The Prescriber's Guide

for

Cidofovir Exposure Registry

Sponsor

Emcure Pharma UK Ltd.

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1. Pre-Enrolment Activities

1.1 Training on the Cidofovir Exposure Registry documents

- Before initiating the enrolment process, you should go through the Cidofovir Exposure Registry Protocol. This will help you understand the essentials of Cidofovir Exposure Registry like rationale and objectives, overall design, methodology, eligibility criteria for patients and protection of their confidentiality and privacy.
- As this Cidofovir Exposure Registry requires recording of medical information in Web based Electronic Data Capture (EDC) system, you are requested to familiarise yourself in advance with the electronic forms (The Baseline Data Form and The Follow-up Data Form) available at the following URL: http://www.cidofovir.eu
- The training on the key aspects of the Cidofovir Exposure Registry may also be provided to you and your study staff by the Cidofovir Exposure Registry representative, if required.

1.2 Identifying patients

- All patients who receive or are exposed to cidofovir are eligible for enrolment in the Cidofovir Exposure Registry.
- There is no fixed limit to the number of patients you can enrol in this Cidofovir Exposure Registry. You can enrol as many patients who are eligible for this Cidofovir Exposure Registry.

Eligibility criteria for patient enrolment

1.3 Informed Consent Document

- As soon you identify a patient requiring cidofovir treatment you are requested to inform the patient regarding this Cidofovir Exposure Registry and offer him/her the informed consent document

(ICD). The ICD consists of the Patient Information Sheet and Informed Consent Form (ICF).

- You or your study staff may offer help to the patient (or a family member or guardian who is legally responsible for the patient) to understand the ICD and any other relevant information regarding the Cidofovir Exposure Registry. Any questions that the patient may have regarding his participation should be answered to his/her satisfaction.

Information to be captured in ICD

- If the patient (or his/her legal representative) agrees to participate in the Cidofovir Exposure Registry, the patient is requested to sign every page of the ICD.
- The original signed ICD should be maintained along with the other medical records.
- The subject should receive a copy of the signed ICD.

1.4 Eligibility Criteria

- After completion of Informed consent process, please check the eligibility criteria of the patient as follows:
  - ✓ Whether the patient is or has been prescribed Emcure's Cidofovir;
  - ✓ Whether the patient (or a family member or guardian who is legally responsible for the patient) has signed the ICD.

1.5 Assigning User Name and Password to the patient

- Once you have received the patient's consent and found him/her eligible, you or your designee will create a profile for your patient by logging into EDC system.
- Further, a User Name and Passwordwill be allotted to every patient. This User Name and Password is unique for each patient and will link the two electronic forms ('Baseline Data Form' and the 'Follow-up Form') for the same patient.
- The electronic forms for an individual patient will be accessible anytime through the assigned User Name and Password.

2. Patient Information

Please note that the patient information is the information collected at the time of enrolment. The information collected at enrolment will be captured in the electronic forms i.e. 'Baseline Data Form' and the 'Follow-up Form'.

Although the naming convention of follow-up form is suggestive of capturing data only at follow-up, the design of the forms allow part of the baseline information to be collected in the 'Follow-up Form'.

The baseline data that has to be completedin the electronic forms by you or the study staff at the time of enrolment are listed below:

- Informed Consent and Eligibility (*in Baseline Data Form*):
  - ✓ The date of signing the ICD;
  - ✓ Whether the patient met eligibility criteria;
  - ✓ The date of assessment
- Demographic data (*in Baseline Data Form*): Following patient demographics should be captured:
  - ✓ Date of Birth;
  - ✓ Gender (Male/Female)
- Medical history (*in Follow-up Form*): The patient's past or concurrent medical condition, illness or any surgical procedures should also be recorded at this time point, if considered relevant. The start date and stop date also need to be captured. If the medical condition is ongoing, the stop date should be *not applicable.*
- Treatment details *(in Baseline form):* The following drug and treatment details need to be captured:
  - ✓ Indication: The medical condition for which you are treating the patient with Cidofovir.
  - ✓ Dose (including units): The total dose of Cidofovir given at baseline.

- ✓ Frequency of administration: The dosing regimen should be captured here (for e.g. once weekly for two consecutive weeks followed by once every two weeks)
- ✓ Route of administration: IV, Intraocular, Topical, etc.
- ✓ Duration of treatment: Please essentially capture the start date and stop date of the treatment. If the treatment is ongoing then stop date should be *not applicable*.
- ✓ If you have anything else to notify regarding treatment details, please comment in the remarks section.

- Results of laboratory investigations *(in Follow-up Form):*
  - ✓ Haematology;
  - ✓ Biochemistry (including urea, creatinine, phosphate, uric acid, bicarbonate);
  - ✓ Urine analysis (including glycosuria);
  - ✓ Serology
  - ✓ Others (Specify)
- Concomitant medications (*in Follow-up Form*): Details of medications given to the patient other than Cidofovir at baseline should be captured. The dose along with units, frequency, route of administration, start date and stop date should also be recorded. If the medication is ongoing then stop date should be *not applicable*.

  Prescriber's Sign Off (*in Baseline Data Form and Follow-up Form*): You are required to digitally sign the electronic forms after reviewing and verifying the information obtained from the patient during the baseline visit.

3. Follow-Up Information

The Follow-up data has to be filled only in the electronic 'Follow-up Form' for all subsequent visits as listed below:

- Treatment details: Please record if any changes in treatment regimen were made from the last visit with regards to indication, dose, frequency and route of administration. Subsequently, the final treatment regimen is to be recorded in the form.
  - ✓ Indication: The medical condition for which you are treating the patient with Cidofovir.
  - ✓ Dose (including units): The total dose of Cidofovir given at that particular follow-up visit.
  - ✓ Frequency of administration: The dosing regimen should be captured here (for e.g. once weekly for two consecutive weeks followed by once every two weeks)
  - ✓ Route of administration: IV, Intraocular, Topical, etc.
  - ✓ Duration of treatment: Please essentially capture the start date and stop date of the treatment. If the treatment is ongoing then stop date should be *not applicable*.
  - ✓ If you have anything else to notify regarding treatment details, please comment in the remarks section.
- Results of laboratory investigations*:*
  - ✓ Haematology;
  - ✓ Biochemistry (including urea, creatinine, phosphate, uric acid, bicarbonate);
  - ✓ Urine analysis (including glycosuria);
  - ✓ Serology
  - ✓ Others (Specify)
- Concomitant medications: Details of medications given to the patient along with Cidofovir at follow-up visit should be captured. The dose along with units, frequency, route of administration, start date and stop date should also be recorded. If the medication is ongoing then stop date should be *not applicable*.
- All adverse events that occur during the course of the Cidofovir Exposure Registry will be documented in the follow-up form with special attention to renal events (including nephrotoxicity including Fanconi syndrome and renal failure), carcinogenic events and serious adverse event (SAE) if any.

- However, for any SAE, besides capturing the event in the electronic form, you or your designee should notify the Sponsor as elaborated in the Section "***Communication with Sponsor***".

  Following details should be recorded for any adverse event:

  - ✓ Event term
  - ✓ Start date and stop date
  - ✓ Whether the event was an SAE
  - ✓ Whether any concomitant medication was given
  - ✓ Record the Cidofovir treatment status:
    - Mark '0' if treatment is not stopped
    - Mark '1' if treatment is temporarily interrupted
    - Mark '2' if treatment is permanently withdrawn
  - ✓ Record the adverse event outcome:
    - Mark '0' if resolved
    - Mark '1' if resolved with sequelae
    - Mark '2' if not resolved
  - ✓ Record the relationship of the adverse event to the study Drug:
    - Mark '0' if is definitely
    - Mark '1' if is probably
    - Mark '2' if is possibly
    - Mark '3' if is unlikely
    - Mark '4' if is not related
    - Mark '5' if is not assessable
- Patient's outcome: At the end of each follow up visit, you would need to evaluate the patient for treatment outcome and enter in the Follow-up Form:

- ✓ Treatment discontinued due to adverse event/SAE
- ✓ Underlying illness resolved
- ✓ Treatment regimen complete
- ✓ Death of patient
- ✓ Lost to follow-up
- ✓ Therapy to continue
- ✓ Withdrawal: Please specify the reason for withdrawal
- ✓ Please specify for any other outcomes

Schedule of events

Study Visits	**Baseline Visit**	**Follow- up Visit***
Parameters		
Informed consent and eligibility	**X**	
Inclusion/ Exclusion Criteria	**X**	
Generating unique patient identification number	**X**	
Demography data	**X**	
Cidofovir treatment details**	**X**	**X**
Relevant medical history	**X**	
Concomitant medication	**X**	**X**
Laboratory Investigations	**X**	**X**
Patient's outcome		**X**

***Follow–up visit(s) can be any time after the baseline visit**
****Includes recording of Indication, dose, frequency, route of administration and duration of treatment**

Data collection for centres in Germany

As per the German Medicines Act the prescriber's need to abide by the following to comply with German law. This is applicable to centres in Germany.

- Patients being treated for off-label indication: The ICD, eligibility criteria, demographic data, treatment regimen and indication will be captured as baseline details in the Baseline Data Form. Further, no details are to be recorded in the Follow-up Form for such patients.
- Patients being treated in line with approved label, the baseline data as well as the follow-up data will be recorded in the Baseline Data Form and Follow-up Form.

4. Communication with Sponsor

The Cidofovir Exposure Registry representative (from Emcure) will be coordinating with you and your study staff for any requirements or clarifications during the study.

The Cidofovir Exposure Registry representative may also provide training on the key aspects of the Cidofovir Exposure Registry to you and your study staff during the course of the Cidofovir Exposure Registry, if required.

The Cidofovir Exposure Registry representative will periodically contact you or your designee to ascertain any adverse events and outcome of treatment and adverse events.

Contact detail of Emcure UK: + 44 (0) 1582 434232

4.1 Adverse events reporting

All adverse events that occur after enrolment of the patient in the Cidofovir Exposure Registry through the final follow-up will be documented in the electronic Follow-up Form.

4.2 Expedited reporting of serious adverse events

Please note that all serious adverse events require expedited reporting. *(A serious adverse reaction corresponds to any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.)*

You are requested to notify the Sponsor about any serious adverse event within 24 hours after its appearance, through any available mode of communication e.g. phone, fax etc. A detailed report on the same will be sent by the Sponsor to the Regulatory Authority within 7 working days.

5. Contact details of Sponsor

Telephone number: + 44 (0) 1582 434232

Department: Pharmacovigilance