[The following text is a response to the use of a dosage of 50 mg/day bicalutamide as a puberty blocker in transgender girls in this 2017 study; Google Scholar link of study; publisher link of study.]

I believe that the 50 mg/day dosage for bicalutamide may be too low. I've come to this conclusion primarily due to the data in this paper of bicalutamide monotherapy in men with prostate cancer. Specifically, the rates of breast events, which I've adapted from the paper as follows:

Side effect	10 mg/day (n = 45)	30 mg/day (n = 75)	50 mg/day (n = 147)	100 mg/day (n = 56)	150 mg/day (n = 66)	200 mg/day (n = 29)
Gynecomastia	4/44 (9%)	14/54 (26%)	50/137 (36%)	44/56 (79%)	50/64 (78%)	23/29 (79%)
Breast tenderness	5/44 (11%)	22/53 (42%)	67/139 (48%)	48/56 (86%)	57/64 (89%)	23/29 (79%)

The rates of gynecomastia with bicalutamide were much higher in the 100 mg/day group (79%) compared to the 50 mg/day group (36%). In contrast, the rates of gynecomastia did not significantly differ between the 100 mg/day, 150 mg/day, and 200 mg/day groups (79%, 78%, and 79%, respectively). These results suggest that the antiandrogenic efficacy of bicalutamide in these men, at least in terms of breast events, was not maximal until a dosage of at least 100 mg/day.

It's also very important to note that the initial testosterone levels in these men were low; they were only about 300 to 400 ng/dL before treatment, and increased to about 450 to 600 ng/dL following introduction of bicalutamide monotherapy. See the following table also adapted from the paper:

Dosage	Before	After[a]	Change
10 mg/day	400 ng/dL	490–520 ng/dL	+21–29%
30 mg/day	320 ng/dL	490–550 ng/dL	+55–73%
50 mg/day	370 ng/dL	550–610 ng/dL	+46–62%
100 mg/day	320 ng/dL	460–490 ng/dL	+45–55%
150 mg/day	290 ng/dL	460–490 ng/dL	+60–70%
200 mg/day	320 ng/dL	520–550 ng/dL	+64–73%
[a] = After 29 to 85 days of treatment.			

Mean testosterone levels in healthy young men are a good amount higher than the initial levels that were present in these older men with prostate cancer. Testosterone levels during puberty in males are low at first but reach near-adulthood levels by roughly age 15, according to the sources I looked through. I've put together a table here:

Life stage	Tanner stage	Age range[1]	Mean age[1]	T levels range[2]	Mean T levels[3]
Child	Stage I	<10 years	–	<30 ng/dL[4]	5.8 ng/dL
Puberty	Stage II	10–14 years	12 years	<167 ng/dL	40 ng/dL
	Stage III	12–16 years	13–14 years	21–719 ng/dL	190 ng/dL
	Stage IV	13–17 years	14–15 years	25–912 ng/dL	370 ng/dL
	Stage V	13–17 years	15 years	110–975 ng/dL	550 ng/dL
Adult	–	≥18 years	–	250–1,100 ng/dL[5]	630 ng/dL

I imagine that in younger men and in males in the latter half of puberty, bicalutamide monotherapy might increase mean testosterone levels to the high end of the normal male range. If we assume that bicalutamide will increase testosterone levels by about 65% (roughly the median of the first table above), that would be mean levels of about 900 ng/dL in 15-year-old pubertal males and mean levels of about 1,000 ng/dL in adult males (based on the values from the second table above). Hence, it's possible that bicalutamide monotherapy could be as much as almost half as potent in younger males relative to older men with prostate cancer.

The preceding was the most important information I have in regards to bicalutamide dosage, but I also have some additional information. According to this Cochrane review, 150 mg/day bicalutamide monotherapy is slightly but significantly less effective than GnRH agonists and surgical castration in the treatment of prostate cancer. However, while very interesting, this statistic is complicated by a couple of factors for our purposes: 1) about 90% of testosterone in the prostate gland is transformed into DHT (source), a significantly more potent androgen, and hence androgen signaling in the prostate gland is estimated to be about 2- to 3-fold higher than in most other parts of the body (source); and 2) while GnRH agonists and surgical castration reduce circulating levels of testosterone by 95 to 97%, they only reduce DHT levels in the prostate gland by about 50 to 75% (source). Hence, the effectiveness of 150 mg/day bicalutamide monotherapy versus GnRH agonists/castration in prostate cancer unfortunately can't directly tell us about their comparative antiandrogenic efficacies elsewhere in the body. Otherwise this might have been very helpful for determining the minimal equivalent dosage of bicalutamide relative to GnRH agonists for use as a puberty blocker. I think it is still potentially useful information to know though as the two aforementioned complicating factors would appear to *very roughly* cancel each other out, suggesting that 150 mg/day bicalutamide monotherapy might indeed be similar to GnRH agonists/castration in terms of general/extraprostatic antiandrogenic efficacy. Certainly take that with a grain of salt though. And of course we should remember that testosterone levels are a good deal lower in older men with prostate cancer relative to younger males, as I wrote on above.

A recent phase III clinical trial of bicalutamide in combination with a combined oral contraceptive for severe hirsutism in women with polycystic ovary syndrome used a dosage of 50 mg/day bicalutamide (link). Testosterone levels are elevated in PCOS, I believe to 50 to 200 ng/dL, and this is probably why the researchers used the higher dosage of bicalutamide than in previous studies of bicalutamide for

hirsutism (which have used 25 mg/day). It's important to note though that the combined oral contraceptive contained ethinylestradiol, which can reduce free levels of testosterone by 40 to 80% via markedly increased production of SHBG (source), and hence itself is a rather efficacious antiandrogen. This suggests that the study authors thought that 50 mg/day bicalutamide was the appropriate necessary dosage for blocking the effects of relatively low levels of testosterone. It is entirely possible that their dosage was overkill though (perhaps intentionally for the purpose of assured maximal effectiveness).

Lastly, the studies of bicalutamide for familial male-limited precocious puberty (testotoxicosis) have used a dosage of 50 mg/day, with significant effectiveness observed. I've only looked through these studies briefly. But I imagine that in these boys, complete blockade of androgen signaling might not be considered essential. Instead, partial blockade of androgen signaling, enough to help reduce pubertal development and delay puberty a bit, might be considered satisfactory. In contrast, maximal blockade of androgen signaling in transgender girls is arguably more critical. If androgen signaling is insufficiently blocked, that could translate into significant and irreversible masculinization (e.g., voice deepening, etc.), effects that would be very undesirable in a transgender girl (but of relatively little importance in a boy with testotoxicosis). And it doesn't take much testosterone to cause some of these changes (namely voice deepening). Hence, I am very cautious on equating the 50 mg/day dosage used as a puberty blocker in testotoxicosis to necessarily be the proper dosage for blocking puberty in transgender girls.

I think that bicalutamide is a great antiandrogen and I very much hope to see it used more both in transgender and cisgender women. It has many advantages over its alternatives. But I think that for transgender girls on its own as a puberty blocker, based on all of the above, there are good indications that the 50 mg/day dosage may be inadequate, at least beyond the earlier stages of puberty. I do not know what the proper dosage would be. But, if I had to make an informed guess, I would assume that it would be more in the area of *at least* 150 to 200 mg/day, again based on all of the above. The 150 mg/day dosage is not approved for use in the United States though, only the 50 mg/day dosage is (for prostate cancer in combination with a GnRH agonist/castration), so that complicates things in terms of insurance coverage and cost in this country. It might ultimately be a better and more certain route in many cases simply to go with a GnRH analogue for blocking puberty in transgender girls unfortunately.

On the other hand, I do think that the combination of lower-dose bicalutamide with an antigonadotropin like an estrogen or progestin to suppress testosterone levels in tandem has excellent potential for use as a puberty blocker. Estrogens and progestins can powerfully suppress testosterone levels, maximally by about 95% and 75%, respectively (e.g., link, link, link). Of course, normal female puberty will occur if an estrogen is used as the antigonadotropin, so it wouldn't exactly be "puberty blockade" in that case per se. But changes that occur in normal female puberty are something that will pretty much happen with bicalutamide on its own similarly, as the study of 50 mg/day bicalutamide as a puberty blocker in transgender girls demonstrated and as we know from women with complete androgen insensitivity syndrome – more or less a biological model of a pure androgen receptor antagonist at a fully efficacious dosage as a puberty blocker in genetic males (link). Hence, simply adding estradiol might be a really favorable route. Puberty "replacement" rather than "blockade", so to speak.

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[The following text is elaboration of the preceding excerpt.]

If there's 90% conversion of T into the more potent AR agonist DHT in the prostate gland, and AR signaling is estimated to be 2- to 3-fold greater in the prostate gland than in the rest of the body because of this, then that is 200 to 300% of the AR signaling of "normal" there. GnRH analogues reduce circulating T levels by 95%, so let's assume that that's the case for T/DHT levels in the prostate gland as well (it's not, but just assume that for now). If 150 mg/day bicalutamide monotherapy is nearly as effective as GnRH analogues for prostate cancer and we're using GnRH analogue efficacy as a proxy for bicalutamide efficacy, then this implies that bicalutamide must be a pretty powerful AR antagonist to be able to overcome all of that DHT. Moreover, it would imply that bicalutamide is having 2- to 3-fold stronger AR antagonist effects elsewhere in the body where AR signaling is lower relative to in the prostate gland.

However, the situation is more complicated and there is more to the story than that. For this part, let's ignore the preceding paragraph and pretend that under normal circumstances the amount of AR signaling in the prostate gland is the same as that in the rest of the body. If GnRH analogues only decrease T/DHT levels in the prostate gland by 50 to 75%, then that implies that GnRH analogues cause AR signaling in the prostate gland to be reduced only to 25 to 50% of normal (relative to 5% or less elsewhere in the body). If we use GnRH analogue efficacy for prostate cancer as a proxy for bicalutamide efficacy again, and if 150 mg/day bicalutamide monotherapy isn't as effective as GnRH analogues for prostate cancer even though GnRH analogues only decrease T/DHT levels in the prostate gland by 50 to 75% (as opposed to 95%+), then this implies that bicalutamide must be a pretty weak AR antagonist. Moreover, it implies that the 150 mg/day monotherapy dosage must be leaving a lot of AR signaling (at least 25 to 50%) left over in the rest of the body and hence is quite inferior to GnRH analogues there.

To get the reality of the situation, we have to combine both factors. If we cross 200 to 300% (AR signaling in the prostate gland normally) and 25 to 50% (remaining AR signaling in the prostate gland with GnRH analogues), we get 50 to 150%, or (surprisingly) a median perfect 100%. In other words, based on this median value, the two opposite and opposing influences have perfectly cancelled each other out; 150 mg/day bicalutamide monotherapy is 100% as effective as GnRH analogues in terms of antiandrogenic efficacy in men with prostate cancer not only in the prostate gland but also elsewhere in the body. However, since we're extrapolating heavily, going based on widely varying ranges rather than more uniform values, and not necessarily accounting for other possible confounding variables that could be present, this is an *extremely rough* estimate of comparative efficacy. Hence why I said "take this with a grain of salt".

Moreover, we also have to keep in mind that 150 mg/day bicalutamide monotherapy is not quite equivalent to GnRH analogues in terms of prostate cancer effectiveness but is actually slightly albeit significantly less effective than them. In addition, we have to remember that testosterone levels are roughly almost twice as high in younger men (or perhaps this is actually men as a group) than in older men. These two facts are of course not in bicalutamide's favor. Hence why it’s quite possible that even 150 to 200 mg/day bicalutamide might not be enough for use as a fully efficacious puberty blocker, at least in late-pubertal transgender girls or pubertal transgender girls with high testosterone levels.