Current PSYCHIATRY

‘I’m sober, Doctor, really’: Best biomarkers for underreported alcohol use

When and how to use highly specific combinations to assess withdrawal risk

Hospitalized patients who are not truthful about their alcohol consumption may be at risk for an unplanned withdrawal. Self-reports of alcohol use—such as CAGE and the Alcohol Use Disorders Identification Test (AUDIT)—are valid, inexpensive, and noninvasive, but patients easily can feign results.[1] Biochemical measures are more objective, and combinations of markers are an effective tool to detect recent heavy drinking in the 10% to 25% of patients who underreport alcohol use.[2]

Biochemical measures can detect acute alcohol intoxication and recent prolonged drinking. Because marker levels return to normal after long-term abstinence, ongoing monitoring can help detect a relapse before a patient admits to it.[3]

This article presents 3 cases in which biochemical markers helped prevent alcohol withdrawal in patients who denied alcohol abuse. We discuss why we ordered biochemical tests and which combinations provided highly sensitive results.

CASE 1

Depression and substance abuse

Ms. C, age 39, presents with bleeding gums due to excessive warfarin, which she takes prophylactically for a history of deep vein thrombosis. She is seen by the psychiatric consultation service for depression—which she says she has experienced since “the day I was born”—and substance abuse that includes a history binge drinking. Ms. C says she has stopped drinking and remained abstinent for the past year because she is fearful of further damaging her kidneys.

BLAIR KELLY FOR CURRENT PSYCHIATRY

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Alcohol use

She also denies psychosis. She does not have a history or symptoms of hepatobiliary or hematologic disease.

Challenge. Despite Ms. C's self-reported 1 year of sobriety, her history of binge drinking and depression calls for evaluating her alcohol withdrawal risk. Laboratory markers of alcohol abuse are the only means to assess her recent drinking behavior.

Discussion. Lab results include serum albumin of 3.4 g/dL, total bilirubin of 0.3 mg/dL, total protein of 6.3 g/dL, aspartate aminotransferase (AST) of 13 U/L, alanine aminotransferase (ALT) of 19 U/L, alkaline phosphatase of 136 U/L, and blood ammonia level of 37 µg/dL. Gamma-glutamyl transferase (GGT) is elevated at 104 U/L (normal range for women: 0 to 45 U/L). Mean corpuscular volume (MCV) is elevated at 101 fL (normal range 80 to 100 fL).

The combination of elevated MCV and GGT has a 95% sensitivity for alcohol abuse.[4] GGT levels become elevated after 24 hours to 2 weeks of heavy alcohol consumption and return to normal within 2 to 6 weeks of abstinence, which allows them to detect binge drinking. MCV takes 6 to 8 weeks of heavy drinking—we which we define as consuming ≥40 grams of alcohol/day[5]—to become elevated and returns to normal within 3 months of abstinence.

These data provide evidence that Ms. C recently consumed substantial amounts of alcohol. As a result, we start her on alcohol withdrawal precautions (AWP).

Clinical Point

Because biomarker levels return to normal after abstinence, ongoing monitoring can help detect relapse

Markers of alcohol abuse

Biochemical markers commonly used to detect alcohol abuse (***Table 1, page 19***) include:

- blood alcohol level (BAL)
- MCV
- liver function tests (LFTs) such as ALT, AST, and GGT
- carbohydrate deficient transferrin (CDT).

BAL can document acute alcohol intoxication, but its use is limited because alcohol has a 4-hour half-life and an elimination rate of 7 grams/hour—equivalent to 1 drink/hour.[6] (A "drink" typically is defined as a 12-ounce bottle of beer or wine cooler, a 5-ounce glass of wine, or 1.5 ounces of 80-proof distilled spirits.) Therefore, BAL will identify as false negatives alcohol-dependent patients who abstain from alcohol within 24 hours of testing.

MCV is an index of the average volume of erythrocytes. Macrocytosis occurs when the volume exceeds 100 fL. Elevated MCV is the most typical morphologic abnormality associated with excessive alcohol consumption[7,8] and macrocytosis—sometimes without associated anemia—is often evident in persons with alcoholism. MCV elevates after 6 weeks of alcohol misuse and may remain elevated for up to 3 months after a person has stopped drinking.[9]

Because patients with disorders unrelated to alcohol use can have elevated MCV, alone it is not a useful screening marker for alcohol abuse.[10] Additionally, because macrocytosis can persist under strictly controlled alcohol abstinence, MCV is not a reliable clinical indicator of relapse.[11]

LFTs measure enzymes and proteins. ALT, AST, and GGT are the most relevant for detecting heavy drinking. An AST:ALT ratio >2:1 supports a suspicion of alcohol abuse.[12] More than 90% of patients with an AST:ALT ratio of 2:1 have alcoholic liver disease. This increases to more than 96% if the ratio is 3:1.[13]

GGT is an enzyme concentrated in the liver, bile ducts, and kidneys; normal range is 0 to 45 U/L (for females) or 53 U/L (for males).[14] GGT levels >30 U/L correlate with alcohol consumption of >4 drinks per day.[15] GGT has a half-life of 14 to 26 days and remains elevated for 4 to 6 weeks after drinking cessation, which make it useful for monitoring abstinence in treatment programs.[16] Sensitivity ranges from 37% to 85% and specificity is as high as 93% in

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Interpreting liver function tests
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Table 1

By the numbers: Biomarkers of excessive alcohol consumption

	Biomarker				
	CDT	GGT	AST	ALT	MCV
Blood test normal range	<60 mg/L	Women: 0 to 45 U/L Men: 0 to 53 U/L	10 to 34 U/L	8 to 37 U/L	80 to 100 fL
Blood test abnormal range	>1.3% of total transferrin concentration	Women: >45 U/L Men: >53 U/L	Levels rarely exceed 500 U/L	Levels rarely exceed 300 U/L	>100 fL
Time to elevation	2 to 3 weeks	24 hours to 2 weeks	3 to 7 days	3 to 7 days	After 6 weeks
Time to descent to normal levels	2 to 4 weeks of abstinence	2 to 6 weeks of abstinence	Half-life 12 to 24 hours	Half-life 37 to 57 hours	3 months
Dose-response of alcohol	60 g/d	80 to 200 g/d	≥40 g/d	≥40 g/d	≥40 g/d
Sensitivity	55% to 90%[a-e]	37% to 85%[b,f,g]	AST:ALT ratio >2:1 has a 70% sensitivity and 92% to 100% specificity for alcoholic-induced liver disease[h-j]		20% to 70%[b,k]
Relapse sensitivity	55% to 76%[a,l,m]	50%[a,e]			20%[a,n]
Specificity	92% to 97%[a,b]	18% to 93%[a,b,e]			64% to 66%[b,k,n]
Positive predictive value	46% to 75%[c,g]	41%[g]			36%[g]
Negative predictive value	72% to 98%[a,c,g]	69% to 92%[a,e,g]			67%[g]

AST: aspartate aminotransferase; ALT: alanine aminotransferase; CDT: carbohydrate deficient transferrin; GGT: gamma-glutamyl transferase; MCV: mean corpuscular volume
Source: For reference citations, see this article on CurrentPsychiatry.com

nonmedical populations.[17] Although non-alcoholic liver disease can elevate GGT in persons who do not abuse alcohol, 50% to 72% of GGT elevations can be explained by excessive alcohol consumption.[18]

CDT is a newer biomarker used to monitor alcohol consumption. The most accurate way to express CDT level is as a percentage of total transferrin concentration. This method accounts for individual variations in transferrin levels, thus minimizing false positives.[18] In persons who consume >4 or 5 drinks per day for 2 weeks or more, CDT is >1.3% of total transferrin.[19] Unfortunately, because it is expensive and requires sophisticated test methodology, CDT testing is not available at most hospitals.[20]

Combinations improve detection

Each biochemical measure has strengths and weaknesses as a marker for determining patients' alcohol consumption (***Table 2, page 20***). CDT and GGT show the highest sensitivity for heavy drinking, and CDT has a higher specificity than GGT (***Table 3, page 21***).[21,22] Relapse to alcohol use after abstinence may be best identified by a simultaneous 30% increase in CDT and GGT.[5]

Because GGT has a longer half-life than CDT, its diagnostic efficiency in detecting alcohol relapse may not develop until 4 weeks after alcohol detoxification, whereas CDT may become clinically useful for detecting relapse as early as 1 week after detoxification.[23]

continued

Clinical Point

Gamma-glutamyl transferase levels >30 U/L reflect alcohol consumption of >4 drinks per day

Alcohol use

Clinical Point

A simultaneous 30% increase in CDT and GGT suggests relapse to alcohol use after abstinence

Table 2

Biomarkers of alcohol use: Strengths and weaknesses

Biomarker	Strengths	Weaknesses
CDT	High specificity for alcohol use; few factors cause false positives High sensitivity in distinguishing alcoholics from social drinkers Marker of relapse and abstinence from drinking Confirmatory test for patients suspected of alcohol abuse	Low sensitivity; more valuable to confirm than exclude heavy drinking Cost (average $30/assay) and low availability of testing Likely less sensitive for women and younger patients compared with men Poor screening tool for alcohol use in general population
GGT	Elevations precede alcohol-induced liver damage High specificity in patients with suspected alcohol abuse Effective marker for patients suspected of binge drinking Inexpensive (<$10)	Can be falsely elevated by liver and biliary disease, smoking, obesity, and medications that induce microsomal enzymes Low sensitivity makes it a poor screening tool in general population Poor marker of relapse
AST:ALT >2:1	Highly sensitive and specific for alcohol-induced liver damage	Enzyme elevations can be detected only after periods of heavy drinking Elevations secondary to liver damage at the hepatocellular level (after fatty changes)
MCV	Accuracy similar in male and female patients Elevations in suspected cases of alcohol use indicate chronicity of drinking Routine laboratory test	Poor biomarker for relapse False positives caused by liver disease, hemolysis, bleeding disorders, anemia, folate deficiency, and medications that reduce folate Low sensitivity and specificity for alcohol use make it a poor screening tool for alcohol abuse

AST: aspartate aminotransferase; ALT: alanine aminotransferase; CDT: carbohydrate deficient transferrin; GGT: gamma-glutamyl transferase; MCV: mean corpuscular volume

There is evidence that combining tests can improve alcohol use detection.[24] For example, Dolman et al[25] found that the ability of the AUDIT questionnaire to correctly predict which patients would experience alcohol withdrawal increases when it is used in combination with biochemical markers. Specifically, the positive predictive value of an AUDIT score ≥8 increased from 17% to 47% when found in combination with ≥2 abnormal biochemical marker levels; the study looked at GGT, ALT, AST, and MCV. Sensitivity was 94% and specificity was 98%.

Similarly, combinations of biochemical markers—especially CDT and GGT—have improved detection of alcohol use and subsequent risk of withdrawal.[26] ***Table 4*** provides a summary of studies that evaluated using combinations of biochemical markers.[4,5,27-31]

Consider patients' comorbidities

Patients at risk for underreporting alcohol use include those with unemployment histories, previous alcohol treatment, and higher scores on the Alcohol Dependence Scale (18.5, SD=8.1).[2] Interpret biochemical testing results in the context of a patient's overall clinical picture.

The following 2 case patients denied or underreported recent alcohol use but we determined they were at high risk for an alcohol disorder because of their medical and/or psychiatric histories. Analysis of biochemical markers helped assess the risk of alcohol withdrawal.

CASE 2

Altered mental status

Family members bring Mr. N, age 44, to the hospital because of his odd behavior. He presents with paranoid delusions and an

Table 3

Interpreting diagnostic test performance

Term	Definition	Applicability
Sensitivity	Percent of persons with disease who test positive	High value is desirable for ruling out disease (low false-negative rate)
Specificity	Percent of persons without disease who test negative	High value is desirable for ruling in disease (low false-positive rate)
Positive predictive value	Percent of positive test results that are true positives	Probability that a person with a positive test result has the disease
Negative predictive value	Percent of negative test results that are true negatives	Probability that a person with a negative test result is disease-free

Source: References 21,22

Table 4

Combining biomarker tests: An effective approach

Combination	Study	Sensitivity*
GGT + MCV	Morgan et al[4]	95%
GGT + CDT	Hietala et al[5] Mundle et al[29] Bell et al[30] Sillanaukee et al[31]	90% 90% 90% 95%
GGT + AST:ALT >2:1	Gluud et al[27] Morgan et al[4]	92% 100%
MCV + AST:ALT >2:1	Kawachi et al[28] Morgan et al[4]	97% 95%
GGT + MCV + AST:ALT >2:1	Morgan et al[4]	100%
GGT + MCV + CDT	Sillanaukee et al[31]	70%

* Sensitivity for detecting excessive alcohol consumption
AST: aspartate aminotransferase; ALT: alanine aminotransferase; CDT: carbohydrate deficient transferrin; GGT: gamma-glutamyl transferase; MCV: mean corpuscular volume

inappropriate elated mood. His medical history includes acquired immune deficiency syndrome (AIDS). After cerebrospinal fluid analysis, computed tomography of the head, electroencephalogram, and metabolic work-up are within normal limits, the patient is diagnosed with human immunodeficiency virus (HIV) mania and is admitted.

On admission, Mr. N denies alcohol use. A blood alcohol/urine toxicity screen is negative. One day after admission, Mr. M develops elevated blood pressure and tachycardia and reports headache and nausea.

Challenge. Gathering a valid history of Mr. N's alcohol use is difficult because of his acutely altered mental status and manic-like state. We use laboratory data to assess his risk of alcohol withdrawal. His liver function tests include an AST of 33 U/L, ALT of 30 U/L, and an alkaline phosphatase of 94 U/L. MCV is normal at 90 fL. Interestingly, the GGT level is elevated almost 4 times normal at 164 U/L.

Discussion. Although Mr. N denied alcohol use and presented with a negative BAL, laboratory data support alcohol dependence. His GGT was elevated well beyond normal limits, without evidence of hepatobiliary disease. GGT has a sensitivity as high as 85%[32] and limited specificity for alcohol abuse. Be-

Clinical Point

Risk factors for underreporting alcohol use include a history of unemployment and previous alcohol treatment

Alcohol use

cause of his high probability of recent alcohol consumption, we place Mr. N on AWP.

We postulate that our patient's autonomic instability, headache, and nausea are related to alcohol withdrawal. We are aware that delirium occurs frequently in patients with HIV infection, and although Mr. N's medical workup is negative, HIV infection can produce an acute encephalopathy that could resemble our patient's clinical picture.[33]

Mr. N's autonomic instability, headache, and nausea abated after treatment for alcohol withdrawal.

CASE 3

Suicide attempt?

Mr. S, age 28, presents to the trauma service with a self-inflicted gunshot wound to the face. He reports feeling depressed for the last year but denies a history of psychotic symptoms or heroin withdrawal symptoms. He also denies recent or past alcohol abuse and does not have a history of biliary tract disease or megaloblastic anemia. His mother tells us Mr. S has had a history of depression since childhood.

Challenge. Based on Mr. S' apparent suicide attempt and history, we feel he is at high risk for alcohol abuse. We use laboratory markers to assess the likelihood of alcohol consumption and possibly decrease his risk of alcohol withdrawal.

Discussion. Mr. S' lab data show an MCV of 91 fL, AST of 95 U/L, alanine ALT of 156 U/L, and alkaline phosphatase of 160 U/L. GGT was elevated at 122 U/L.

Although Mr. S' MCV is within the normal range, his GGT is elevated, and the combination of an elevated GGT and MCV has a 95% sensitivity for the diagnosis of alcohol abuse. We place Mr. S on alcohol withdrawal precautions and discuss with him the potential life-threatening complications of alcohol withdrawal. Confronted with this information and the possible implication of his elevated LFTs, the patient admits his alcohol history—which consists of drinking 12 beers/day for at least the past 2 years. He admits this despite exhibiting no signs or symptoms of alcohol withdrawal.

Clinical Point

Interpret biomarker results in the context of the patient's overall clinical picture

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Bottom Line

Because CDT—the most accurate biomarker—is not available at most hospitals, we recommend using combinations of other measures to detect unreported recent alcohol consumption. If GGT and MCV are elevated, GGT is elevated and AST:ALT is >2:1, or MCV is elevated and AST:ALT is >2:1, consider initiating alcohol withdrawal precautions.

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NSAIDs, Aspirin, and Warfarin)- Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of case-control and cohort design have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. These studies have also shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Altered anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with warfarin. Patients receiving warfarin therapy should be carefully monitored when Pristiq is initiated or discontinued. **Ethanol-** A clinical study has shown that desvenlafaxine does not increase the impairment of mental and motor skills caused by ethanol. However, as with all CNS-active drugs, patients should be advised to avoid alcohol consumption while taking Pristiq. **Potential for Other Drugs to Affect Desvenlafaxine-** Inhibitors of CYP3A4 (ketoconazole)- CYP3A4 is a minor pathway for the metabolism of Pristiq. Concomitant use of Pristiq with potent inhibitors of CYP3A4 may result in higher concentrations of Pristiq. Inhibitors of other CYP enzymes- Based on *in vitro* data, drugs that inhibit CYP isozymes 1A1, 1A2, 2A6, 2D6, 2C8, 2C9, 2C19, and 2E1 are not expected to have significant impact on the pharmacokinetic profile of Pristiq. **Potential for Desvenlafaxine to Affect Other Drugs-** Drugs metabolized by CYP2D6 (desipramine)- *In vitro* studies showed minimal inhibitory effect of desvenlafaxine on CYP2D6. Clinical studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. Concomitant use of desvenlafaxine with a drug metabolized by CYP2D6 can result in higher concentrations of that drug. Drugs metabolized by CYP3A4 (midazolam)- *In vitro*, desvenlafaxine does not inhibit or induce the CYP3A4 isozyme. Concomitant use of Pristiq with a drug metabolized by CYP3A4 can result in lower exposures to that drug. Drugs metabolized by CYP1A2, 2A6, 2C8, 2C9 and 2C19- *In vitro*, desvenlafaxine does not inhibit CYP1A2, 2A6, 2C8, 2C9, and 2C19 isozymes and would not be expected to affect the pharmacokinetics of drugs that are metabolized by these CYP isozymes. **P-glycoprotein Transporter-** *In vitro*, desvenlafaxine is not a substrate or an inhibitor for the P-glycoprotein transporter. The pharmacokinetics of Pristiq are unlikely to be affected by drugs that inhibit the P-glycoprotein transporter, and desvenlafaxine is not likely to affect the pharmacokinetics of drugs that are substrates of the P-glycoprotein transporter. **Electroconvulsive Therapy-**There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy combined with Pristiq treatment. **USE IN SPECIFIC POPULATIONS: Pregnancy-** Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy. Teratogenic effects – Pregnancy Category C- There are no adequate and well-controlled studies of Pristiq in pregnant women. Therefore, Pristiq should be used during pregnancy only if the potential benefits justify the potential risks. Non-teratogenic effects- Neonates exposed to SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), or SSRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome [*see Warnings and Precautions (5.2)*]. When treating a pregnant woman with Pristiq during the third trimester, the physician should carefully consider the potential risks and benefits of treatment [*see Dosage and Administration (2.2)*]. **Labor and Delivery-** The effect of Pristiq on labor and delivery in humans is unknown. Pristiq should be used during labor and delivery only if the potential benefits justify the potential risks. **Nursing Mothers-** Desvenlafaxine (O-desmethylvenlafaxine) is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Pristiq, a decision should be made whether or not to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Only administer Pristiq to breastfeeding women if the expected benefits outweigh any possible risk. **Pediatric Use-** Safety and effectiveness in the pediatric population have not been established [*see Box Warning and Warnings and Precautions (5.1)*]. Anyone considering the use of Pristiq in a child or adolescent must balance the potential risks with the clinical need. **Geriatric Use-**Of the 3,292 patients in clinical studies with Pristiq, 5% were 65 years of age or older. No overall differences in safety or efficacy were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. For elderly patients, possible reduced renal clearance of desvenlafaxine should be considered when determining dose [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Renal Impairment-** In subjects with renal impairment the clearance of Pristiq was decreased. In subjects with severe renal impairment (24-hr CrCl < 30 mL/min) and end-stage renal disease, elimination half-lives were significantly prolonged, increasing exposures to Pristiq; therefore, dosage adjustment is recommended in these patients [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.6) in the full prescribing information*]. **Hepatic Impairment-**The mean $t_{1/2}$ changed from approximately 10 hours in healthy subjects and subjects with mild hepatic impairment to 13 and 14 hours in moderate and severe hepatic impairment, respectively. No adjustment in starting dosage is necessary for patients with hepatic impairment.

OVERDOSAGE: Human Experience with Overdosage- There is limited clinical experience with desvenlafaxine succinate overdosage in humans. In premarketing clinical studies, no cases of fatal acute overdose of desvenlafaxine were reported. The adverse reactions reported within 5 days of an overdose > 600 mg that were possibly related to Pristiq included headache, vomiting, agitation, dizziness, nausea, constipation, diarrhea, dry mouth, paresthesia, and tachycardia. Desvenlafaxine (Pristiq) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of Pristiq) is presented below; the identical information can be found in the *Overdosage* section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of Pristiq) has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdosage include tachycardia, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting. Electrocardiogram changes (e.g., prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, rhabdomyolysis, vertigo, liver necrosis, serotonin syndrome, and death have been reported. Published retrospective studies report that venlafaxine overdosage may be associated with an increased risk of fatal outcomes compared to that observed with SSRI antidepressant products, but lower than that for tricyclic antidepressants. Epidemiological studies have shown that venlafaxine-treated patients have a higher pre-existing burden of suicide risk factors than SSRI-treated patients. The extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdosage, as opposed to some characteristic(s) of venlafaxine-treated patients, is not clear. Prescriptions for Pristiq should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose. **Management of Overdosage-**Treatment should consist of those general measures employed in the management of overdosage with any SSRI/SNRI. Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Gastric lavage with a large-bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Induction of emesis is not recommended. Because of the moderate volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for desvenlafaxine are known. In managing an overdose, consider the possibility of multiple drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the Physicians Desk Reference (PDR®).

This brief summary is based on Pristiq Prescribing Information W10529C002, revised April 2008.

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Related Resources

- National Institute on Alcohol Abuse and Alcoholism Data/Statistical Tables. www.niaaa.nih.gov/Resources/DatabaseResources/QuickFacts.
- Maisto SA, Connors GJ, Allen JP. Contrasting self-report screens for alcohol problems: a review. *Alcohol Clin Exp Res* 1995;19(6):1510-6.
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Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Acknowledgement

The authors acknowledge Daiana Radac, BA, a third-year medical student at Eastern Virginia Medical School, for her contributions to this article.

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