FIXED-RATIO COMBINATION PRODUCTS

Documentation Required

A. FDA approved indications

1. Perphenazine and Amitriptyline (Etrafon, Triavil)
   - Depression with anxiety
   - Psychosis with depression

2. Olanzapine and Fluoxetine (**Symbyax**)
   - Bipolar disorder, depressive
   - Treatment Resistant Depression (MDD in adults who do not respond to 2 separate trials of different antidepressants of adequate dose and duration in the current episode.)

3. Amitriptyline and Chlordiazepoxide (**Limbitrol**)
   - Depression with anxiety, moderate to severe

Documentation Required

B. Minimal documentation

All standard outpatient and inpatient requirements

Documentation Required

C. Maximum dosage – see Table 1 or MDD Medication Summary

Documentation Required

D. Duration

1. For Outpatient: Document rationale when making any drug change.
2. For Inpatient: Document rationale when making more than 3 changes in any 7-day period.

Documentation Required

E. Polypharmacy

For these products, polypharmacy is defined as using >1 agent with the same mechanism of action in relation to each component of the fixed-ration combination product. If polypharmacy is necessary, clearly document the necessity for such a regimen. Documentation regarding failed monotherapy must include specifics such as: dosage, duration of therapy and the clinical response

Documentation Required

F. Drug-Drug Interactions – Refer to www.epocrates.com

Document

G. Black Box Warnings

Assessment of Following:

1. Antidepressants along with antipsychotics with MDD FDA approved indication increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Short –term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior.
2. Antipsychotics-Elderly patients w/ dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.

Documentation Required

H. Standard Laboratory and Examination Requirements

1. For Inpatient: Basic laboratory studies on admission.
2. For Outpatient:
   All other requirements for both the antipsychotic and antidepressant medications specified in these guidelines must be met.
3. More frequent and/or additional monitoring should be considered depending on the clinical situation and whenever there is a change in the patient's status.

Documentation Required

I. Pregnancy and Lactation – Refer to agent specific sections

Attachment: Table 1 FDA-Approved Indications and Maximum Dose

References: Epocrates, Micromedex, Drug specific Prescribing Information

Fixed Ratio Combination Agents

Table 1: FDA-Approved Indications and Maximum Dose

Agent	Brand	Max Daily Dose	FDA-Approved Indications
Amitriptyline and Chlordiazepoxide	**Limbitrol**	100mg/40mg	Depression with anxiety, mod-severe
Amitriptyline and Perphenazine	Etrafon, Triavil	200mg/32mg	• Depression w. anxiety • Psychosis w. depression
Olanzapine and Fluoxetine	**Symbyax**	18mg/75mg	• Bipolar DO, depressive • Treatment resistant depression

References: Epocrates, Micromedex, Prescribing Information