.0)                          |
| Risperidone                 | 34 (1.3)     | 17 (0.9)                          | 17 (2.3)                         |
| Haloperidol decanoate       | 11 (0.4)     | 9 (0.5)                           | 2 (0.3)                          |
| Fluphenazine decanoate      | 10 (0.4)     | 2 (0.1)                           | 8 (1.1)                          |
| Non-LAI AP                  |              |                                   |                                   |
| Perphenazine                | 76 (2.8)     | 51 (2.6)                          | 25 (3.3)                         |
| Fluphenazine                | 58 (2.1)     | 43 (2.2)                          | 15 (2.0)                         |
| Paliperidone                | 120 (4.4)    | 84 (4.5)                          | 36 (4.8)                         |
| Olanzapine                  | 454 (16.7)   | 336 (17.1)                        | 118 (15.7)                       |
| Risperidone                 | 648 (23.9)   | 485 (24.7)                        | 163 (21.7)                       |
| Aripiprazole                | 553 (20.4)   | 404 (20.6)                        | 149 (19.8)                       |
| Clozapine                   | 156 (5.8)    | 84 (4.3)                          | 72 (9.6)                         |
| Quetiapine                  | 581 (21.4)   | 432 (22.0)                        | 149 (19.8)                       |
| Haloperidol                 | 199 (7.3)    | 155 (7.9)                         | 44 (5.9)                         |

\(*P values are for the comparison of the incident schizoaffective disorder and prevalent schizoaffective disorder study cohorts.*

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TABLE 3. Frequency of Polypharmacy During the Follow-Up Period of the Overall Study Population With Schizoaffective Disorder and Study Cohorts With Incident and Prevalent Schizoaffective Disorders

| Polypharmacy                                                                 | All N = 2713 | Incident Schizoaffective Disorder n = 1961 | Prevalent Schizoaffective Disorder n = 752 | P*          |
|------------------------------------------------------------------------------|--------------|------------------------------------------|-------------------------------------------|-------------|
| APs and mood stabilizers/antiepileptics                                     | 861 31.7     | 627 32.0                                 | 234 31.1                                  | 0.668       |
| APs and antidepressants                                                    | 418 15.4     | 301 15.4                                 | 117 15.6                                  | 0.893       |
| APs and anxiolytics                                                        | 544 20.1     | 408 20.8                                 | 136 18.1                                  | 0.113       |
| Antidepressants and mood stabilizers/antiepileptics                        | 233 8.6      | 182 9.3                                  | 51 6.8                                    | 0.038       |
| Anxiolytics and mood stabilizers/antiepileptics                            | 336 12.4     | 259 13.2                                 | 77 10.2                                   | 0.036       |
| Antidepressants and anxiolytics                                             | 169 6.2      | 130 6.6                                  | 39 5.2                                    | 0.164       |
| Use of ≥3 drug classes                                                     | 494 18.2     | 372 19.0                                 | 122 16.2                                  | 0.097       |

*P values are for the comparison of the incident schizoaffective disorder and prevalent schizoaffective disorder study cohorts.

DISCUSSION

This national large-scale claims study identified 1961 patients with incident schizoaffective disorder and 752 patients with prevalent schizoaffective disorder. Prevalent patients tended to be older and have greater comorbidities, as measured by CCI score, partially reflecting that these patients had been diagnosed with schizoaffective disorder already and would be expected to have a greater mean age than the incident population. The results of this study showed that, in the commercially insured study population of patients with schizoaffective disorder, approximately 75% were treated with APs; however, less than 50% of patients treated with APs were adherent to AP medications as measured by MPR and PDC, with greater proportions of patients with an MPR of 80% or greater and a PDC of 80% or greater in the prevalent schizoaffective disorder cohort versus the incident schizoaffective disorder cohort. In addition, among the study population many patients were frequently treated with multiple psychiatric medications, with an AP and a mood stabilizer/antiepileptic being the most frequent combination. A higher prevalence of anxiety, depression, and other disease-related comorbidities was observed among patients with incident versus prevalent schizoaffective disorder, which was reflected in their greater use of combinations of antidepressants and mood stabilizers/antiepileptics and of anxiolytics and mood stabilizers/antiepileptics. Importantly, we also observed that, although existing evidence suggests that LAI AP treatments may help increase medication adherence and improve patient outcomes,12-14 their use is remarkably low (<3%) among commercially insured patients with schizoaffective disorder.

Although the prevalence of schizoaffective disorder seems lower than that of schizophrenia, a US National Hospital Discharge Survey in 2005 reported that a slightly greater number of hospital-discharged patients had schizoaffective disorder than had schizophrenia.15-16 An older study conducted by Svarstad et al16 reported a hospitalization rate of 23% for patients with schizoaffective disorder in a 12-month period from 1989 to 1990. In addition, Svarstad et al16 found that patients with schizophrenia or schizoaffective disorder who used medications (eg, APs, lithium, antidepressants) irregularly were nearly twice as likely to be rehospitalized and had 12% higher inpatient costs than patients who used their medication regularly. A more recent study by Karve et al17 of 1193 hospitalized patients with a primary diagnosis of schizoaffective disorder reported that, in the first 60 days after relapse, approximately 11% of patients had 1 or more...
disease-related inpatient stay. Furthermore, in this study, medication adherence was lowest in the first 60 days after the inpatient stay for relapse. Two studies have reported that patients with schizoaffective disorder are more likely than patients with schizophrenia to be rehospitalized. Few studies have been published in the last decade that have examined the medication adherence and/or hospitalization rates specifically of patients with schizoaffective disorder. Based on the results of our study, we found that nonadherence to AP medications is widespread among commercially insured patients with schizoaffective disorder. Therefore, it will be important to study the impact of newer AP medications, including LAIs, on medication adherence, the prevention of relapses, and the functioning of patients with schizoaffective disorder in the real-world setting.

Relapses, in the context of schizophrenia, are personally debilitating and have large societal and economic burdens, with the average cost of first episodes reported at $38,672 (2014 cost level). In the long-term PP1M versus placebo relapse-prevention study, patients with schizoaffective disorder treated with PP1M had a lower risk of relapse, and PP1M was effective as a monotherapy and as an adjunctive therapy with mood stabilizers, antidepressants, and other mental health–related medications. Using an economic model based on the clinical trial event rates observed in the long-term PP1M versus placebo relapse-prevention study, it was estimated that total mean annual medical costs were $7,140 lower for patients with schizoaffective disorder who are treated with PP1M versus placebo. The reductions in annual medical costs in patients treated with PP1M versus placebo were largely attributed to reduced risk of relapse. There are no other randomized clinical trials that have specifically evaluated the efficacy and safety of other APs for the treatment of schizoaffective disorder. Although LAI risperidone was shown to be effective for improving functional recovery, as measured with the Social and Occupational Functioning Assessment Scale and 2 other quality-of-life measures, within a study population composed of patients with schizophrenia or schizoaffective disorder, other studies have shown that, in the context of schizophrenia, LAI AP treatments may help increase medication adherence, improve patient outcomes, and reduce health care costs. Further study in the real-world setting is warranted.

A large study of AP drug utilization across multiple health care systems revealed that approximately one fifth of patients with schizophrenia and other psychiatric disorders received AP polypharmacy. These data are similar to ours in that approximately 18% of patients with schizoaffective disorder received 3 or more drug classes of psychiatric medications. There is limited evidence, however, that AP polypharmacy is efficacious for the treatment of psychotic disorders. A review of the literature conducted by Lochmann van Bennekom et al reported that AP polypharmacy is associated with increased mortality, metabolic syndrome, decreased cognitive function, nonadherence, and increased health care costs among patients with psychiatric disorders. A second review found that AP polypharmacy is also associated with increased global side effect burden, including parkinsonian side effects, anticholinergic use, sexual dysfunction, and diabetes. Patients with schizoaffective disorder and other psychotic disorders are also frequently treated with multiple disease-related medications, but the Olsson et al study observed that the use of complex pharmacologic regimens was more prominent among patients with schizoaffective disorder than among patients with schizophrenia. Because of the complexity of schizoaffective disorder, patients with the disease may represent a population in which strategies to simplify treatment may improve patient medication adherence, clinical outcomes, and health care costs; however, more studies are warranted, especially in the real-world setting.

Strengths and Limitations

A critical limitation of this study is that only commercially insured patients with schizoaffective disorder were included in the study population. Therefore, the findings may not generalize well to patients with schizoaffective disorder insured by other types of coverage, such as Medicaid. In addition, our study population only included patients with continuous health care and prescription coverage, so treatment patterns and medication adherence are likely to differ among patients with schizoaffective disorder who do not receive continuous care for reasons such as intermittent insurance coverage. Although we consider these as limitations of our study on the generalizability of the findings, we also consider them as strengths because little information exists on the treatment patterns and medication adherence of commercially insured patients with schizoaffective disorder. The diagnosis/coding of schizoaffective disorder is based on clinical judgment and not on rating scales or criteria that may be used in other clinical research studies. In addition, our study used MPR and PDC as surrogate measurements of medication adherence and that the collection of a prescription does not necessarily mean that it was taken as prescribed. Thus, nonadherence rates may have been underestimated in this study. However, the use of different medication adherence measurements did show similar trends among patient groups and also shows the variation in adherence rates when measured with 2 different approaches. Paliperidone palmitate once-monthly received US Food and Drug Administration approval in 2009 for the treatment of schizophrenia and in 2014 for the treatment of schizoaffective disorder. Thus, overall use of PP1M may have been limited in 2009. Another potential limitation is that the Clinformatics Data Mart database consists of claims submitted by health care providers to insurance companies for reimbursement on behalf of individuals, and such claims are subject to possible coding errors or coding for the purpose of ruling out the disease rather than coding for the actual disease itself. In addition, all diagnoses may not have been coded by the health care provider. Finally, because the Clinformatics Data Mart database is based on a large convenience sample and is not random, it may contain biases or fail to generalize well to other patient populations of schizoaffective disorder.

CONCLUSIONS

Based on the results of this national large-scale claims study, we determined that most patients with schizoaffective disorder are treated with AP medications, but less than half who are treated with APs adhere to treatment, as measured by MPR and PDC. Furthermore, among this commercially insured population, many patients are treated with multiple psychiatric medication classes. Long-acting injectable AP treatments may potentially help increase medication adherence and improve patient outcomes among patients with schizoaffective disorder.

AUTHOR DISCLOSURE INFORMATION

Krusi Joshi, Dong-Jing Fu, and Erik Muser are employees of Janssen Scientific Affairs and are Johnson & Johnson stockholders. Jay Lin and Melissa Lingohr-Smith are employees of Novasys Scientific Affairs in connection with the conduct of this study and the development of this manuscript.

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