REXULTI (BREXPIPRAZOLE) SNAPSHOT

Brand name: Rexulti
Generic name: Brexpiprazole

Indications: Rexulti (brexpiprazole) is an atypical antipsychotic indicated for treatment of schizophrenia, and as an adjunctive therapy to antidepressant for treatment of major depressive disorder (MDD).

Mechanism of Action: Rexulti (brexpiprazole) has unknown mechanism of action. However, it is assumed to be through a combination of partial agonist activity at serotonin 5-HT1A and dopamine D2 receptors, and antagonist activity at serotonin 5-HT2A receptors. Together, these pharmacological actions at the receptors work to balance their effects in the brain such as reward/arousal (dopamine), and mood/appetite (serotonin).

Pharmacokinetics: **Peak plasma:** 4 hours post-dose; $t_{1/2}$: 91 hours (Rexulti (brexpiprazole)), 86 hours (DM-3411, major metabolite); **Time to Steady State:** 10-12 days; **Absolute oral BA:** 95%; **Plasma Protein Binding:** > 99%; **Metabolism:** CYPs 3A4 and 2D6. **Excretion:** 25% urine, 46% feces and 14% recovered unchanged.

Dosing:

Indication	Starting Dose	Recommended Dose	Maximum Dose
MDD	0.5 – 1 mg/day	2 mg/day	3 mg/day
Moderate to Severe Hepatic Impairment (Child-Pugh score ≥7)			2 mg/day
Moderate, Severe or End-Stage Renal Impairment (CLcr<60 mL/minute)			2 mg/day
Schizophrenia	1 mg/day	2 to 4 mg/day	4 mg/day
Moderate to Severe Hepatic Impairment (Child-Pugh score ≥7):			3 mg/day
Moderate, Severe or End-Stage Renal Impairment (CLcr<60 mL/minute)			3 mg/day

- Rexulti (brexpiprazole) can be taken once daily with or without food.
- CYP2D6 Poor Metabolizers → Decrease dosage by 50%

Dosage adjustment:

CYP2D6 Poor Metabolizers	
CYP2D6 poor metabolizers	Administer half of the usual dose
Known CYP2D6 poor metabolizers taking strong/moderate CYP3A4 inhibitors	Administer a quarter of the usual dose
Patients Taking CYP2D6 Inhibitors and/or CYP3A4 Inhibitors	
Strong CYP2D6 inhibitors * [maybe exempt for patients with MDD taking e.g. paroxetine, fluoxetine]	Administer half of the usual dose
Strong CYP3A4 inhibitors	Administer half of the usual dose
Strong/moderate CYP2D6 inhibitors with strong/moderate CYP3A4 inhibitors	Administer a quarter of the usual dose
Patients Taking CYP3A4 Inducers	
Strong CYP3A4 inducers	Double usual dose over 1 to 2 weeks

Common Adverse effects:

Adverse Effect	Incidence rate in MDD (N=643)	Incidence rate in Schizophrenia (N=852)
Akathisia	9%	6%
Nasopharyngitis	4%	-
Tremor	4%	3%
Weight gain	7%	4%
Extrapyramidal movements	6%	-
Constipation	2%	-
Headache	7%	-
Somnolence	5%	-
Dyspepsia/Diarrhea	-	3%

Place in therapy:

Rexulti (brexpiprazole) is marketed as a successor to Abilify (aripiprazole). However, Abilify (aripiprazole) has more FDA-approved indications for adults and pediatrics than Rexulti (brexpiprazole). Rexulti (brexpiprazole) is claimed to have improved tolerability profile as compared to Abilify (aripiprazole). Package inserts support the claim: 3% of patients (n=643) taking Rexulti (brexpiprazole) versus 6% of patients (n=371) taking Abilify (aripiprazole) discontinued clinical trials due to adverse reactions. Common adverse reactions in Rexulti (brexpiprazole) group were constipation, fatigue and nasopharyngitis while Abilify (aripiprazole) group were akathisia, restlessness, insomnia, constipation, fatigue, and blurred vision. Rexulti (brexpiprazole)'s effectiveness is similar to other second-generation antipsychotics. But Rexulti (brexpiprazole) has lesser incidence of side effects such as weight gain compared to Zyprexa (olanzapine).

Counseling points:

1. Take medication as directed, at about the same time every day.
2. Monitor adverse effects, and the risk of suicidal thoughts.
3. Do NOT take medication if you have hyperglycemia, seizures, hypertension, stroke and low white blood cell count.

References:

1. *Rexulti* [package insert]. Rockville, MD: Otsuka America Pharmaceuticals, Inc; July 2015.
2. Celada P, Puig M, Amargós-bosch M, Adell A, Artigas F. The therapeutic role of 5-HT1A and 5-HT2A receptors in depression. J Psychiatry Neurosci. 2004;29(4):252-65.