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Guidance and Tools to Strengthen Pharmacovigilance for Pediatric Medicines with a Focus on New Antiretroviral Treatment Regimens in Resource-Limited Settings

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Introduction

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine/vaccine-related problem.[1]

It is imperative to strengthen national pharmacovigilance (PV) systems to monitor acceptability, tolerability, and adverse drug reactions (ADRs) of new pediatric medicines, including the transition to Dolutegravir (DTG) as both first- and second-line regimens for children and adolescents living with HIV (CALHIV). An ADR is an unwanted or harmful response to a medicine or combination of medicines that is unintended and occurs at doses normally used in humans.[2] Studies reporting antiretroviral (ARV)-associated ADRs in children and adults highlight the need for an active approach to PV to ensure that drugs are not only effective but also safe. ARV-associated ADRs are diverse and can lead to poor tolerance, non-adherence to treatment, negative health outcomes, and the development of HIV-drug resistance. Signs of intolerance — such as vomiting, spitting up, or sleep disturbance — can be identified soon after a child is initiated on or switched to a new drug, while other ADRs can take months to identify. Examples of significant ARV-associated ADRs include immune reconstitution inflammatory syndrome, weight gain, hyperlipidemia, and central nervous system complications (e.g., depression, sleep disturbance, and irritability).

Global guidance and a number of tools for pediatric PV already exist and are available on the World Health Organization (WHO) website,[3] including a Module 10 on Pharmacovigilance in the 2018 *WHO Toolkit for research and development of paediatric antiretroviral drugs and formulations.*[4] There is, however, a need to provide simplified and focused guidance that aims to strengthen the capacity of health care workers (HCWs) and caregivers to actively identify, document and report, and respond to information on ARV-associated ADRs in resource-limited settings.

Goal and Objectives

This package of guidance and tools aims to support active PV of ARVs, especially pediatric DTG (pDTG), with a focus on collecting and responding to short-term data on acceptability, tolerability, and clinically symptomatic ADRs among CALHIV, followed by long-term monitoring for other significant ADRs. ART optimization plans, at both national and facility levels, should include an assessment of the acceptability and tolerability of a newly introduced ARV. Information on assessing ARV tolerance and ADRs should be enhanced in HCW training materials, and relevant elements should be included in caregiver treatment-literacy materials. HCWs play an important role in collecting facility-level PV data that can be collated and analyzed at a program level, with mechanisms to provide feedback to the end user about data trends and data quality. The use of electronic medical records is desirable, but PV practices can be adapted for use with paper-based tools as well.

Target Audience

This guidance is intended to assist national, subnational, and facility-level health care teams, as well as stakeholders engaged in ensuring PV is integrated within efforts to optimize pediatric ARVs. The guidance can be used by national and facility teams to adapt the already-existing PV activities and tools and to sensitize caregivers to signs of ARV intolerance and ADRs. It also can be used by facility staff who assess, report, and manage PV-related activities.

Approach to Active PV for New Pediatric Medicines

Monitoring of ADRs frequently involves a clinical assessment, which incorporates the overall ADR profile of the product, including both symptomatic side effects and asymptomatic laboratory, radiographic, and clinical events. PV typically involves two complementary approaches: (1) the short-term assessment and monitoring of the acceptability and tolerability of ARVs; and (2) the longer-term assessment and monitoring of the wider array of ARV-associated ADRs.

Acceptability is the ability and willingness of the patient to use and the caregiver to administer the medicine as intended. *Tolerability* is the degree to which the new drug is tolerated by the patient. ADRs that are clinically symptomatic and bothersome to the patient are key factors in the assessment of tolerability, compared with ADRs — such as laboratory abnormalities — that may go unnoticed by the patient.

Early recognition and management of ADRs can improve ART adherence and treatment outcomes. ADRs can be classified as short-term or long-term adverse events in relationship to the associated ARV exposure. Short-term ADRs are those that may occur in the immediate post–ARV initiation/transition, and long-term ADRs are those that may occur after the first six months post–ARV initiation/transition. ADR assessment and monitoring should have a tiered approach to accommodate short-term and long-term ADRs. Short-term ADRs associated with ARV drugs may include dizziness and gastrointestinal disorders, as well as cognitive and sleep disorders. Longer-term ADRs may include weight gain, changes in body fat distribution (lipodystrophy), glucose abnormalities, cognitive disorders, and negative effects on bone health.[5]

ADRs also can be graded as mild, moderate, or serious based on clinical or laboratory manifestations. They also can be graded as expected or unexpected. Mild ADRs can be tolerated and rarely lead to discontinuation of treatment, while moderate and serious ADRs typically result in drug/regimen discontinuation or substitution. Recommendations for grading systems are provided in the 2018 WHO resource: *WHO implementation tool for monitoring the toxicity of new antiretroviral and antiviral medicines in HIV and viral hepatitis programmes.*[6]

This guidance applies a two-tiered PV approach, with the first level assessing the acceptability and tolerability (AT) of pediatric ARVs from the perspective of the client/caregiver, and the second level assessing the wider array of ARV-associated ADRs primarily from the perspective of HCWs, with client/caregiver input when appropriate. Program teams should adopt active PV monitoring at the facility level and routine monitoring at the national surveillance level. Routine ADR monitoring, also known as passive PV, is already integrated into the monitoring and evaluation (M&E) of national HIV treatment programs using existing patient-monitoring tools and ART reporting systems. This guidance document differs from and compliments current passive PV systems at the national surveillance level because it encourages active PV monitoring at the facility level to increase identification, management, and reporting of ADRs, including mild ones. The proposed *active* PV is a system in which measures are taken to detect the presence or absence of ADRs through specifically designed tools. Active PV complements routine PV by enabling enhanced monitoring and data capture of ADRs, including their management and outcomes. Active PV can focus on specific ARVs and in a select number of ART sites or, if resources allow, in all ART facilities. ADRs may be detected by interviewing patients, by performing specific targeted investigations, or by screening patient records.

Assessment and Management of Short-Term Acceptability and Tolerability

AT should be assessed soon after a child is transitioned to a new ARV regimen, keeping in mind that changes in caregivers can impact AT over time. For all children initiated on or transitioned to a DTG-based regimen, an AT assessment tool should be administered to the caregiver and/or client *at the first clinical visit* after ART initiation or transition. The same tool should be administered at subsequent visits *until six months post–ART initiation* or *transition*. Ideally, the AT tool should be administered within *one month, two months, three months, and six months post–new ARV introduction*. The tool should include the name of the caregiver, the ARV regimen in use, the dosages of the ARVs, the time of day they are administered, and the weight of the child (to assess if the correct dose is administered). The inclusion of the brand name of the ARVs issued (along with the generic name) should be considered because patients frequently refer to the package name of the drug. It should be noted that changes in the brand of the same ARV products occasionally can cause tolerability issues because components of the medicine that are not drug-specific but relate to things like solubility (i.e. excipients), which may differ between brand. The AT tool should also include a select list of symptoms that may indicate intolerance to the ARVs.

The AT assessment tool also should include the following elements:

- Tolerance of the taste (note that even child-friendly dispersible formulations may have an unpleasant taste or aftertaste)
- Ability to swallow the formulation (solid and/or liquid) as prescribed
- Experience of the pill/dosing burden (such as food/drug or drug/drug co-administration considerations)

Appendix 2 contains a generic AT assessment tool that can be adapted to the context, including the new ARVs introduced. It is titled *New pediatric antiretroviral regimen acceptability and tolerability (AT) assessment tool (Version, February 2023).* The AT assessment tool is also available in Excel format to facilitate its adaptation to a country's context.

The following steps should be taken to introduce and conduct pediatric ARV AT assessments:

1. Adapt the generic AT assessment tool to be used at healthcare facility level, including a reporting tool format. If possible, the tool should be used on a digital platform, such as Open Data Kit (ODK software). The use of an electronic version of this tool is desirable, especially if it can be linked to a central database. With this, the facility and programs will be able to monitor both the utilization of the tool as well as the data collected, and provide appropriate support. Completed forms can be printed and inserted into patient files.

2. Identify facility and other related HCWs and staff to be trained on the use of the AT assessment tool and reporting database. Staff responsible for PV can include, for example, clinicians, pharmacy staff, adherence counselors, and peer counselors. Clear distributions of roles and responsibilities (as data collectors and/or data managers) should be specified. The program may decide to target the use of the AT assessment tool in a few sentinel surveillance sites or roll it out in all main facilities.

3. Map the client flow in the facility jointly with the staff selected for training. The mapping of client flow should include the following points: the ART initiation visit, the ARV transition visit, and ARV follow-up visits within one month, two months, three months, and six months. The mapping will help identify the points in the flow where AT assessments can be done.

4. Train and strengthen the capacity of the selected staff in the use of the AT assessment and reporting tools. The training may be done on or off site. When feasible, it is preferable that the training is carried out in a way that does not interfere with health services. Training should include several opportunities for hands-on practice with completing the AT tool, such as mock AT assessment exercises combined with entering mock AT data into a PV database, as well as a review of the client flow for ART initiation, ARV transition, and ART follow-up visits. Based on the results of the AT assessment of each client, HCWs should assess the severity of the challenges reported and whether they require counseling and assurance or medical intervention. Training should emphasize the critical importance of weighing a child at every clinic or follow up visit, documenting the weight in the AT assessment tool, and reviewing the dose according to the weight-band of the child. Training also should instruct HCWs to manage AT and ARV-associated ADRs according to national clinical guidelines and best clinical practice and ensure that all trained staff understand their roles in the AT assessment and reporting process, including reporting all ADRs identified through the tool through the national system.

5. Ensure that all service-delivery points are equipped with the AT assessment tool and that there is a clear, designated process for collecting assessments once the training is complete. The AT assessment tool should be inserted in each client's file if hard copies are used. If digital files are used, it should be attached to the electronic client file, with a pop up to remind HCWs to complete the AT assessment.

6. Plan for post-training follow-up and/or mentoring to assess how the tool is being used, check that the AT assessment tool is being completed correctly and that ADRs are being reported, and give feedback based on what the follow-up assessment finds. Implement an M&E plan with regular check-ins beyond the initial assessment. Include AT assessment as part of the facility's monthly or quarterly data review.

Assessment and Management of Long-Term, Adverse Events

To achieve and sustain safe and durable viral suppression over a lifetime, both short-term and long-term ADRs must be anticipated, discussed with the client/caregiver, and managed according to national clinical guidelines. When selecting an ARV regimen, clinicians must consider potential ADRs, as well as an individual's comorbidities, concomitant medications, and prior experiences of drug toxicity and/or intolerance. ADRs can lead to reduced quality of life, treatment interruption, treatment failure, avoidable morbidity, death, and added costs for health care services (e.g. hospitalization).

Long-term, active monitoring of ADRs is important during new or expanded use of ARVs because exposure and reactions to such treatments are relatively new. As part of ADR identification and management, there should be systems and tools in place for national and subnational programs to collect, collate, and analyze PV reports and provide feedback to HCWs on ADR trends. This will improve the ability of HCWs to assess and manage ADRs. Monitoring of ADRs also provides data on the frequency and clinical relevance of various types of ADRs, which can be used to improve the management of ADRs in patients as well as to inform national treatment policies. **Table 1** lists major toxicities associated with commonly used ARVs, which should be included in long-term ADR monitoring.

Table 1. Major toxicities associated with commonly used ARVs

	Drug	Liver	Renal	Bone	CVD	Metabolic	Hematologic	CNS	Skin	GI intolerance	Muscular
NRTI	ABC				X				XX		
	AZT					X	XX		X	XX	X
	TDF		XX	XX							
NNRTIs	EFV	X				X		XX			
	NVP	X							XX		
PI	ATV/r		XX		X	X					
	DRV/r	X			X	X			XX		
	LPV/r	X			X	XX				XX	
INSTI	DTG	X						XX	XX		
	RAL	X						X	XX		X

Legend:

CVD: cardiovascular disease
CNS: central nervous system
GI: gastrointestinal
ABC: Abacavir
AZT: Zidovudine
TDF: Tenofovir disoproxil fumarate
EFV: Efavirenz
NVP: Nevirapine
ATV/r: Atazanavir/ritonavir
DRV/r: Darunavir/ritonavir
LPV/r: Lopinavir/ritonavir
DTG: Dolutegravir
RAL: Raltegravir
X: reported
XX: most commonly reported

Source: World Health Organization.[7]

Long-term, active monitoring of ADRs should focus on specific ARVs in a select number of ART sites, or in all ART facilities, if there are sufficient resources and capacity. ADRs may be detected by interviewing patients, by performing specific targeted investigations, or by screening patient records.

The main criteria for selecting clinical sites for active, long-term PV include:

- Number of CALHIV initiating DTG, pDTG, or other new ARV drugs: ART sites with significant number of patients initiating or transitioning to DTG or other new ARV drugs are generally preferable.

- Availability of electronic medical records (EMRs): Sites with EMRs are preferable to support data capture and reporting. The PV module ideally should be incorporated into an existing EMR platform and include a drop-down list to capture all signs and symptoms of ADRs related to the drugs in question.

- Human resource capacity: Sites with the greatest availability, willingness, commitment, and capacity of HCWs to identify, manage, and report ADRs associated with new ARVs are preferable. Staff should be assigned to fill in the required data and to associate the ADRs with specific drugs (possibly trained physicians/clinicians).

- Laboratory testing: Sites with the capacity for detection, identification, and confirmation of laboratory abnormalities as well as the assessment of treatment efficacy are preferable.

- Data management and record keeping: The availability of unique patient identifiers, linkages to pharmacy databases, and longitudinal patient data including ART, clinical, and ADR data at a site is preferable. The protocol for follow-up assessments with individuals receiving new ARVs should require proper identification of the ADR, assessment of its relation to the new ARV drug, and documentation of the timeline and outcome.

Appendices 1 and 2 below provide an example AT assessment tool as well as guidance for adapting the tool to a country's context and medicines of interests, and for introducing the tool into health care facilities and a country's PV system. The example AT assessment tool in Appendix 2 is available in Excel format to facilitate adaptation of the tool.

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APPENDIX 1:

Guidance for Adapting the New Pediatric ARV Acceptability and Tolerability Assessment Tool and for Introducing It into Health Care Facilities

Adapting the AT Assessment Tool to the National Context

National programs should review and adapt the generic AT assessment tool to ensure that it reflects national HIV case management guidelines as well as the tolerability and adverse drug reaction profiles associated with the pediatric drugs being used in the country. As part of the adaptation process, it is recommended to integrate the tool into the national pharmacovigilance system as much as possible to ensure that cases of acceptability, tolerability, and adverse drug reactions are reported, aggregated, reviewed, and responded to at both health care facility and national levels.

The adaptation process should include the following:

- ***Page 1:*** Review and update the language on page one to ensure that the tool accurately reflects the types of health care facilities that will use the tool, that the instructions align with national HIV case management guidelines, and that the drug tables reflect the types of drugs that will be monitored by the tool.

- ***First, second, and third visit headings:*** After initiation or transition to a new drug or drug regimen, HCWs using the tool should schedule follow up clinic visits in accordance with national case management guidelines. For the first, second, and third follow up visits, the number of days, weeks, or months after initiation or transition to the new drug should be updated in the AT assessment tool, as needed, to align with national guidelines. To capture acceptability and tolerability challenges, it is important to schedule the first visit from two weeks to one month after initiating or transitioning to a new drug.

- ***List of questions for each follow up visit:*** In the generic AT assessment tool, the list of questions for each follow up visit (first, second, and third visit) was developed and piloted with a focus on acceptability, tolerability and adverse reactions to pediatric Dolutegravir 10mg dispersible tablets (pDTG 10mg). When adapting the tool, it is recommended to review and update the list of questions to ensure they capture the tolerability and ADR profile of the pediatric medicines that are being introduced or used by the national program. For example, if a new drug is difficult to swallow, but should not be cut or crushed, then the AT assessment form should include a question about the practice of cutting or crushing tablets.

- ***Integrating the AT assessment tool into electronic patient records systems:*** For countries that use an electronic patient record system, it is recommend to integrate the tool into the system, with a prompt or pop-up to ensure that the set of questions are asked at each follow up clinical visit.

- ***Reporting ADRs to the national PV reporting system*:** Countries should use information from the AT assessment tool to report to the national PV system. Any ADR recorded in the AT tool should be reported. Mild adverse events will not be overlooked in the reporting since the AT tool helps identify them.

Introducing the AT Assessment Tool at Health Care Facilities

How can the tool be integrated into the patient flow of those services?
The tool shall be used by all health care providers including community health workers. It can be availed in electronic format or printed. The tool can be filled at different service delivery points, including at triage, clinician's desk, adherence assessment, and the pharmacy level. It therefore should be integrated in the patient records or included in a physical patient file. Actions taken from information provided in the tool shall be recorded in the patient records and a report sent to the national pharmacovigilance system by a trained clinician.

Who should receive an orientation to the tool (e.g. supervisors, administrators, data managers)?
All managers in health care facilities and regional levels should be sensitized on the use of the AT assessment tool. Heads of public health programs, those performing clinical trials, sentinel sites and facility managers should also be included in the sensitization on the use of the tool.

Who should be trained to use the tool?
All HCWs, including community health workers, and adherence support staff should receive information on the tool and supported to use it when a new drug is available. These workers come in contact with the children receiving care and their caregivers. Their knowledge on the use of the tool will allow for immediate identification of any ADRs and reporting of the same.

How should the users of the tool be trained?
The training of HCWs and all users of the tool should be through a formal training on pharmacovigilance where the tool will be introduced in situations where there is a new drug to be monitored for acceptability and tolerability. The training should be designed to build both knowledge and skills through hands-on practice using the tool with mock patients and data.

HCWs should be trained in: (1) how to ask the questions and record the responses in the AT assessment tool; (2) how to analyze the information and responses collected; and (3) how to manage AT and ARV-associated ADRs according to national clinical guidelines and best practices. For example, a child's weight should be taken during each follow-up visit. The HCW should use the opportunity to check if the correct dose of ARVs are being given to the child. In addition, the training should provide an overview of common ADRs and how they should be managed.

How should the users of the tool be supported after training (e.g. on-site supervision, mentoring visits, site-level quality improvement reviews)?
After training of the users, ongoing support should be provided though site visits and on-the-job training. The use of quality improvement approaches should be adopted to institutionalize the use of the tool across facilities. Gaps identified during supervision visits can be filled through mentorship support as follow up of the QI projects.

Challenges with Using the Tool and Suggestions for Overcoming Them

The following table lists some challenges that could be experienced when introducing the AT assessment tool, as well as suggestions for overcoming them. It is recommended to highlight these challenges and solutions during the orientations and trainings on the tool.

Scenario	Proposed Solution
1. Page 1: Listing the drug regimen in the table, especially for fixed-dose combination (FDC) treatments.	• Each individual drug in a regimen should be listed separately in the table. For example, if ABC/3TC + DTG is prescribed, ABC/3TC (which is an FDC) should be listed as Drug 1 and DTG listed as Drug 2. • If the drug is a fixed dose combination, such as TLD, then it should be listed on one line. • If the drug is a generic then this should be indicated in the brand name section
2. Caregiver does not adhere to scheduled clinic appointments or is coming without the child.	• Conduct follow-up phone calls to: (1) remind the caregiver to keep appointments; and (2) inquire about any ADR, especially if the caregiver missed the first clinic appointment following initiation or transition. • Flex clinic schedules (e.g., schedule clinic appointments on weekends, align appointments with school schedules, etc.) • Joint planning with caregiver on appointment scheduling
3. Inputting a visit in the AT assessment tool if the child and/or caregiver comes after the recommended time for the first, second, or third visit or misses an appointment.	• For each follow up visit (first, second, or third visit), the tool suggests a number of weeks or months after the initiation or switch to a new drug or regimen to complete that visit. If the child returns after the recommended time, simply fill in the actual date that the child returned and complete the form for the corresponding first, second, or third visit. • Schedule the next clinical visit as follows: - If the child/caregiver misses the first appointment, but comes within one month of ART initiation/transition, document it as the first follow-up visit. The next appointment should be adjusted based on previous honored appointment but within the recommendations. - If the child/caregiver misses the first follow-up appointment and comes more than one month after ART initiation/transition, document it as the second visit. On the AT form, note that the client missed the first follow-up clinic appointment.

(Continued on next page)

Scenario	Proposed Solution
4. A different caregiver brings the child back for a follow-up clinical visit.	• Indicate if the caregiver that brought the child to the visit is the new primary caregiver, and confirm if they support/observe administering medicine to the child.
5. Weight is not taken at a follow up visit or a caregiver does not bring the child with them to a follow-up visit.	• Taking a child's weight is critical to ensure accurate weight-based dosing • HCWs should weigh a child and document their weight at each clinic visit • As a child's weight changes, the dosage of each drug should also change to ensure that it is still effective but not toxic. • If the dosage is too high for a child's weight, it could lead to an ADR. If the dosage is too low for a child's weight, the drug could be less effective (e.g., lead to high viral load) • HCWs should encourage caregivers to bring the child with them to each follow-up visit. If the caregiver cannot bring a child, then the child should be weighed in the community within one week of the visit.
6. Incomplete/non-documentation of AT tool by the clinical team.	• Sensitize more facility technical staff through CME on how and the importance of complete documentation. • Provide hands-on, directly observed practice in using the tool, including identifying, managing, and reporting administration challenges and ADRs identified through the tool.
7. AT tool not filled during the clinic visit	• The AT tool should be filled at every clinic visit according to the schedule. • Place a reminder (e.g., sticker, note) in the patient file. Put a copy of the tool in the patient's record when they start or switch to a new ARV and include a pop-up in the EMR to remind HCWs to complete the tool. • If the AT tool is not filled in during a clinic visit date, it is a missed opportunity. However, a follow up can be done with the caregiver either by phone or through a home visit. • Ensure the tool is filled in subsequent visits • One staff member should be assigned the responsibility of ensuring the tool is filled for all eligible children on a clinic day, usually the last one in contact with the child before completing the visit.
8. Some health care facility staff or not oriented on the use of the tool.	• Include use of the AT tool in facility-based capacity building (i.e., CME, OJT, mentorship) to ensure that all HCWs are oriented to the tool and how to use it.

APPENDIX 2:

New Pediatric ARV Regimen Acceptability and Tolerability Assessment Tool

Generic Version for National Adaptation

Version 1.0: February 2023

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New Pediatric Antiretroviral Regimen Acceptability and Tolerability (AT) Assessment Tool

Facility Name [Insert Name]	**Facility Code** [Insert Code]	**HIV Clinic Number** [Insert Number]
Patient Name [Insert Name]	**Date of Birth** [Insert DOB]	**Patient Weight** [Insert Weight]
Caregiver Name [Insert Name]	**Start Date of Old Regimen/Drug** [Insert Date]	**Start Date of New Regimen/Drug** [Insert Date]

This form should be completed by a clinician, nurse, or other appropriate staff member when a child or adolescent age 0–14 years is initiated on, or switched to, a new antiretroviral (ARV) regimen or other related drug (e.g. TB treatment). When the child starts the new ARV regimen or drug, enter the new drugs being given in the table below. If a fixed-dose combination therapy is prescribed, enter it as one drug only (e.g. Drug 1). Place the original copy of this form in the patient's file to be completed during future visits. Complete relevant sections of the form at or around **# weeks, # month, and # months post new ARV regimen introduction or transition**. At each visit, review the results of the previous visit, weigh the child, and ensure that the drug dosages are correct for the child's weight. Ask the caregiver and/or patient the questions corresponding to the visit number (i.e. visit 1, 2 or 3), and record the responses on the form. Children 10 years of age or older generally can respond with or without the caregiver.

Reason for new ARV regimen or other new drug (check one):

- ◯ Initiation of ART for newly-diagnosed patient (e.g. first-line)
- ◯ Switch to a new optimal ARV regimen (e.g. from LPV/r to DTG)
- ◯ Failure on current ARV regimen
- ◯ Other (intolerance, adverse events, procurement challenge, TB treatment, etc.), please specify:

[*Please specify*]_____

New ARV Regimen

ARV Regimen	Name	Brand (Manufacturer)	Strength (mg, ml)	Dosage	Frequency	Adherence counselling provided?
Example Drug	*ABC/3TC (FDC)*	*Generic (Mylan)*	*120/60mg*	*1 tab*	*Once per day*	☐ Yes ☐ No
Drug 1						☐ Yes ☐ No
Drug 2						☐ Yes ☐ No
Drug 3						☐ Yes ☐ No

Other New Drug (e.g. TB treatment)

Other Regimen	Name	Brand (Manufacturer)	Strength (mg, ml)	Dosage	Frequency	Adherence counselling provided?
Drug 1						☐ Yes ☐ No
Drug 2						☐ Yes ☐ No

Acceptability and tolerability questions after ARV (and/or other new drug) initiation/transition

1st Visit—# weeks after ARV (and/or other new drug) initiation/transition

Date [Insert Date] **Name of Caregiver** [Insert Name] **Weight of child** (write N/A if not available) [Insert Weight]

Was the child's weight taken during the visit?
☐ Yes ☐ No IF NO, explain why: [insert text]

Has the child been taking the ARVs (and/or other new drug) EVERY DAY during the last month?
(check the quantity of the remaining drug)
☐ Yes ☐ No IF NO, explain why: [insert text]

Is the dosage taken correct for the weight? (ask caregiver/child how much drug is given and how often)
☐ Yes ☐ No IF NO, explain: [insert text]

What time(s) of the day are ARVs or drugs given/taken?
☐ AM ☐ Mid-day ☐ PM

Is the timing of ARVs or drugs working for you?
☐ Yes ☐ No

Is the frequency, or the number of tablets, or volume of liquids difficult to administer/take?
☐ Yes ☐ No IF YES, which ARV/drug? [insert text]

Does the child have difficulty taking the ARV/drug (spitting up, vomiting) due to the taste, size, or feeling?
☐ Yes ☐ No IF YES, which ARV/drug? [insert text]

Does the child have any of the following symptoms when taking ARVs/drugs?
(Read aloud the following symptoms of adverse drug reactions (ADRs) and check all that apply)

Gastrointestinal: ☐ Vomiting ☐ Diarrhea ☐ Nausea
If yes, for how long? [insert text] How often? [insert text]

Skin: ☐ Itching of the skin ☐ Rash on the skin ☐ Other skin problem
If yes, examine/explain: [insert text]

Central Nervous System: ☐ Difficulty sleeping ☐ Increased sleepiness ☐ Dizziness ☐ Headache
If yes, explain: [insert text]

Metabolic: ☐ Increased appetite ☐ Decreased appetite ☐ Yellowness of eyes ☐ Rapid or excessive weight gain ☐ Rapid or excessive weight loss
If yes, examine/explain: [insert text]

☐ Other changes or concerns (specify): [insert text]

Summary of Findings

Check if a challenge or ADR was reported in the previous visit. Ask further questions, as needed, such as how many times per day, for how long (days/weeks/months), if the problem is increasing or decreasing, etc. Summarize the main findings below.

[insert text]

Actions Taken and Recommendations

List the actions taken and/or advice given. For example, provided counselling, asked caregiver to demonstrate giving the drug, ordered diagnostic test, changed ARV regimen, etc. If an ADR was reported, grade the severity of the ADR and decide on a course of action (e.g. hospitalize, change regimen, closely monitor). If no action was taken, write "No Action Taken".

[insert text]

Reporting of Adverse Drug Reactions (ADRs)

Was an ADR reported to the appropriate regulatory authority? ☐ Yes ☐ No ☐ Don't know
If yes, name of the ADR: [insert text] ADR report number: [insert number]

2nd Visit—# month after ARV (and/or other new drug) initiation/transition

Date [Insert Date]

Name of Caregiver [Insert Name]

Weight of child (write N/A if not available) [Insert Weight]

Was the child's weight taken during the visit?
☐ Yes ☐ No IF NO, explain why: [insert text]

Has the child been taking the ARVs (and/or other new drug) EVERY DAY during the last month?
(check the quantity of the remaining drug)
☐ Yes ☐ No IF NO, explain why: [insert text]

Is the dosage taken correct for the weight? (ask caregiver/child how much drug is given and how often)
☐ Yes ☐ No IF NO, explain: [insert text]

What time(s) of the day are ARVs or drugs given/taken?
☐ AM ☐ Mid-day ☐ PM

Is the timing of ARVs or drugs working for you?
☐ Yes ☐ No

Is the frequency, or the number of tablets, or volume of liquids difficult to administer/take?
☐ Yes ☐ No IF YES, which ARV/drug? [insert text]

Does the child have difficulty taking the ARV/drug (spitting up, vomiting) due to the taste, size, or feeling?
☐ Yes ☐ No IF YES, which ARV/drug? [insert text]

Does the child have any of the following symptoms when taking ARVs/drugs?
(Read aloud the following symptoms of adverse drug reactions (ADRs) and check all that apply)

Gastrointestinal: ☐ Vomiting ☐ Diarrhea ☐ Nausea
If yes, for how long? [insert text] How often? [insert text]

Skin: ☐ Itching of the skin ☐ Rash on the skin ☐ Other skin problem
If yes, examine/explain: [insert text]

Central Nervous System: ☐ Difficulty sleeping ☐ Increased sleepiness ☐ Dizziness ☐ Headache
If yes, explain: [insert text]

Metabolic: ☐ Increased appetite ☐ Decreased appetite ☐ Yellowness of eyes
☐ Rapid or excessive weight gain ☐ Rapid or excessive weight loss
If yes, examine/explain: [insert text]

☐ Other changes or concerns (specify): [insert text]

Summary of Findings

Check if a challenge or ADR was reported in the previous visit. Ask further questions, as needed, such as how many times per day, for how long (days/weeks/months), if the problem is increasing or decreasing, etc. Summarize the main findings below.

[insert text]

Actions Taken and Recommendations

List the actions taken and/or advice given. For example, provided counselling, asked caregiver to demonstrate giving the drug, ordered diagnostic test, changed ARV regimen, etc. If an ADR was reported, grade the severity of the ADR and decide on a course of action (e.g. hospitalize, change regimen, closely monitor). If no action was taken, write "No Action Taken".

[insert text]

Reporting of Adverse Drug Reactions (ADRs)

Was an ADR reported to the appropriate regulatory authority? ☐ Yes ☐ No ☐ Don't know
If yes, name of the ADR: [insert text] ADR report number: [insert number]

3rd Visit—# months after ARV (and/or other new drug) initiation/transition

Date [Insert Date] **Name of Caregiver** [Insert Name] **Weight of child** (write N/A if not available) [Insert Weight]

Was the child's weight taken during the visit?
☐ Yes ☐ No IF NO, explain why: [insert text]

Has the child been taking the ARVs (and/or other new drug) EVERY DAY during the last month?
(check the quantity of the remaining drug)
☐ Yes ☐ No IF NO, explain why: [insert text]

Is the dosage taken correct for the weight? (ask caregiver/child how much drug is given and how often)
☐ Yes ☐ No IF NO, explain: [insert text]

What time(s) of the day are ARVs or drugs given/taken?
☐ AM ☐ Mid-day ☐ PM

Is the timing of ARVs or drugs working for you?
☐ Yes ☐ No

Is the frequency, or the number of tablets, or volume of liquids difficult to administer/take?
☐ Yes ☐ No IF YES, which ARV/drug? [insert text]

Does the child have difficulty taking the ARV/drug (spitting up, vomiting) due to the taste, size, or feeling?
☐ Yes ☐ No IF YES, which ARV/drug? [insert text]

Does the child have any of the following symptoms when taking ARVs/drugs?
(Read aloud the following symptoms of adverse drug reactions (ADRs) and check all that apply)

Gastrointestinal: ☐ Vomiting ☐ Diarrhea ☐ Nausea
If yes, for how long? [insert text] How often? [insert text]

Skin: ☐ Itching of the skin ☐ Rash on the skin ☐ Other skin problem
If yes, examine/explain: [insert text]

Central Nervous System: ☐ Difficulty sleeping ☐ Increased sleepiness ☐ Dizziness ☐ Headache
If yes, explain: [insert text]

Metabolic: ☐ Increased appetite ☐ Decreased appetite ☐ Yellowness of eyes
☐ Rapid or excessive weight gain ☐ Rapid or excessive weight loss
If yes, examine/explain: [insert text]

☐ Other changes or concerns (specify): [insert text]

Summary of Findings

Check if a challenge or ADR was reported in the previous visit. Ask further questions, as needed, such as how many times per day, for how long (days/weeks/months), if the problem is increasing or decreasing, etc. Summarize the main findings below.

[insert text]

Actions Taken and Recommendations

List the actions taken and/or advice given. For example, provided counselling, asked caregiver to demonstrate giving the drug, ordered diagnostic test, changed ARV regimen, etc. If an ADR was reported, grade the severity of the ADR and decide on a course of action (e.g. hospitalize, change regimen, closely monitor). If no action was taken, write "No Action Taken".

[insert text]

Reporting of Adverse Drug Reactions (ADRs)

Was an ADR reported to the appropriate regulatory authority? ☐ Yes ☐ No ☐ Don't know
If yes, name of the ADR: [insert text] ADR report number: [insert number]