

Put Resmetirom in Perspective for NASH Treatment

Resmetirom (*Rezdiffra*) will be the first med approved for treatment of nonalcoholic steatohepatitis (NASH) with fibrosis in adults.

About 5% of adults in the US have NASH...liver fat and inflammation that can progress to fibrosis or scarring and cirrhosis.

You will start to hear NASH called **metabolic dysfunction-associated steatohepatitis (MASH)**...to reflect its link with cardiometabolic risk factors (diabetes, dyslipidemia, obesity, etc).

Until now, we've relied on lifestyle changes, controlling comorbidities, and in some cases pioglitazone or semaglutide.

New Rx resmetirom activates thyroid hormone receptor-beta in the liver...to increase liver fat metabolism and reduce fat buildup.

It's a specialty med...and costs about \$4,000/month.

Using oral resmetirom in patients with MASH with fibrosis for 12 months...plus diet and exercise...leads to MASH resolution (minimal to no inflammation, etc) in about 1 of 6 patients treated versus placebo.

Plus about 1 in 10 patients have fibrosis improvement.

Keep in mind, these outcomes are based on short-term data. It's too soon to say if resmetirom decreases risk of cirrhosis, liver transplant, or death...or has long-term safety risks.

Head-to-head data are lacking...and many trials are ongoing.

For instance, limited evidence shows semaglutide or tirzepatide leads to MASH resolution in about 1 of 3 patients treated versus placebo. But they don't seem to improve fibrosis yet.

Anticipate that specialists will save resmetirom for patients who have MASH with moderate to advanced liver fibrosis despite optimizing diet, exercise, and meds for other comorbidities (diabetes, obesity, etc).

If patients get resmetirom, caution that GI side effects (diarrhea, nausea, etc) may persist for a few months...and to promptly report severe GI pain, which can be a red flag for rare gallbladder problems.

Also educate about possible liver injury and ensure periodic liver function monitoring. Tell patients to report nausea, jaundice, etc.

Expect patients who weigh less than 100 kg to usually get resmetirom 80 mg/day...and those 100 kg or more to get 100 mg/day.

Stay alert for interactions. For instance, recommend limiting resmetirom to 60 mg/day for patients under 100 kg taking a moderate CYP2C8 inhibitor (clopidogrel, etc).

Or if adding resmetirom, advise a max of 20 mg/day of rosuvastatin or simvastatin...or 40 mg/day of pravastatin or atorvastatin...to limit statin side effects (myalgias, etc).

Use our resource, *Drug Interactions: Cytochrome P450 (CYP), P-glycoprotein, and More*, to sort through other resmetirom interactions.

Key References:

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