

Annex 4 - Specific adverse drug reaction follow-up forms

Liver Injury

Targeted Follow-up Checklist for Liver Injury (Jan 2016)

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided.

Event Description:

1. Diagnosis and date of diagnosis_____

2. Did the patient present with any of the following signs or symptoms? Check all that apply:

- ☐ Jaundice ☐ Ascites ☐ Asterixis (flapping tremor)
- ☐ Dark urine ☐ Fever ☐ Altered mental status
- ☐ Pale stool ☐ Fatigue ☐ Abdominal pain (specify location)
- ☐ Pruritus ☐ Bleeding (specify location) ☐ Anorexia
- ☐ Nausea ☐ Spider angiomas ☐ Variceal Bleeding
- ☐ Caput medusae ☐ Peripheral edema ☐ Feter hepaticus
- ☐ Gynecomastia ☐ Muscle wasting ☐ Other (specify)
- ☐ None

3. Were any of the following diagnostic tests performed?

► If yes, please specify the dates and results including reference range and pre- and post- treatment values:

- ☐ Liver function tests
- ☐ Serology & PCR testings for Hepatitis A, B, C &/or E virus
- ☐ Autoantibody tests
- ☐ Abdominal or hepatobiliary ultrasound (with or without Doppler's)
- ☐ Abdominal CT scan
- ☐ Liver biopsy
- ☐ Liver transplant (planned or completed)
- ☐ Other (specify)
- ☐ None

4. Does the patient have a history of any of the following prior to the start of the suspect drug? Check all that apply and include date(s) of onset as well as status (i.e. active/inactive) and details:

- ☐ Previously elevated liver enzymes ☐ Tattoos
- ☐ Hepatitis ☐ Transfusion or blood product administration
- ☐ Other hepatobiliary disease or dysfunction ☐ Gilbert's disease
- ☐ Autoimmune disease (specify type) ☐ Alcohol intake (quantify if possible) ☐ Active or chronic pancreatitis ☐ Drug abuse

- ☐ Diabetes mellitus (Type I or II) ☐ Foreign travel
☐ Non-alcoholic steatohepatitis ☐ Active gall bladder disease
☐ Cirrhosis ☐ Portal hypertension
☐ Ascites ☐ Variceal bleeding/esophageal varices ☐ Spider angiomas ☐ Thrombocytopenia
☐ None ☐ Other (specify)

5. Has the patient recently (i.e. within the past 6 months) taken any of the following? Check all that apply:

- ☐ Sulfonamides ☐ Furosemide ☐ ACE Inhibitors
☐ Valproic acid ☐ NSAIDs (e.g. ibuprofen) ☐ Estrogens (oral contraceptives) ☐ Metronidazole ☐
Acetaminophen/Paracetamol ☐ Amiodarone
☐ COX II inhibitors (e.g. celecoxib) ☐ Tetracycline ☐ Steroids
☐ Thiazide diuretics ☐ 6-Mercaptopurine ☐ Statins
☐ Nicotinic acid ☐ Methotrexate ☐ Other (specify)
☐ None

Targeted Follow-up Checklist for

Pancreatitis and Amylase & Lipase Elevations (version 2, 2016)

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided.

Event Description:

Did the patient present with any of the following signs or symptoms? **Check all that apply:**

- ☐ Upper abdominal pain ☐ Indigestion
☐ Swollen and tender abdomen ☐ Weight loss
☐ Nausea and vomiting ☐ Steatorrhea
☐ Fever ☐ Dehydration
☐ Clammy skin ☐ Diarrhea
☐ Hypotension ☐ Bloating
☐ Jaundice ☐ Radiation of pain to back/flank
☐ Cullen's sign ☐ Tachycardia
☐ Reduced bowel sounds
☐ None of the above

Were any of the following diagnostic tests performed? **Check all that apply and specify including dates and results:**

- ☐ Abdominal ultrasound ☐ None of the above

- ☐ CT scan
- ☐ Amylase and Lipase
- ☐ Abdominal MRI
- ☐ Any additional blood test abnormalities (**specify**):

Relevant medical history (concurrent and pre-existing conditions)***(Please specify medical condition and date of onset)***Did the patient have a history of any of the following prior to the start of the suspect drug? **Check all that apply**

- ☐ Gallstones ☐ Hyperparathyroidism
- ☐ Heavy alcohol use ☐ Hypertriglyceridemia
- ☐ Other gallbladder (biliary disease) ☐ Cystic Fibrosis
- ☐ Pancreatic or common bile duct surgical procedures ☐ Cigarette smoking
- ☐ Traumatic Injury ☐ Viral infections
- ☐ Pancreatic cancer ☐ Other relevant history (*please specify*)
- ☐ Hypercalcemia ☐ Abdominal surgery
- ☐ Endoscopic retrograde cholangiopancreatography (ERCP) ☐ Family history of pancreatitis
- ☐ None of the above

Was the patient taking any of the following drugs? **Check all that apply:**

- ☐ Estrogens ☐ Corticosteroids
- ☐ Thiazide diuretics ☐ Azathioprine

Lactic Acidosis**Galvus/Eucreas targeted follow-up checklist (v1.1, Mar 2017)****Targeted Follow-up Checklist**

Lactic acidosis with vildagliptin/metformin FDC

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided.

Information on daily dose of vildagliptin/metformin FDC:

Medicinal product		Average daily dose (mg/day)	Dose level at last date taken	Time of last dose	Plasma Level (metformin) if done/date	Concentration in erythrocyte (metformin) if done/ date

	Start Date	Last date drug taken					
Vildagliptin/metformin FDC							
Total Metformin (including concomitant additional metformin)							

Event Description

For this adverse event, did the patient present with any of the following signs or symptoms? **Check all that apply**

- | | | | | |
|--|--|---|---|--|
| <input type="checkbox"/> Arrhythmias | <input type="checkbox"/> Hypotension | <input type="checkbox"/> Chest pain | <input type="checkbox"/> Deep rapid breathing | <input type="checkbox"/> Acidotic dyspnea |
| <input type="checkbox"/> Altered mental status | <input type="checkbox"/> Decreased visual acuity | <input type="checkbox"/> Coma | <input type="checkbox"/> Seizure | <input type="checkbox"/> Nausea |
| <input type="checkbox"/> Vomiting | <input type="checkbox"/> Diarrhea | <input type="checkbox"/> Abdominal pain | <input type="checkbox"/> Bone pain | <input type="checkbox"/> Muscle wasting/weakness |
| <input type="checkbox"/> Muscle cramps | <input type="checkbox"/> Asthenia | <input type="checkbox"/> Hypothermia | <input type="checkbox"/> None of the above | <input type="checkbox"/> Other (please specify) |

Diagnostic/Laboratory tests:

Were any of the following diagnostic tests performed for this adverse event? **Check all that apply.**

(Please specify tests, dates, results. For all laboratory results, please specify units)

Name	Values before the event (dd/mm/yyyy)	Unit / Reference Range	Values during the event (dd/mm/yyyy)	Unit / Reference Range	Follow-up measurement (dd/mm/yyyy)	Unit / Reference Range
Blood pH						
Bicarbonate						
Plasma lactate level						
Anion gap						
Urinary ketones						
β-hydroxybutyrate						
[Na ⁺]						
[K ⁺]						
[Cl ⁻]						
[HCO ₃ ⁻]						
eGFR						
Blood creatinine						
Blood BUN						

Relevant medical history (concurrent and pre-existing conditions)

(Please specify medical condition and date of onset)

- | | |
|--|---|
| <input type="checkbox"/> Excessive alcohol use | Further details (e.g. date of onset etc.) |
| <input type="checkbox"/> Exposure to contrast media | |
| <input type="checkbox"/> Infection/sepsis | |
| <input type="checkbox"/> Renal disease | |
| <input type="checkbox"/> Diarrhea/vomiting | |
| <input type="checkbox"/> Dehydration | |
| <input type="checkbox"/> Malnutrition | |
| <input type="checkbox"/> Acute heart failure | |
| <input type="checkbox"/> Acute myocardial infarction | |
| <input type="checkbox"/> Other conditions with hypoxia | |

Concomitant medications

Please list concomitant drugs being taken by the patient at the time of the event

(Please specify drug, indication, dose, route, date and duration)

Drug	Indication	Dose & Route	Date & Duration

Treatment of lactic acidosis

Please list the relevant treatments for the adverse event

(Please specify relevant treatment[s], dates and outcomes)

Treatment	Dates	Outcome

Myopathies including Rhabdomyolysis**Targeted Follow-up Checklist****Myopathies including Rhabdomyolysis (Sep 2015)**

Targeted Follow-up Checklist

Myopathies including Rhabdomyolysis

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided and/or confirmed.

Event Description:

Did the patient present with any of the following signs or symptoms? Check all that apply

- ☐ Muscle tenderness ☐ Walking difficulty ☐ Fatigue
☐ Muscle stiffness ☐ Respiratory difficulty ☐ Acute renal failure
☐ Muscle aching (myalgia) ☐ Dark or red color urine ☐ Disseminated
☐ Muscle weakness ☐ General weakness ☐ Intravascular coagulation
☐ Muscle spasms ☐ Frequent falls ☐ Compartment syndrome
☐ Muscle hypotonicity ☐ Poor balance ☐ Thyroid disorder (hypo/
☐ Muscle hypertonicity ☐ Joint pain ☐ Hyperthyroidism
☐ Muscle swelling ☐ None of the above

Were abnormalities detected in any of the following diagnostic tests? Check all that apply and please specify which test(s), dates and results

- ☐ Electrolyte levels (i.e. hyperkalemia, hypocalcaemia)
- ☐ CPK, myoglobin, aldolase, albumin (hypoalbuminemia)
- ☐ Urinalysis including casts, hemoglobin, myoglobin
- ☐ Renal tests indicating renal insufficiency (Serum creatinine, BUN)
- ☐ Muscle biopsy
- ☐ None of the above

Patient History:

Had the patient been exposed to hazardous toxins in the past? ☐ Yes (please describe) ☐ No ☐ Unknown

Does the patient have evidence of any of the following? Check all that apply

- ☐ Metabolic or genetic disorders (e.g. disorders of muscle carbohydrate metabolism, carnitine palmitoyltransferase deficiency)
- ☐ Exertional rhabdomyolysis
- ☐ Crush injury or trauma
- ☐ Alcoholism or alcohol abuse (please specify)
- ☐ Hypothermia
- ☐ Drug or substance abuse (please specify)
- ☐ Malignant hyperthermia
- ☐ Electrical injuries
- ☐ Neuroleptic malignant syndrome
- ☐ Viral infection (e.g. EBV, CMV, HIV, Herpes virus)
- ☐ Hyperthermia
- ☐ Endocrine abnormality (e.g. diabetic ketoacidosis)
- ☐ Bacterial infection
- ☐ Seizures/Epilepsy
- ☐ Genetic abnormality (e.g. hereditary metabolic abnormality)
- ☐ Arterial thrombosis
- ☐ Snake or insect envenomation (please specify)
- ☐ None of the above

Has the patient recently taken any of the following? Check all that apply

- ☐ HMG-CoA reductase inhibitors (statins)
- ☐ Nucleoside reverse transcriptase inhibitors (NRTIs)
- ☐ Gemfibrozil
- ☐ Corticosteroids
- ☐ Niacin
- ☐ Injection of iron-dextran
- ☐ Cyclosporine
- ☐ Erythromycin
- ☐ Itraconazole
- ☐ Neuroleptics (phenothiazines)
- ☐ MAOIs (esp. in combination with SSRIs, lithium, tri-cyclic antidepressants)
- ☐ SSRIs/SNRIs
- ☐ Colchicine
- ☐ D-penicillamine
- ☐ Chloroquine
- ☐ Hydroxychloroquine
- ☐ None of the above

Was there any evidence of drug-drug-interactions leading up to this event?

- ☐ Yes (please specify, including medications) ☐ No ☐ Unknown