PediCAP

Oral stepdown and Discharge

v2.0 01-Oct-2020

EDCTP

PediCAP is part of the EDCTP2 programme supported by the European Union under Grant Agreement RIA2017MC - 2023.

Summary

- Oral stepdown
  - When to stepdown
  - Prescribing
  - Dosing
  - Preparing the oral medication
- Discharge
  - When to discharge
  - Meeting with the parent/carer
  - Drug Information Leaflet

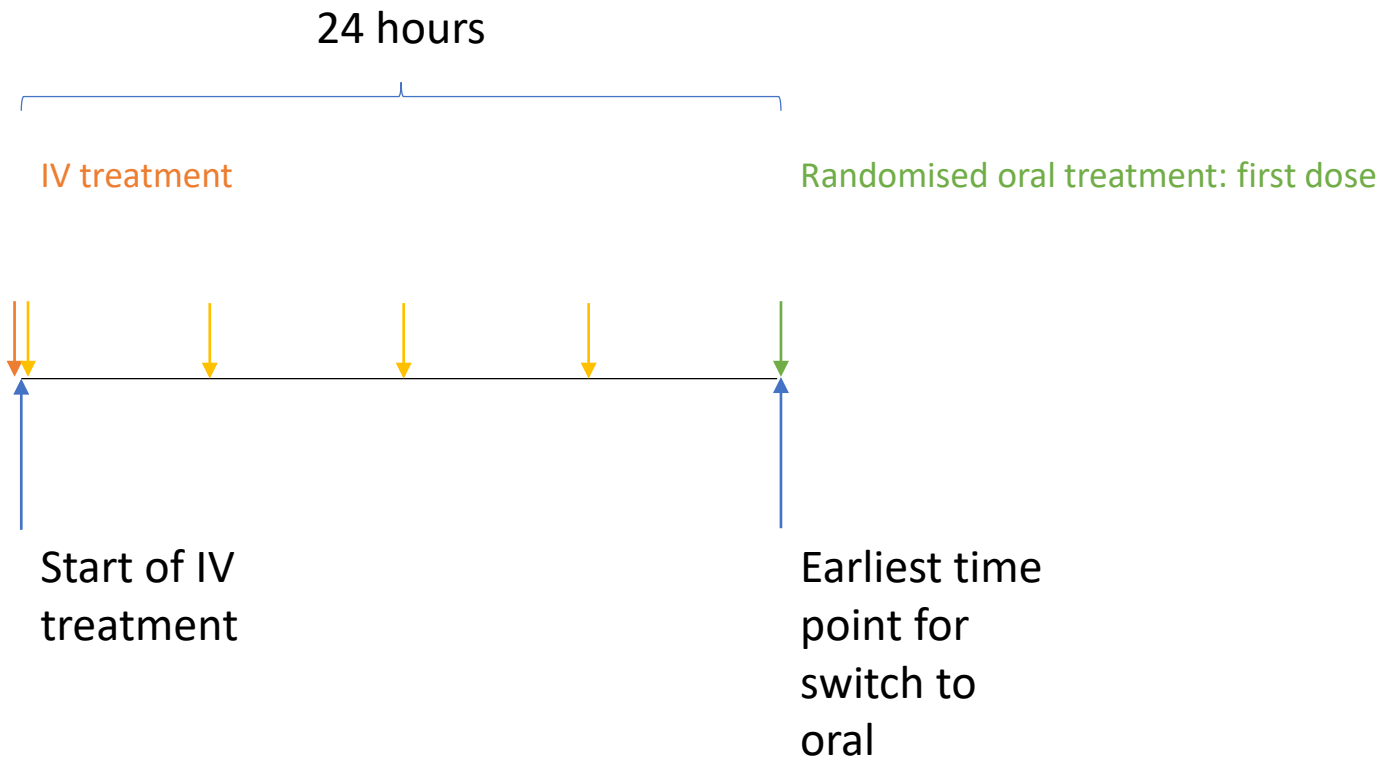
Oral Stepdown

Study IMP

- In PediCAP-A the Investigational Medicinal Products (IMP) are the oral stepdown drugs:
  - Amoxicillin
  - Co-amoxiclav 7:1 (amoxicillin:clavulanate)
- Both study drugs are administered orally as dispersible tablets.

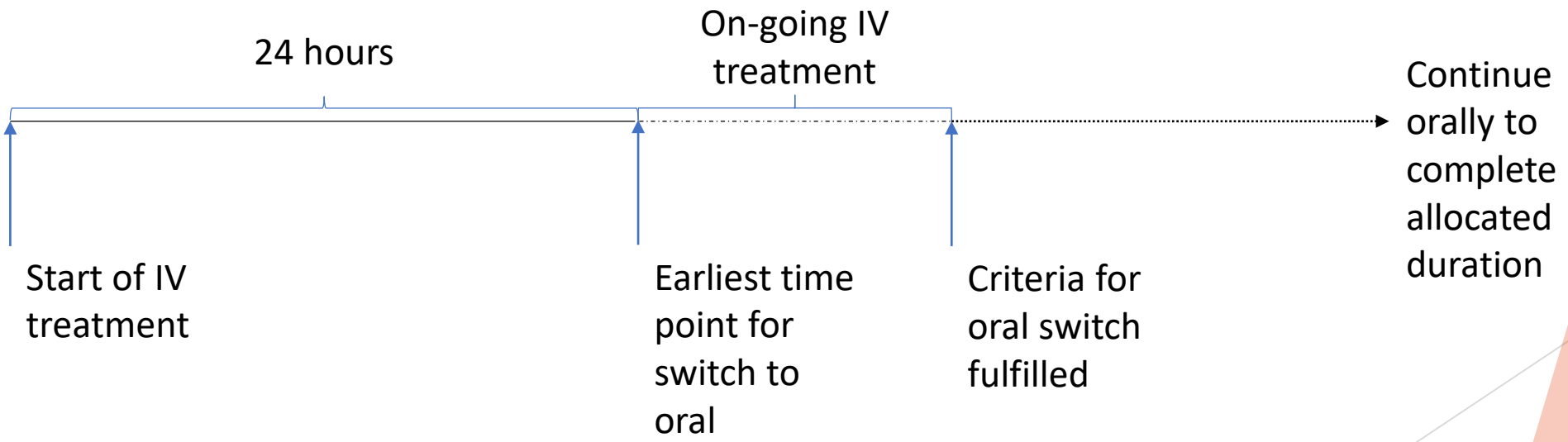
When to stepdown?

- All children will receive at least 24 hours of intravenous (IV) antibiotics regardless of their randomisation allocation.
- This means that if randomised to oral stepdown, the earliest timepoint for the first dose of oral treatment is 24 hours after the first dose of IV medication.



When to stepdown?

- Once the patient has received 24 hours of IV antibiotics, they should switch to oral antibiotics as soon as they have improved clinically and are well enough to take medication by mouth.
- They should continue on IV treatment until this criteria is fulfilled.



When to stepdown?

- The child's clinician should decide when the patient is well enough to start oral antibiotics, however the following should be considered to ensure standardisation across sites:
  - The patient should have received at least 24 hours of IV antibiotics.
  - The patient should have improved overall clinically, be currently clinically stable or continuing to improve.
  - The patient should be well enough to tolerate oral medication (not vomiting and able to take fluids orally).
  - The patient should not require IV fluids and should not meet the criteria for **severe** dehydration.
  - The patient does not need to be ready for discharge to step down to oral treatment, and may need to stay in hospital to receive oxygen.

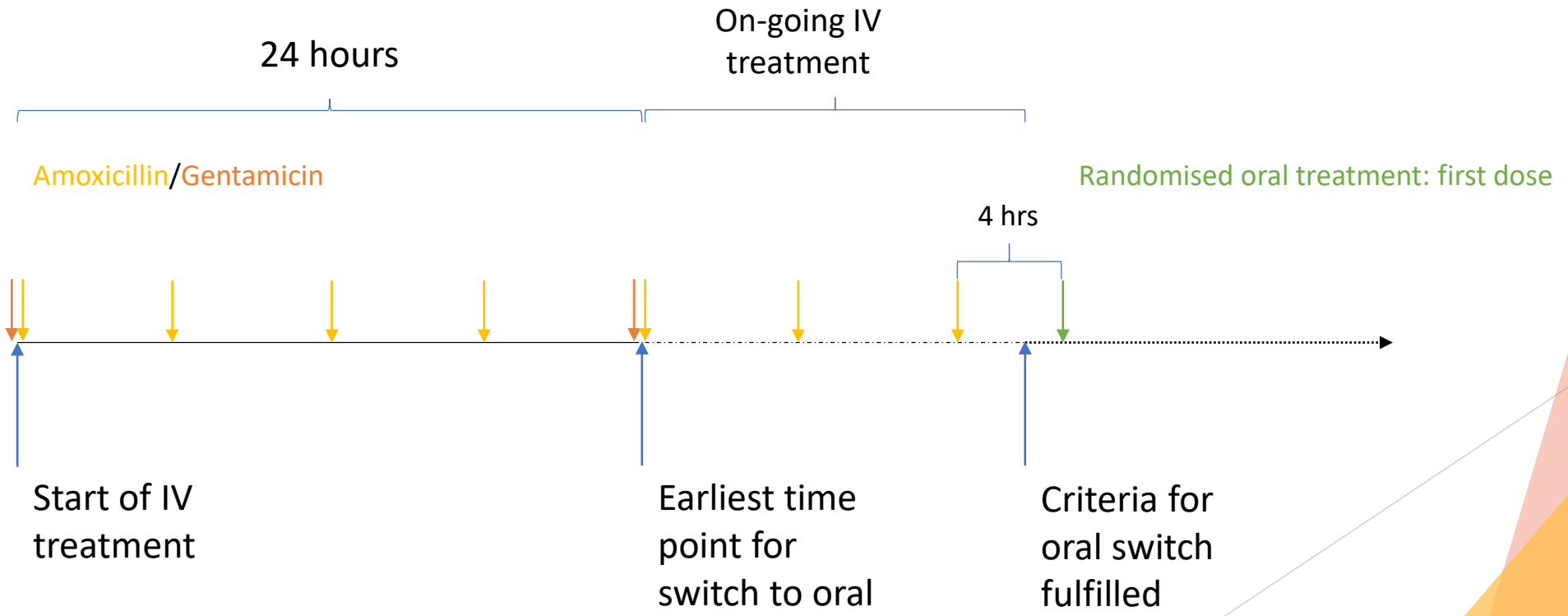
Dehydration Classification

Classification	Signs or symptoms
Severe dehydration	Two or more of the following signs: • lethargy or unconsciousness • sunken eyes • unable to drink or drinks poorly • skin pinch goes back very slowly (≥ 2 s)*
Some dehydration	Two or more of the following signs: • restlessness, irritability • sunken eyes • drinks eagerly, thirsty • skin pinch goes back slowly
No dehydration	Not enough signs to classify as some or severe dehydration

*skin pinch should be done on exposed abdominal skin to assess for decreased skin turgor

When to give first oral dose?

- There must be at least 4 hours between initiation of the last IV dose and giving the first oral dose of treatment.
- The time may be longer than 4 hours and may depend on the IV drug that is given.
- Care should be taken to ensure sufficient IV dosing until the first oral dose.



Prescribing

- Oral medication should always be prescribed and dispensed on the day of oral step-down, never in advance.
- The PediCAP trial prescription should be used to prescribe the oral medication.
- The PediCAP dosing tool should be used to help calculate the correct number of tablets to prescribe.
- Children will be prescribed the duration of antibiotics needed to complete the randomised total antibiotic course (starting at the time intravenous antibiotics were administered, excluding any antibiotics taken in the community prior to admission). For example:
  - A child randomised to total 8 days antibiotics who is well enough to start taking oral antibiotics after 3 days of intravenous antibiotics will receive 5 days oral antibiotics
  - A child who is randomised to total 4 days antibiotics who is well enough to start taking oral antibiotics after 2 days of intravenous antibiotics will receive 2 days oral antibiotics
- One extra dose should be prescribed to account for any lost or vomited doses.

Dosing

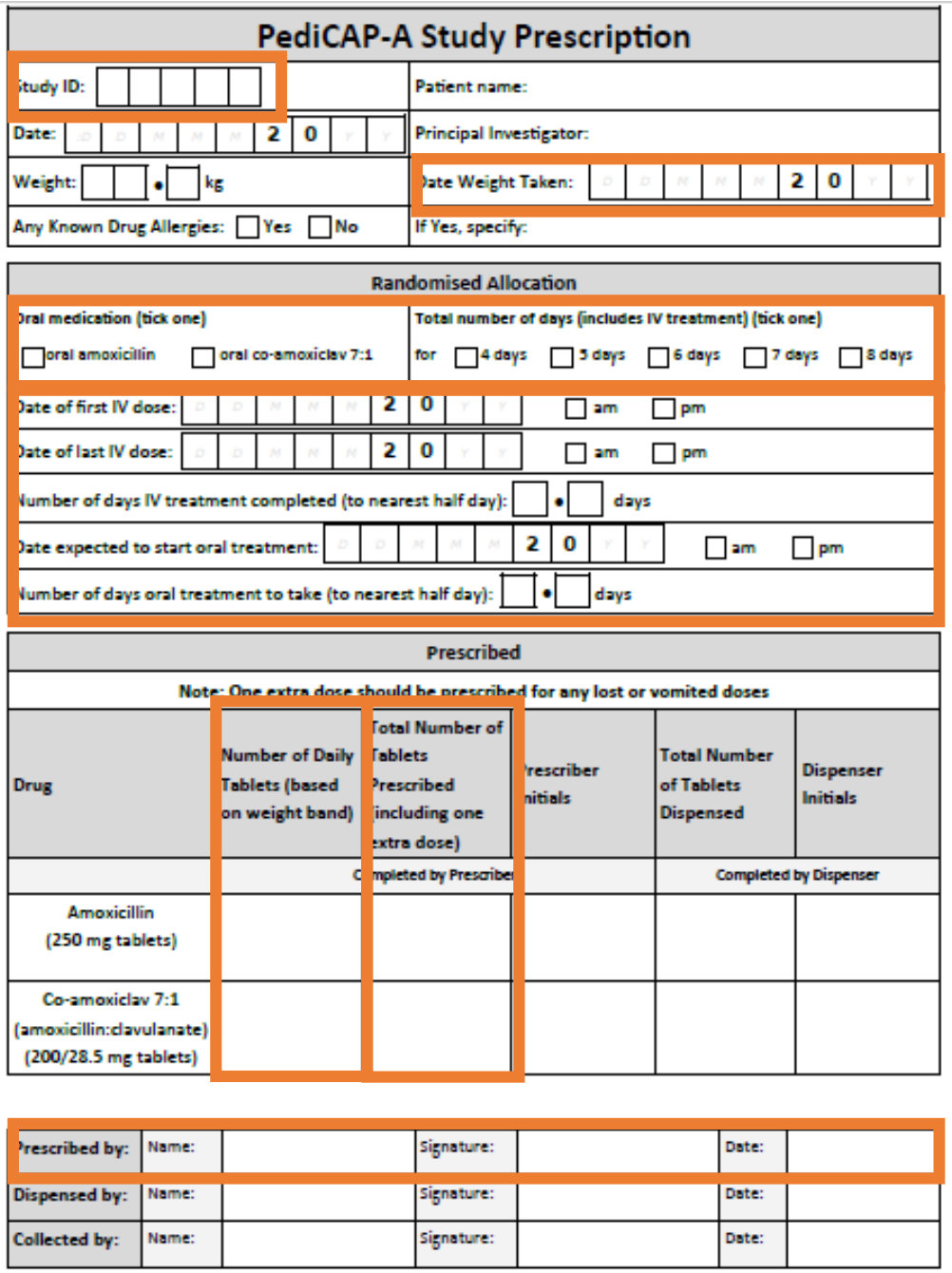
- Dosing is based on the child's weight.
- It is important to weigh the child on the day of oral step-down to ensure correct dosing, as the child's weight may have changed considerably since admission.

Formulation	Weight Band	# Tablets am	# Tablets pm	# Tablets Daily	Daily Dose (mg)
Amoxicillin (250mg tablets)	3 - <6kg	1	1	2	500
	6 - <10kg	2	1	3	750
	10 - <14kg	2	2	4	1000
	14 - <20kg	3	3	6	1500
	20 - <25kg	4	4	8	2100
	25 - <35kg	5	5	10	2500
Co-amoxiclav 7:1 (200/28.5mg tablets)	3 - <6kg	1	1	2	400/57
	6 - <10kg	2	2	4	800/114
	10 - <14kg	3	2	5	1000/142.5
	14 - <20kg	4	4	8	1600/228
	20 - <25kg	5	5	10	2000/285
	25 - <35kg	6	6	12	2400/342

Ensure to complete the Study ID

Confirm the randomised allocation on the Individual Visit Schedule

The prescribing doctor should have signed the PediCAP Signature and Delegation Log and been delegated the responsibility of prescribing by the Principal Investigator



PediCAP-A Study Prescription

Study ID: | Patient name:

Date: D D M M M 2 0 Y Y | Principal Investigator:

Weight: [ ][ ] • [ ] kg | Date Weight Taken: D D M M M 2 0 Y Y

Any Known Drug Allergies: ☐ Yes ☐ No | If Yes, specify:

Randomised Allocation

Oral medication (tick one)
☐ oral amoxicillin ☐ oral co-amoxiclav 7:1

Total number of days (includes IV treatment) (tick one)
for ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐ 8 days

Date of first IV dose: D D M M M 2 0 Y Y ☐ am ☐ pm

Date of last IV dose: D D M M M 2 0 Y Y ☐ am ☐ pm

Number of days IV treatment completed (to nearest half day): [ ][ ] • [ ] days

Date expected to start oral treatment: D D M M M 2 0 Y Y ☐ am ☐ pm

Number of days oral treatment to take (to nearest half day): [ ][ ] • [ ] days

Prescribed

Note: One extra dose should be prescribed for any lost or vomited doses

Drug	Number of Daily Tablets (based on weight band)	Total Number of Tablets Prescribed (including one extra dose)	Prescriber Initials	Total Number of Tablets Dispensed	Dispenser Initials
	Completed by Prescriber			Completed by Dispenser	
Amoxicillin (250 mg tablets)					
Co-amoxiclav 7:1 (amoxicillin:clavulanate) (200/28.5 mg tablets)					

Prescribed by:	Name:		Signature:		Date:	
Dispensed by:	Name:		Signature:		Date:	
Collected by:	Name:		Signature:		Date:	

The weight should be taken on the same day that the prescription is written

Calculate the number of days oral treatment to take to the nearest half day

The number of daily tablets should be based on the weight band (check dosing table in protocol and MOP)

Prescribe one extra dose for lost or vomited doses

Total Duration of Antibiotics for PediCAP

RANDOMISATION ALLOCATION

IV antibiotics

5 days total

1 day — 24 hours compulsory IV antibiotics

4 days — Continue IV antibiotics

7:1 Oral Coamoxiclav for 6 days

6 days total

1 day — 24 hours compulsory IV antibiotics

3 days — Ready for oral step down **after 4 days** IV treatment

2 days — Oral antibiotics for 2 days

Oral Amoxicillin for 4 days

4 days total

1 day — 24 hours compulsory IV antibiotics

2 days — Ready for oral stepdown **after 3 days** IV treatment

1 day — Oral antibiotics for 1 day

am or pm?

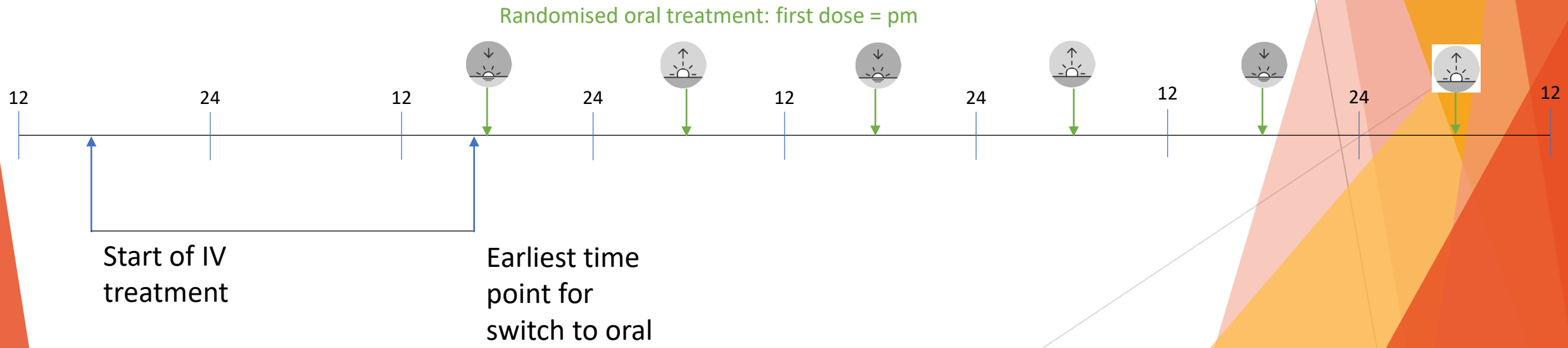
- The time that the first dose of oral and IV treatment is given also needs to be considered.
- The number of days should be calculated to the nearest half day.
- If the first dose of IV treatment was given in the afternoon, this means the last dose of oral treatment should be given in the morning.

Treatment day	am	pm
1		
2		
3		
4		
5		
6		
7		

- This patient was randomised to 6 days total duration of treatment.
- Their first dose of IV treatment was in the afternoon.
- To complete 6 full days of treatment, this means that their last dose will be on the morning of treatment day 7.

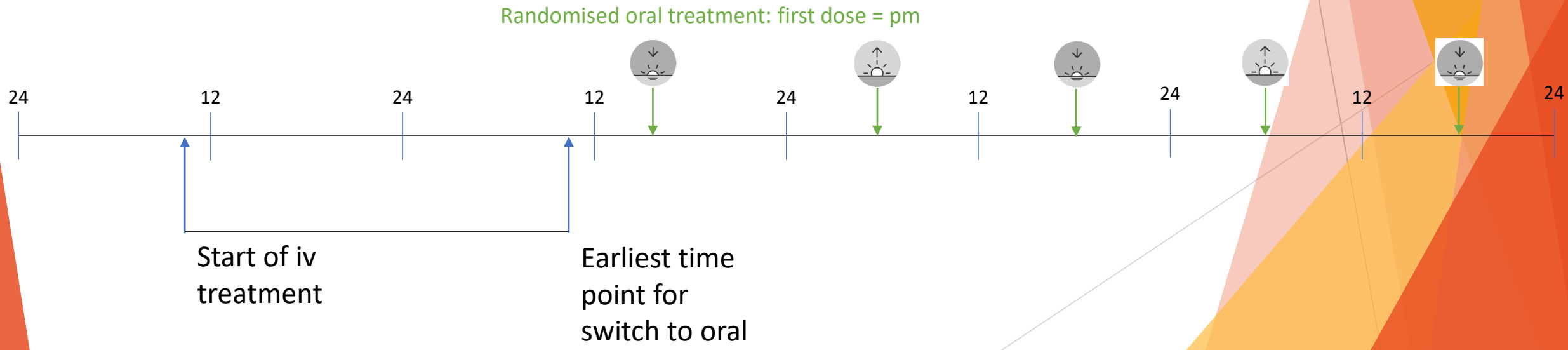
Example 1:

- This patient was randomised to 4 days total duration.
- Their first dose of IV treatment was in the afternoon.
- They had 24 hours of IV treatment (1 day duration).
- 4 days (total duration) minus 1 day (IV treatment) = 3 days oral treatment (6 doses)
- Their first dose of oral treatment was in the afternoon.
- Their last dose of oral treatment was in the morning.



Example 2:

- This patient was randomised to 4 days total duration.
- Their first dose of IV treatment was in the morning.
- They had 1.5 days of IV treatment.
- 4 days (total duration) minus 1.5 day (IV treatment) = 2.5 days oral treatment (5 doses)
- Their first dose of oral treatment was in the afternoon.
- Their last dose of oral treatment was also in the afternoon.



Dosing calculator tool demonstration

Preparing the oral medication

- The ward nurse will prepare and administer the tablets whilst the patient is still in hospital.
- Tablets should be dissolved in clean water or another liquid such as breast milk.
- Transfer the tablet directly from the packaging to the liquid in which it will be dissolved (do not leave outside of packaging for any period of time). Ensure the whole tablet is dropped into the liquid.
- The tablet should be dissolved in approximately 10ml (two teaspoons) of liquid. Wait until the tablet is fully dissolved (approximately 3-4 minutes).
- Swallow down with water or another liquid. Ensure the child drinks all the liquid in which the tablet was dissolved.
- They should never be swallowed whole, divided, chewed or crushed.
- Ideally the tablets should be administered at the start of a meal to prevent gastrointestinal intolerance.

Discharge

When to discharge?

- Children will be hospitalised throughout their entire course of IV antibiotics.
- After completing their IV antibiotics children may be discharged (depending on their randomised allocation this will be either after 5 days or at some point after moving to oral antibiotics).
- Children should not be discharged if they are not clinically stable or still show any signs of **severe** pneumonia.

Pneumonia Classification

Classification	Signs or Symptoms

Severe Pneumonia	Cough or difficulty in breathing with:
	• Oxygen saturation < 90% or central cyanosis
	• Severe respiratory distress (e.g. grunting, very severe chest indrawing)
	• Signs of pneumonia with a general danger sign:
	  ○ inability to breastfeed or drink
	  ○ lethargy or reduced level of consciousness
	  ○ convulsions

Pneumonia	• Fast breathing:
	  ○ ≥ 50 breaths/min in a child aged 2–11 months
	  ○ ≥ 40 breaths/min in a child aged 1–5 years
	• Chest indrawing

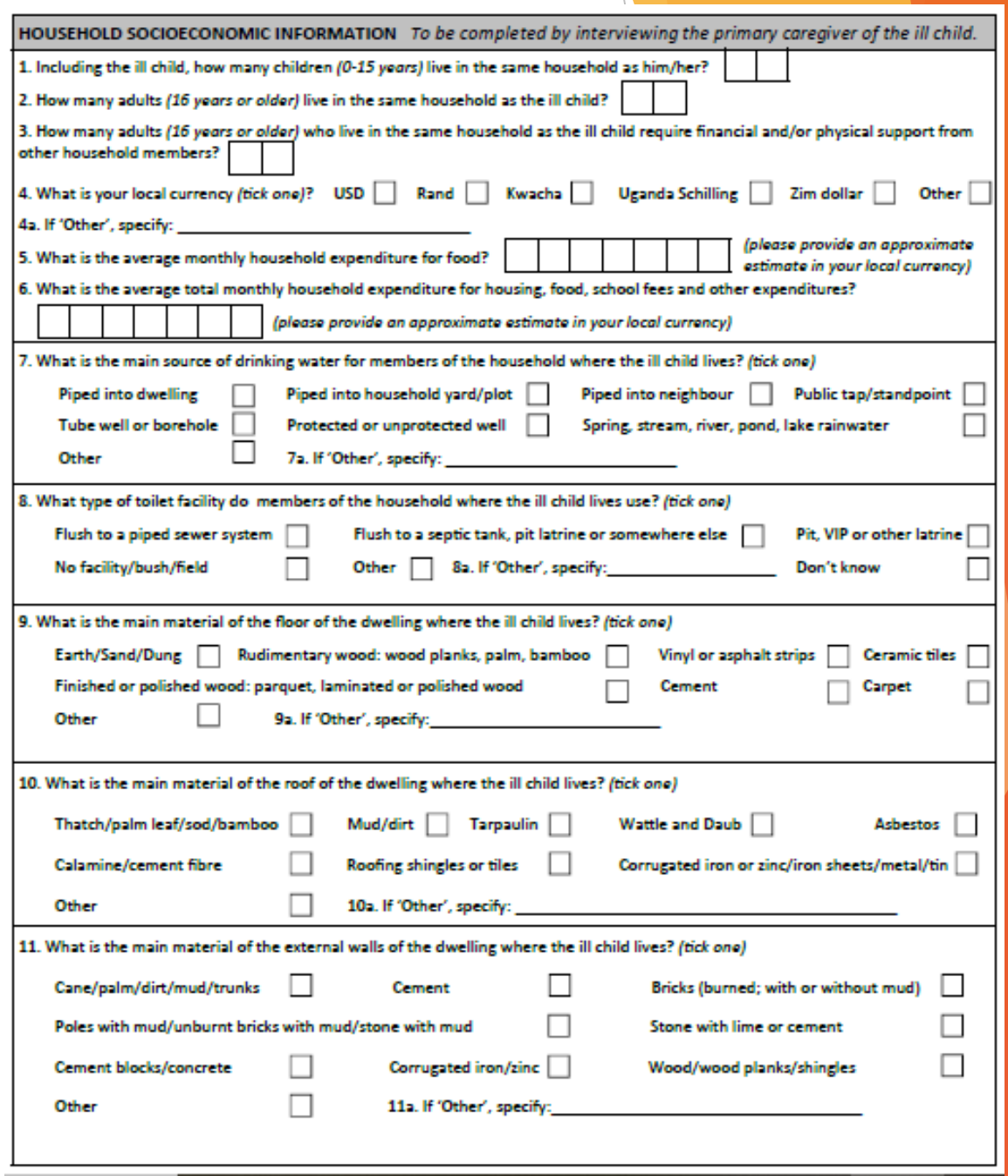
No pneumonia	No signs of pneumonia or severe pneumonia

Discharge Checklist

- ☑ The child does not show any signs of severe pneumonia
- ☑ If stepping down to oral medication, the child has received and not vomited at least one dose of oral antibiotics.
- ☑ The parents understand the signs of severe pneumonia and when to return.

Meeting with parent/carer

- The child's doctor/nurse should meet with the parent/carer at discharge.
- For children who have stepped down to oral antibiotics, CRF07 – Antibiotic Acceptability should be completed together with the parent/carer to assess the tolerability of the oral medication.
- It should be confirmed that CRF15 - Household Socioeconomic has been completed previously and if not, this should also be completed by interviewing the parent/carer of the child.



HOUSEHOLD SOCIOECONOMIC INFORMATION *To be completed by interviewing the primary caregiver of the ill child.*

1. Including the ill child, how many children *(0-15 years)* live in the same household as him/her? ☐☐
2. How many adults *(16 years or older)* live in the same household as the ill child? ☐☐
3. How many adults *(16 years or older)* who live in the same household as the ill child require financial and/or physical support from other household members? ☐☐
4. What is your local currency *(tick one)*? USD ☐ Rand ☐ Kwacha ☐ Uganda Schilling ☐ Zim dollar ☐ Other ☐
   4a. If 'Other', specify: _____
5. What is the average monthly household expenditure for food? ☐☐☐☐☐☐☐ *(please provide an approximate estimate in your local currency)*
6. What is the average total monthly household expenditure for housing, food, school fees and other expenditures?
   ☐☐☐☐☐☐☐ *(please provide an approximate estimate in your local currency)*

7. What is the main source of drinking water for members of the household where the ill child lives? *(tick one)*
   Piped into dwelling ☐ Piped into household yard/plot ☐ Piped into neighbour ☐ Public tap/standpoint ☐
   Tube well or borehole ☐ Protected or unprotected well ☐ Spring, stream, river, pond, lake rainwater ☐
   Other ☐ 7a. If 'Other', specify: _____

8. What type of toilet facility do members of the household where the ill child lives use? *(tick one)*
   Flush to a piped sewer system ☐ Flush to a septic tank, pit latrine or somewhere else ☐ Pit, VIP or other latrine ☐
   No facility/bush/field ☐ Other ☐ 8a. If 'Other', specify: _____ Don't know ☐

9. What is the main material of the floor of the dwelling where the ill child lives? *(tick one)*
   Earth/Sand/Dung ☐ Rudimentary wood: wood planks, palm, bamboo ☐ Vinyl or asphalt strips ☐ Ceramic tiles ☐
   Finished or polished wood: parquet, laminated or polished wood ☐ Cement ☐ Carpet ☐
   Other ☐ 9a. If 'Other', specify: _____

10. What is the main material of the roof of the dwelling where the ill child lives? *(tick one)*
    Thatch/palm leaf/sod/bamboo ☐ Mud/dirt ☐ Tarpaulin ☐ Wattle and Daub ☐ Asbestos ☐
    Calamine/cement fibre ☐ Roofing shingles or tiles ☐ Corrugated iron or zinc/iron sheets/metal/tin ☐
    Other ☐ 10a. If 'Other', specify: _____

11. What is the main material of the external walls of the dwelling where the ill child lives? *(tick one)*
    Cane/palm/dirt/mud/trunks ☐ Cement ☐ Bricks (burned; with or without mud) ☐
    Poles with mud/unburnt bricks with mud/stone with mud ☐ Stone with lime or cement ☐
    Cement blocks/concrete ☐ Corrugated iron/zinc ☐ Wood/wood planks/shingles ☐
    Other ☐ 11a. If 'Other', specify: _____

Meeting with parent/carer

- The doctor should always feel confident that the parent/carer leaves the hospital with a thorough understanding of how to administer the trial medication. The following should be discussed:
  - The tablets should be given to the child twice a day.
  - How many tablets the child should be given (this is dependent on their weight and may be a different number in the morning and evening).
  - How to prepare the tablets (these instructions may be provided by the nurse, doctor or pharmacist depending on local procedures).
  - The tablets should be given with food where possible.
  - Reinforce the importance of adherence to the trial drugs.
  - Confirm whether their last dose will be taken in the morning or evening (this will depend on when the first dose was given).
  - What to do in the event of a missed or vomited dose, including guidance on the extra dose provided. If the child is in a weight band that has a different number of tablets in the am to pm, ensure to explain that in the event of vomiting, the child should only re-take the number of tablets that were vomited.

Missed or Vomited doses

Missed doses

- If a dose is missed and **less than 6 hours** have passed since the usual dosing time - give the missed tablets as soon as possible. Give the next usual dose as prescribed.
- If a dose is missed and **more than 6 hours** have passed since the usual dosing time - do not give the missed tablets. Instead, give the next usual dose as prescribed.

Vomited doses

- If your child vomits **within 30 minutes** of giving a dose – give an extra dose as soon as possible.
- If your child vomits **after 30 minutes** of giving a dose – do not give an extra dose. Instead, give the next usual dose as prescribed.

- In all situations, the next dose should be given at the usual time.

Meeting with the parent/carer

- Instruct the parent/carer to contact the study team if they have any concerns, lose more than one dose, if the child takes more than the prescribed dose, or if the child has persisting symptoms.
- Encourage the parent/carer to bring the child back to the site if they become acutely unwell during the follow-up period.
- Verify the locator information collected at enrolment. Ring the telephone numbers provided when the parent/carer is present to confirm that the correct details are recorded.
- Give the parent/carer a PediCAP contact card (if local ethics body allows). Complete the study team's contact details and details of the follow-up appointments.

If you have any concerns contact the study team:

Name of doctor/nurse:

Telephone number:

Address:

Next Appointments:

		Date	Time
1	Telephone		
2	Telephone		
3	Telephone		
4	In clinic		

Drug Information Leaflet

The parent/carer should be given a Drug Information Leaflet to take home with them.

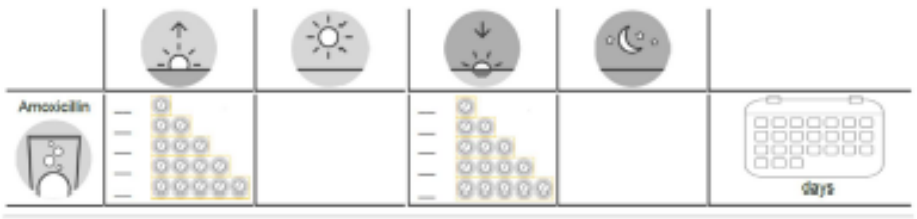
Complete the number of extra tablets they have been provided and point this out to them, explaining that they should bring this many tablets back with them at the week 4 visit unless they lose a dose or their child vomits a dose

Drug Information Leaflet: Amoxicillin

PediCAP: Impact of oral step-down to amoxicillin or co-amoxiclav and of duration of antibiotic therapy on effectiveness, safety and selection of antibiotic resistance in severe childhood community-acquired pneumonia (CAP): a randomised controlled trial

- Please read this information carefully.
- If you have any questions, please contact your study doctor/nurse.
- **It is very important that even if your child seems better, they must continue to take all the tablets for the all the days prescribed.**

Your child's treatment



- You should give your child's medicine in the morning and in the evening.
- Your child should take the indicated number of tablets each time.
- Your child should take the tablets provided for the indicated number of days.

How should the tablets be taken?

- The tablets should be taken with food at the start of a meal.
- The tablets should be taken at roughly the same time each day.
- Tablets should be dissolved in clean water or another liquid such as breast milk.
- Leave the tablet in approximately 10ml (2 teaspoons) of the liquid to completely dissolve, and then swallow down with water or another liquid.
- The tablets should never be swallowed whole, divided, chewed or crushed.

Wh… treatment?

You have been provided with ☐ extra tablets.

…et or your child vomits a dose (please see instructions below on missed and vomited doses). **These are the only times your child should take the extra tablets.**

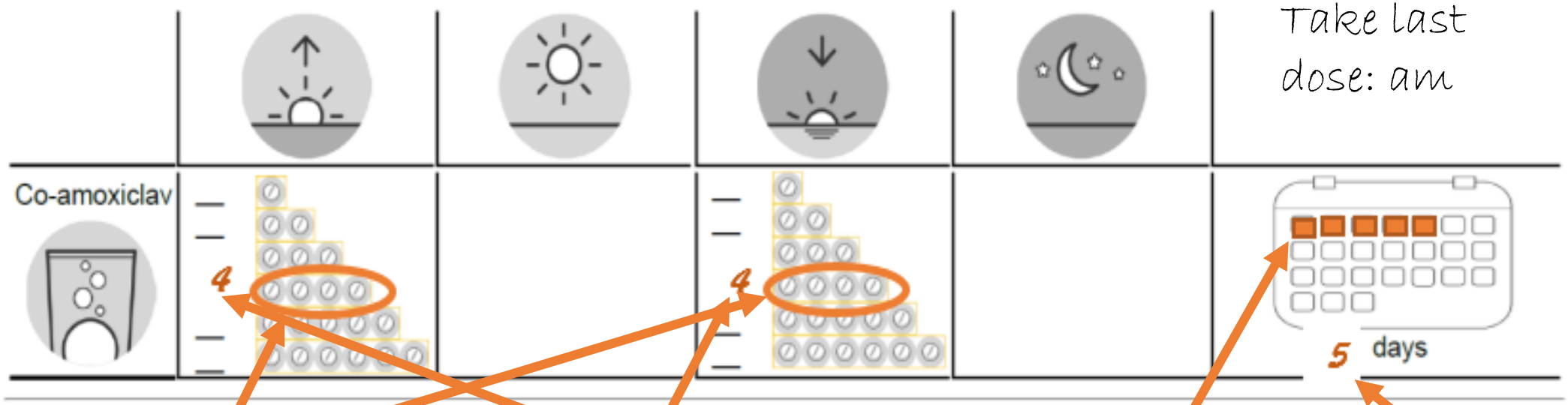
- Any tablets left over should be brought back to the clinic on your week 4 visit.

Ensure to give the leaflet for the correct drug.

Complete the details on the pictogram.

Completing the pictogram

Add a reminder of whether the last dose will be taken in the am or pm



Circle the correct number of tablets that the child should taken in the morning and evening

Write the number of tablets next to the picture

Fill in the number of days that the child should take the tablets for

Write the number of days underneath