RUCAM Causality Assessment

Drug: _____ Initial ALT: _____ Initial Alk P: _____ R ratio = [ALT/ULN] ÷ [Alk P/ULN] = _____ ÷ _____ = _____

The R ratio determines whether the injury is hepatocellular (R > 5.0), cholestatic (R < 2.0), or mixed (R = 2.0 – 5.0)

	Hepatocellular Type		Cholestatic or Mixed Type		Assessment
1. Time to onset					
	Initial Treatment	**Subsequent Treatment**	**Initial Treatment**	**Subsequent Treatment**	**Score** (check one only)
o From the beginning of the drug:					
• Suggestive	5 – 90 days	1 – 15 days	5 – 90 days	1 – 90 days	☐ +2
• Compatible	< 5 or > 90 days	> 15 days	< 5 or > 90 days	> 90 days	☐ +1
o From cessation of the drug:					
• Compatible	≤ 15 days	≤ 15 days	≤ 30 days	≤ 30 days	☐ +1
Note: If reaction begins before starting the medication or >15 days after stopping (hepatocellular), or >30 days after stopping (cholestatic), the injury should be considered unrelated and the RUCAM cannot be calculated.					
2. Course	**Change in ALT between peak value and ULN**		**Change in Alk P (or total bilirubin) between peak value and ULN**		**Score** (check one only)
After stopping the drug:					
• Highly suggestive	Decrease ≥ 50% within 8 days		Not applicable		☐ +3
• Suggestive	Decrease ≥ 50% within 30 days		Decrease ≥ 50% within 180 days		☐ +2
• Compatible	Not applicable		Decrease < 50% within 180 days		☐ +1
• Inconclusive	No information or decrease ≥ 50% after 30 days		Persistence or increase or no information		☐ 0
• Against the role of the drug	Decrease < 50% after 30 days **OR** Recurrent increase		Not applicable		☐ -2
o **If the drug is continued:**					
• Inconclusive	All situations		All situations		☐ 0
3. Risk Factors:	**Ethanol**		**Ethanol or Pregnancy (either)**		**Score** (check one for each)
o Alcohol or Pregnancy	Presence Absence		Presence Absence		☐ +1 ☐ 0
o Age	Age of the patient ≥ 55 years Age of the patient < 55 years		Age of the patient ≥ 55 years Age of the patient < 55 years		☐ +1 ☐ 0

4. Concomitant drug(s):	**Score** (check one only)
o None or no information or concomitant drug with incompatible time to onset	☐ 0
o Concomitant drug with suggestive or compatible time to onset	☐ -1
o Concomitant drug known to be hepatoxic with a suggestive time to onset	☐ -2
o Concomitant drug with clear evidence for its role (positive rechallenge or clear link to injury and typical signature)	☐ -3

5. Exclusion of other causes of liver injury:		**Score** (check one only)
Group I (6 causes): o **Acute viral hepatitis** due to **HAV** (IgM anti-HAV), or o **HBV** (HBsAg and/or IgM anti-HBc), or o **HCV** (anti HCV and/or HCV RNA with appropriate clinical history) o **Biliary obstruction** (By imaging) o **Alcoholism** (History of excessive intake and AST/ALT ≥ 2) o **Recent history of hypotension, shock or ischemia** (within 2 weeks of onset) **Group II (2 categories of causes):** o Complications of underlying disease(s) such as autoimmune hepatitis, sepsis, chronic hepatitis B or C, primary biliary cirrhosis or sclerosing cholangitis; or o Clinical features or serologic and virologic tests indicating acute CMV, EBV, or HSV.	o All causes in Group I and II ruled out	☐ +2
	o The 6 causes of Group I ruled out	☐ +1
	o Five or 4 causes of Group I ruled out	☐ 0
	o Less than 4 causes of Group 1 ruled out	☐ -2
	o Non drug cause highly probable	☐ -3

6. Previous information on hepatotoxicity of the drug:	**Score** (check one only)
o Reaction labeled in the product characteristics	☐ +2
o Reaction published but unlabeled	☐ +1
o Reaction unknown	☐ 0

7. Response to readministration:			**Score** (check one only)
o Positive	Doubling of ALT with drug alone	Doubling of Alk P (or bilirubin) with drug alone	☐ +3
o Compatible	Doubling of the ALT with the suspect drug combined with another drug which had been given at the time of onset of the initial injury	Doubling of the Alk P (or bilirubin) with the suspect drug combined with another drug which had been given at the time of onset of the initial injury	☐ +1
o Negative	Increase of ALT but less than ULN with drug alone	Increase of Alk P (or bilirubin) but less than ULN with drug alone	☐ -2
o Not done or not interpretable	Other situations	Other situations	☐ 0
		TOTAL (add the checked figures)	

Abbreviations used: ALT, alanine aminotransferase; Alk P, alkaline phosphatase; ULN, upper limit of the normal range of values
Modified from: Danan G and Benichou C. J Clin Epidemiol 1993; 46: 1323-30.