**Appendix 2: Puberty Induction Algorithm**

**Pubertal induction**

* BOYS: transdermal testosterone commencing as ½ a sachet of Testogel® 50mg sachets daily or 2 actuations of Testogel® pump, then increasing slowly to 1 sachet/day (for sachets) or 4 actuations daily (for pump) at 6 months, 2 sachets/day (for sachets) or 8 actuations daily (for pump) at 12 months to mimic normal pubertal progress. Maximum dose of 2 sachets daily (for sachets) or 8 actuations daily (for pump).

Pump or sachet choice will be dependent on availability of product.

An equivalent product can be given if the PI deems it to be appropriate.

* GIRLS: transdermal oestrogen commencing at standard dosing of half a Climara® 25 (2mg oestradiol) patch weekly, with slow increases, to full patch at 6 months, then Climara® 50 (3.8mg oestradiol) patch at 12 months, to mimic normal pubertal progress Maximum dose of Climara® 50 patch weekly

Please see algorithm for dose changes below: All dosing changes are based on the participant’s preceding visit.

**BOYS:**

|  |  |  |
| --- | --- | --- |
| **Duration of dosing** | **Participant changes** | **Dose changes** |
| Screening – 3 months | All participants will start at ½ Sachet or 2 actuations of Testogel® daily |
| At 3 months visit  | Increase of AT LEAST one level of Tanner staging | No changes |
| No changes to puberty | Increase to 1 sachet /day (for sachets) or 4 actuations daily (for pump) |
| At 6 months visit | Increase of AT LEAST one level of Tanner staging | No changes |
| No changes to puberty | If patient is currently on ½ sachet/2 actuations of Testogel®, increase to 1 sachet/4 actuations daily of Testogel® If patient is currently on 1 sachet/4 actuations of Testogel®, increase to 2 sachets daily/8 actuations daily of Testogel®  |
| At 9 months visit | Increase of AT LEAST one further level of Tanner staging | No changes |
| No changes to puberty | If patient is currently on ½ sachet/2 actuations of Testogel®, increase to 1 sachet/4 actuations daily of Testogel® If patient is currently on 1 sachet/4 actuations of Testogel®, increase to 2 sachets daily/8 actuations daily of Testogel®If patient is currently on 2 sachets daily/8 actuations daily, make no further changes as this is the maximum dose. |
| At 12 months visit | Increase of AT LEAST one further level of Tanner staging | No changes |
| No changes to puberty | If patient is currently on ½ sachet/2 actuations of Testogel®, increase to 1 sachet/4 actuations daily of Testogel® If patient is currently on 1 sachet/4 actuations of Testogel®, increase to 2 sachets daily/8 actuations daily of Testogel®If patient is currently on 2 sachets daily/8 actuations daily, make no further changes as this is the maximum dose. |
| From 12- 24 months visit | No further changes to dosage |

**GIRLS:**

|  |  |  |
| --- | --- | --- |
| **Duration of dosing** | **Participant changes** | **Dose changes** |
| Screening – 3 months | All participants will start at ½ patch of Climara® 25, weekly |
| At 3 months visit  | Increase of AT LEAST one level of Breast Tanner staging | No changes |
| No changes to puberty | Increase to one patch of Climara® 25 weekly |
| At 6 months visit | Increase of AT LEAST one level of Breast Tanner staging | No changes |
| No changes to puberty | If patient is currently on ½ patch of Climara® 25 weekly, increase to 1 full patch of Climara® 25 weeklyIf patient is currently on 1 full patch of Climara® 25 weekly, increase to 1 and a half patches of Climara® 25 weekly |
| At 9 months visit | Increase of AT LEAST one level of Breast Tanner staging | No changes |
| No changes to puberty | If patient is currently on ½ patch of Climara® 25 weekly, increase to 1 full patch of Climara® 25 weeklyIf patient is currently on 1 full patch of Climara® 25 weekly, increase to 1 and a half patches of Climara® 25 weeklyIf patient is currently on 1 and half patches of Climara® 25 weekly, increase to one patch of Climara® 50 weekly |
| At 12 months visit | Increase of AT LEAST one level of Breast Tanner staging | No changes |
| No changes to puberty | If patient is currently on ½ patch of Climara® 25 weekly, increase to 1 full patch of Climara® 25 weeklyIf patient is currently on 1 full patch of Climara® 25 weekly, increase to 1 and a half patches of Climara® 25 weeklyIf patient is currently on 1 and half patches of Climara® 25 weekly, increase to one patch of Climara® 50 weeklyIf patient is currently on 1 full patch of Climara® 50 weekly, then no changes |
| From 12- 24 months visit | No further changes to dosage |

**Appendix 2 – Telephone interview questionnaire for phase 1**

1. Why was puberty/low sex hormones a concern initially?
2. What hormonal treatment(s) did you / your child receive?
3. What age was this commenced?
4. Did you / your child experience any problems giving this medication?
	1. Testogel: female carer any concerns?
	2. Swallowing difficulties for oral medications
	3. Patches (oestrogen/testosterone): falling off
	4. Injections of hormone eg testosterone for boys
	5. Bisphosphonates? Any side effects
5. Do you /your child think there was any useful benefit from receiving this medication and if so, please describe what you felt to be helpful?
6. Were there any benefits to mood or cognition/understanding after receiving this medication?
7. Did you notice any possible side effects or problems associated with this medication?
8. Were there any problems with behaviour or mood after starting this medication?
9. (Females only) Were there any problems with periods if female hormone treatment was used? If yes, specify (heavy bleeding, painful bleeding, irregular bleeding, difficulty with maintaining hygiene)
	1. (Males only) Were there any problems with aggression after starting this medication? If yes, could you please briefly describe the nature of the problem
10. Do you continue to take sex hormones? Can you briefly describe the reason the treatment has been continued or why it was stopped
11. If you / your child is continuing to have hormone treatment who supervises this for you? If yes, how often do you see a specialist?
12. (No follow up patients) What have been the difficulties, (if any) with following up this issue?
13. Have you/ your child had any fractures (breaks in long bones) in the past?
	1. If so: can you briefly describe which bone was involved, what happened to cause the break, if you know, and what treatment was needed eg plaster cast, operation …
	2. How do the timing of the fractures relate to the use of the hormone replacement?
14. Do you have any persistent aches and pains?
15. Have you had a bone density scan? If so could you please tell us where it was done and roughly when so we can check it for you.
16. Please tell us about whether you/your child can stand or walk and if so for how long each day
17. Do you have any concerns about body size or weight? – too heavy, too light?