CASE AUTH/3137/12/18

VIIV HEALTHCARE v GILEAD SCIENCES

Promotion of Biktarvy (bictegravir, emtricitabine and tenofovir)

ViiV Healthcare Ltd complained about material used by Gilead Sciences Europe Ltd to promote Biktarvy (bictegravir/emtricitabine/tenofovir) at the HIV Drug Therapy Conference in Glasgow, 28-31 October 2018. Biktarvy was used in the treatment of adults infected with human immunodeficiency virus-1 (HIV-1). ViiV promoted, *inter alia*, Juluca (dolutegravir (DTG)/rilpivirine) for the treatment of HIV-1 infection in adults.

ViiV stated that its complaint related to a stand panel and videos (original and revised) that appeared on the stand.

The case preparation manager decided that inter-company dialogue on the original video was successful and therefore that complaint did not proceed. The matter in relation to the revised video did proceed.

The detailed response from Gilead is set out below.

Gilead explained that four different items appeared on the stand including two static image stand panels (BIK\IHQ\18-09\\1177b and BIK\IHQ\18-09\\1177c), the revised video (BIK\IHQ\18-09\\1177a(1)) which was shown as three separate videos looping simultaneously in different areas of the stand and another standalone looping video (BIK\IHQ\18-09\\1177d).

Gilead requested that the Authority considered the complaint in the context of all claims and imagery available on all four separate items.

1 Claim 'Better tolerated than DTG-containing regimens'

This claim was prominently displayed on the stand panel and as part of the revised video. The claim was accompanied by a dagger symbol which referred the reader to the statement 'Significantly fewer all grade treatment-related AEs [adverse events] compared to DTG plus ABC/3TC [abacavir/lamivudine] or FTC/TAF [emtricitabine/ tenofovir alafenamide] (secondary endpoint)'.

ViiV alleged that the claim was not fair or balanced and was misleading. The claim overstated the differences in tolerability profiles comparing Biktarvy with dolutegravir (DTG)-containing regimens. The footnote, in smaller print below the claim, only referred to all-grade treatment-related adverse events from the treatment naïve studies GS-1489 (Gallant *et al* 2017) and GS-1490 (Sax *et al* 2017), and did not refer to the full tolerability profile of the study comparators in those treatment-naïve studies or refer to study GS-1844 (Molina *et al* 2018*)*. Detailed review of all of the tolerability and safety sections of

these studies led to the conclusion that the overall tolerability and safety profiles of these regimens were similar.

ViiV alleged that the deliberate use of highly selected data from a larger dataset to qualify, as a footnote to a much broader unsubstantiated claim were breaches of the Code including not maintaining high standards. Tolerability was the ability to tolerate a medicine and was not defined by the single parameter of all grade adverse events. It was more usually assessed by other measures such as the rate of drug-related discontinuations and/or more severe adverse events.

The Panel noted that the claim 'Better tolerated than DTG-containing regimens' which appeared on the stand panel (BIK\IHQ\18-09\\1177b) and in the revised video (BIK\IHQ\18-09\\1177a(1)) specifically referred to by ViiV was referenced to Gilead Data on File, Gallant *et al*, Sax *et al*, and contrary to ViiV's submission, Molina *et al*. In both materials, directly above the claim, it stated 'In Phase 3 clinical trials' and directly below the claim was the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)'. The Panel noted that although the statement appeared within the same visual field as the claim, it was in much smaller, less prominent font than the claim 'Better tolerated than DTG-containing regimens'.

The Panel noted that although the statement appeared to reflect the information in studies GS-1489, GS1490 and GS1844 with regard to all-grade treatment-related adverse events, it did not reflect the results with regards to the other factors within these studies which might contribute to the tolerability profiles of the medicines or the overall conclusions of the studies with regard to tolerability. The Panel considered that the immediate impression of the claim 'Better tolerated than DTG-containing regimens' to readers, would be that Biktarvy was better tolerated than all DTG-containing regimens which was misleading and could not be substantiated by the referenced studies and the statement immediately beneath did not negate this misleading impression. Further, in the Panel's view, better tolerability might imply statistically significant differences in measures other than all grade treatment-related adverse events eg rates of discontinuation. In this regard, the Panel noted Gilead's submission that the rates of discontinuation between the treatment groups in GS-1489, GS-1490 and GS-1844 were not statistically significantly different. The Panel considered therefore that the claim 'Better tolerated than DTG-containing regimens' was misleading, exaggerated Biktarvy's properties, was not capable of substantiation and was not qualified by the statement that followed. Breaches of the Code were ruled including that high standards had not been maintained. These rulings were upheld on appeal from Gilead.

2 Use of imagery showing a rose which had shed many of its thorns

This imagery described by ViiV appeared on the stand panel (ref BIK\IHQ\18-09\\1177c) which was not specifically referred to by ViiV and only the image of a rose head appeared in the revised video referred to by ViiV (BIK\IHQ\18-09\\1177a(1)).

The stand panel included an image of a rose which had shed a number of thorns which lay beside it. Above it stated 'The beauty of what is possible' followed by 'Biktarvy (BIC/FTC/TAF) combines bictegravir – a novel INSTI – with DESCOVY▼ (FTC/TAF), a durable guideline-preferred dual-NRTI backbone'.

The revised video contained a number of claims including the claim at Point 1.

ViiV alleged that the depiction of a rose with most of its thorns shed, immediately after the contested claim suggested an overstated tolerability and safety profile improvement with Biktarvy compared with DTG-containing therapy. This could not be substantiated by the body of evidence from the studies as outlined above. The imagery implied that Biktarvy was 'safe' or 'safer'. ViiV alleged that the use of the words 'safe' and 'safer' were in breach of the Code.

ViiV alleged that associations between the rose, loss of thorns and the claim appeared throughout the booth and were clearly meant to imply that Biktarvy had a superior tolerability profile (dropping of thorns) and that DTG-containing regimens might cause pain or harm to HIV patients. ViiV alleged that if the campaign misrepresented safety and disparaged a competitor then it also brought the industry into disrepute.

In the Panel's view, on the balance of probabilities, most readers would associate the picture of the rose as representing Biktarvy. The Panel considered that thorns on a rose stem would be seen as something injurious rather than representing different attributes as described by Gilead; the imagery implied that Biktarvy might cause less injury in comparison with a 'rose' with more thorns. The Panel considered that within the context of the stand, it appeared that Biktarvy was being compared to DTG-containing regimens as acknowledged by Gilead.

The Panel noted that although only the rose head appeared throughout the revised video, the video was displayed within the context of the stand and, in the Panel's view, visitors to the stand would make a connection between the rose with thorns beside it on the stand panel and the rose head in the revised video. The Panel noted that the revised video was made up of three separate videos looping simultaneously in different areas of the stand.

The Panel noted that within the three video loops, an image of the rose head appeared directly before and/or directly after the following claims, which all included the caveat 'In Phase 3 clinical trials': Better tolerated than DTG-containing regimens; Small STR with flexible daily dosing; >90% efficacy and 0 resistance. In the Panel's view, ViiV had not established that the flower head image within the three video loops was a hanging comparison as alleged and therefore no breach was ruled in that regard.

The Panel considered, on the balance of probabilities, that visitors to the stand would associate the image of the rose head in the videos appearing before and after the claims including 'Better tolerated than DTG-containing regimens' with the image of the rose with some dropped thorns on the stand panel. The Panel considered, therefore, that the video, by association with the imagery and claim on the stand panel and the claim 'Better tolerated than DTG-containing regimens' within the video loops, implied that Biktarvy was less hazardous than DTG-containing regimens and it considered that this implication could not be substantiated and disparaged DTG-containing regimens. Breaches of the Code were ruled. These rulings were upheld on appeal by Gilead.

The Panel did not consider that the rose head depicted in the video implied that Biktarvy was safe as alleged; no breach was ruled.

The Panel ruled a breach as Gilead had failed to maintain high standards. This ruling was upheld on appeal from Gilead.

On balance, the Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use.

3 Claim 'The beauty of what is possible … Biktarvy … is now a reality'

This claim appeared within the revised video (ref BIK\IHQ\18-09\\1177a(1)) specifically referred to by ViiV.

ViiV alleged that the claim could not be substantiated; it promised a brighter future, even a utopian state of antiretroviral treatment beyond what other regimens delivered. At best, this was ambiguous and at worst it overstated the benefits of Biktarvy.

The Panel noted Gilead's submission that the claim at issue was meant to introduce the subsequent claims (>90% efficacy and 0 resistance (Non-inferior vs comparator in all registrational studies), better tolerated than DTG-containing regimens (significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF) and small, single tablet regimen with flexible daily dosing), and add to this that Biktarvy was now available.

The Panel considered that the claim 'The beauty of what is possible … Biktarvy … is now a reality' when considered in isolation was not necessarily unreasonable. However, the context of the claim within the material and in relation to all the materials on the stand was relevant. The Panel noted its comments and rulings above at Points 1 and 2 and considered that they were relevant here. The Panel considered that linking the claim 'The beauty of what is possible … Biktarvy … is now a reality' in the video (ref BIK\IHQ\18-09\\1177a(1)) which also included the claim 'Better tolerated than DTG-containing regimens' and the rose imagery was misleading and exaggerated the properties of Biktarvy. The Panel therefore ruled breaches of the Code. These rulings were upheld on appeal by Gilead.

ViiV Healthcare Ltd complained about material used by Gilead Sciences Europe Ltd to promote Biktarvy (bictegravir/emtricitabine/tenofovir) at the HIV Drug Therapy Conference 2018 held in Glasgow, 28-31 October. Biktarvy was used in the treatment of adults infected with human immunodeficiency virus-1 (HIV-1). ViiV promoted, *inter alia*, Juluca (dolutegravir (DTG)/rilpivirine) for the treatment of HIV-1 infection in adults.

COMPLAINT

ViiV stated that its complaint related to items: BIK\IHQ\18-09\\1177b which was a stand panel and videos BIK\IHQ\18-09\\1177a (original) and BIK\IHQ\18-09\\1177a(1)) (revised) which appeared on the stand.

The case preparation manager decided that inter-company dialogue on the original video was successful and therefore the complaint did not proceed. The matter in relation to the revised video did proceed.

Gilead explained that four different items appeared on the stand including two static image stand panels (BIK\IHQ\18-09\\1177b and BIK\IHQ\18-09\\1177c, the revised video (BIK\IHQ\18-09\\1177a(1)) which was shown as three separate videos looping simultaneously in different areas of the stand and another standalone looping video (BIK\IHQ\18-09\\1177d).
Gilead described the four materials and requested that the Authority considered the complaint in the context of all claims and imagery available on all four separate items.

The largest panel (BIK\IHQ\18-09\\1177c) introduced the campaign with the title 'The Beauty of What is Possible' followed by the claim 'Biktarvy (BIC/FTC/TAF) combines bictegravir-a novel INSTI-with DESCOVY (FTC/TAF), a durable guideline-preferred dual NRTI-backbone', alongside the Biktarvy logo. This was accompanied with an image of a rose with thorns, alongside some thorns which were removed from the stem.

The second panel (BIK\IHQ\18-09\\1177b), which was specifically referred to by ViiV had the same subheading 'Biktarvy (BIC/FTC/TAF) combines bictegravir- a novel INSTI-with DESCOVY (FTC/TAF), a durable guideline-preferred dual NRTI-backbone' and included three claims each of which were stated on three separate panels:

- In Phase III clinical trials:>90% efficacy and 0 resistance
- In Phase III clinical trials: Better tolerated than DTG-containing regimens
- In Phase III clinical trials: small STR [single tablet regimen] with flexible daily dosing.

Gilead stated that the videos that formed part of ref BIK\IHQ\18-09\\1177a(1), which was the revised video referred to by ViiV, contained a combination of the same copy described above, with one additional question posed at the front of the looping video 'How does Biktarvy achieve durability for what's ahead?'. These videos were depicted visually by a combination of moving shapes that transitioned periodically to a rose, focused on the image of the flower.

Finally, the second video BIK\IHQ\18-09\1177d looped through to repeatedly show the Biktarvy logo and intermittently included the statement flow 'The beauty of what is possible … Biktarvy … is now a reality'. There was no image of the rose, or rose and thorns as part of this video.

1 Claim 'Better tolerated than DTG-containing regimens'

This claim was prominently displayed on the stand panel referred to by ViiV (BIK\IHQ\18-09\\1177b) and as part of the revised video referred to by ViiV which was available as three separate videos looping simultaneously in different areas of the stand (BIK\IHQ\18-09\\1177a(1)). The claim was accompanied by a dagger symbol which referred the reader to the statement 'Significantly fewer all grade treatment-related AEs [adverse events] compared to DTG plus ABC/3TC [abacavir/lamivudine] or FTC/TAF [emtricitabine/ tenofovir alafenamide] (secondary endpoint)'.

COMPLAINT

ViiV alleged that the claim was not fair or balanced and was misleading. The claim overstated the differences in tolerability profiles comparing Biktarvy with dolutegravir (DTG)-containing regimens. The footnote, in smaller print below the claim, only referred to all-grade treatment-related adverse events from the treatment naïve studies GS-1489 (Gallant *et al* 2017) and GS-1490 (Sax *et al* 2017), and did not refer to the full tolerability profile of the study comparators in those treatment-naïve studies or refer to study GS-1844 (Molina *et al* 2018*)*. In Molina *et al*

which compared switching to Biktarvy with continuing DTG/abacavir/lamivudine, the discontinuation rate due to adverse events was numerically higher in the Biktarvy arm compared with the comparator arm which contained DTG.

Detailed review of all of the tolerability and safety sections of these studies led to the conclusion that the overall tolerability and safety profiles of these regimens were similar. Regulatory bodies had assessed these data and the European Medicines Agency (EMA) had concluded the following in the Biktarvy European Public Assessment Report for study GS-1490 (Sax *et al*): 'As expected, the safety profile of B/F/TAF is similar to DTG+FTC/TAF'. It went on to state 'Discontinuation due to adverse events: the rate of discontinuation due to AE with B/F/TAF is low (≤2%), similarly to the comparators groups'. The Food and Drug Administration (FDA) also made a similar assessment of the overall data.

There were other adverse event line listings from these studies where the numerical differences sometimes favoured Biktarvy and sometimes favoured the comparator (DTG-containing regimen). For example, the clinically important categories of 'Any SAE [serious adverse event], Grade 3-4 AEs and drug-related grade 3/4 AEs', were numerically in favour of DTG-containing regimens in the naïve studies.

ViiV alleged that the deliberate use of highly selected data from a larger dataset to qualify, as a footnote to a much broader unsubstantiated claim was a breach of Clauses 7.2, 7.3, 7.4 and 7.10 and did not maintain high standards in breach of Clause 9.1. Tolerability was the ability to tolerate a medicine and was not defined by the single parameter of all grade adverse events. It was more usually assessed by other measures such as the rate of drug-related discontinuations and/or more severe adverse events.

ViiV noted that during inter-company dialogue Gilead had submitted that the footnote was in fact a bullet point. However, the use of both a smaller font size and the superscript dagger (†) footnote indicator adjacent to the references and the claim indicated otherwise. ViiV asserted that the annotation implied this was a footnote and it was disingenuous to imply otherwise.

On request, Gilead provided the reference (data on file) related to study GS-1489, week 48 data only, where one DTG-containing regimen (ABC/3TC/DTG) acted as the comparator. The document again asserted this was relevant for 'DTG Regimens': 'This data is internal information to support the calculation of the p value of <0.001 for Drug-Related Adverse Events through Week 48 in study 1489 - B/F/TAF vs. DTG Regimens'. The raw figures from the data on file appeared in Gallant *et al* which was also referenced to support the claim. Yet the authors interpreted the data differently to the way the main claim implied and to the data on file provided.

Gallant *et al* presented results from study GS-1489 which evaluated Biktarvy vs Triumeq (DTG/ABC/3TC (dolutegravir, abacavir, and lamivudine)) in treatment-naïve patients. Biktarvy was a co-formulation of bictegravir, emtricitabine and tenofovir alafenamide and was compared against Triumeq. ViiV alleged that the Gilead claim was disingenuous as it implied dolutegravir was the key differentiating agent in the co-formulation. However, Gallant *et al* claimed that tolerability differences (nausea) were driven by other agents within the co-formulations ie tenofovir alafenamide within Biktarvy vs abacavir within Triumeq. Specifically, the authors stated:

i) ‘Both regimens were well tolerated; adverse events leading to study discontinuation were noted in no participants in the bictegravir, emtricitabine, and tenofovir alafenamide group and 1% of participants in the dolutegravir, abacavir, and lamivudine group’.

ii) ‘We recorded more nausea adverse events in the dolutegravir, abacavir, and lamivudine group. This observation is most likely to be attributable to differences in gastrointestinal tolerability between tenofovir alafenamide and abacavir, since gastrointestinal tolerability was similar in the Phase 2 and 3 trials comparing bictegravir with dolutegravir when both were combined with emtricitabine and tenofovir alafenamide’.

In short, the GS-1489 manuscript conclusions did not match or corroborate the claim.

With regard to study GS-1490 (Sax *et al*), ViiV asserted that the highly selective use of adverse event data gave a misleading overall impression of the study results and an exaggerated claim. Study drug-related adverse events were less common in the bictegravir group than in the dolutegravir group (57 [18%] of 320 vs 83 [26%] of 325, p=0·022). However, the authors also stated that ‘Adverse events leading to study drug discontinuation were uncommon, occurring in five (2%) of 320 participants in the bictegravir group and one (<1%) of the 325 in the dolutegravir group’. The authors concluded that ‘Discontinuations due to adverse effects ascribed to study medications occurred rarely in both groups and none occurred in more than one participant, indicating a lack of a pattern to these events’.

Finally, ViiV alleged that the claim was too broad as it referred to all DTG-based regimens although the supporting data only included comparisons between Biktarvy and two DTG-containing regimens: Triumeq and DTG plus F/TAF. However, other DTG-containing regimens were also used in clinical practice. Therefore, such an all-embracing, misleading claim was exaggerated and could not be substantiated.

RESPONSE

Gilead noted that the claim in full read ‘In Phase 3 clinical trials: Better tolerated than DTG-containing regimens’ and where the claim was made, it was prominently and immediately accompanied by the qualifying statement, ‘Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF (secondary endpoint)’. This was not a footnote placed away from the headline claim at the foot of the page, but a clear statement placed next to the headline claim. The layout of the claim ensured that the reader was clear about how ‘better-tolerated’ was defined (all grade treatment-related adverse events), and the comparators against which the claim was made (DTG plus ABC/3TC or F/TAF). Gilead noted that it had also included a prominent reference to the fact that these findings were a secondary endpoint of the study, ensuring that the reader knew that the clinical trials were not designed specifically to assess these measures, which further ensured that he/she could form his/her own opinion of the therapeutic value of the medicine.

With regard to the claim, ‘Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF (secondary endpoint)’ (a claim in itself that ViiV did not dispute), the Biktarvy clinical trial registration program included four studies, three of which involved a randomised double-blind comparison against dolutegravir (DTG) in combination with either abacavir/3TC (ABC/3TC) or emtricitabine/tenofovir alafenamide (F/TAF) (Gallant *et al*, Sax *et al*,

Molina *et al*). The table below summarised the rate of all grade treatment-related adverse events for Biktarvy compared with DTG plus ABC/3TC or FTC/TAF in each of the three studies. This represented the totality of data available for this type of comparison, and within the material at issue, all supporting figures were included in small font for each study, wherever the parent claim was made, including details of all appropriate references.

			Rate of all grade treatment-related AEs (%)			
Study	**Comparators**	**Treatment population**	**Week 48**	p value	**Week 96**	p value
GS-1489	**Biktarvy**	**Naïve**	26%		28%	
(Gallant *et al*)	**DTG + ABC/3TC**		40%	p<0.001	40%	p=0.002
GS-1490	**Biktarvy**	**Naïve**	18%		20%	
(Sax *et al*)	**DTG + F/TAF**		26%	p=0.022	28%	p=0.02
GS-1844	**Biktarvy**	**Virologically Suppressed**	8%		NA*	
(Molina *et al*)	**DTG + ABC/3TC**		16%	p=0.01	NA*	

*Randomised comparison ended at Week 48 for Study GS-1844

Gilead stated that although the 96 week data was not available when the materials at issue were developed, they were presented at the end of 2018 at two international conferences, and were included here to illustrate that the legitimacy of the claims used at week 48 were maintained as more data emerged at week 96.

Gilead stated that although it made no claim about patient-reported outcomes (PROs) within the context of the materials, this observation was supported by significantly more favourable PROs for Biktarvy across multiple domains in validated scales in both registrational studies that compared Biktarvy with DTG + ABC/3TC (Wohl *et al* 2018) (data had not been evaluated comparing PROs between Biktarvy and the combination of DTG + F/TAF). Thus, not only were the claims sufficiently qualified, but they were capable of substantiation.

The claim was that in Phase 3 clinical trials Biktarvy was better tolerated than DTG-containing regimens with the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF (secondary endpoint)' that immediately and prominently followed the claim clarifying for the reader the measure of tolerability that was being used.

The claim was fair, balanced, was not misleading and appropriately stated the difference in the tolerability profile of Biktarvy compared with dolutegravir (DTG)-containing regimens observed in the Phase 3 clinical studies performed and clearly referenced.

Gilead disagreed that the absence of 'discontinuation data due to AEs' as part of this claim rendered it any less accurate or capable of substantiation. Tolerability was not, by default, defined by discontinuation rates due to AEs (ie, patients might have difficulty tolerating a

medicine but not discontinue taking it during the course of the study) and it was clear that this was not the measure relied on nor communicated in this claim. Other measures of tolerability might be an important consideration if any significantly favoured DTG + ABC/3TC or F/TAF, but this was not the case across all studies in which Biktarvy was compared with DTG + ABC/3TC or F/TAF (see table below for a summary of data across all studies for the measure 'discontinuation due to AEs'). It was also important that the claim was a tolerability claim and not a safety claim and Gilead's stand did not contain a promotional claim about safety.

			Discontinuations due to AEs (%)			
Study	**Comparators**	**Treatment population**	**Week 48**	p value	**Week 96**	p value
GS-1489	**Biktarvy**	**Naïve**	0%[1]		0%[4]	
	DTG + ABC/3TC		1%[1]	p=NS	1.6%[4]	p=NS
GS-1490	**Biktarvy**	**Naïve**	2%[2]		1.9%[5]	
	DTG + F/TAF		<1%[2]	p=NS	1.6%[5]	p=NS
GS-1844	**Biktarvy**	**Virologically Suppressed**	2%[3]		NA*	
	DTG + ABC/3TC		1%[3]	p=0.29	NA*	

*Randomised comparison ended at Week 48 for Study GS-1844

[1] – Gallant *et al*, [2] – Sax *et al*, [3] – Molina *et al,* [4] – Wohl *et al*, [5] – Stellbrink *et al*

The statement, 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF (secondary endpoint)' cross referenced three studies (Gallant *et al*, Sax *et al*, Molina *et al*). Contrary to the complaint letter, study GS-1844 was referenced as were all randomised double-blind studies where Biktarvy was compared against dolutegravir (DTG) in combination with either abacavir/3TC (ABC/3TC) or emtricitabine/tenofovir alafenamide (F/TAF).

Gilead noted ViiV's position that the claim was unacceptable because there were other adverse event line listings from the referenced studies (eg 'Any SAE, Grade 3-4 AEs and drug-related grade 3/4 AEs') where the numerical differences sometimes favoured Biktarvy and sometimes favoured the comparator (DTG-containing regimen). Gilead did not agree that not including these other measures of adverse events as part of the claim rendered the promotional claim any less accurate or capable of substantiation. As noted by ViiV, only small numerical differences were observed across these measures, the direction of which sometimes favoured Biktarvy and sometimes favoured comparator. Given these measures essentially neutralised each other, any differences in tolerability (to support the claim 'better tolerated') were driven by significant differences in all grade treatment-related adverse events, a claim which ViiV had acknowledged was capable of substantiation.

Overall, given the clear layout of the claims, it was clear that the claim 'better tolerated' was based solely on differences in all grade treatment-related adverse events, thus health

professionals could understand the basis of the claim and assess whether or not it was a clinically relevant measure in the treatment of HIV.

Gilead noted ViiV's submission that tolerability, the ability to tolerate a medicine, was not defined by the single parameter of all grade adverse events and was more usually assessed by other measures such as the rate of drug-related discontinuations and/or more severe adverse events. Gilead maintained that the basis upon which the 'better tolerated' claim was made was clear, capable of substantiation, and enabled the reader to assess the therapeutic value of the medicine. Gilead did not accept ViiV's assertion that tolerability was usually assessed by other measures such as the rate of drug-related discontinuations and/or more severe adverse events; this was merely an opinion and not based on any guidance provided by regulatory authorities or within the Code.

Gilead noted that ViiV indicated in its complaint that Gilead had provided, on request, the reference BVY002 (data on file) and commented on the data provided. The data available in BVY002 was the same as that in Gallant *et al* and therefore it was unclear what ViiV had asserted.

ViiV then discussed Gallant *et al* and the authors' conclusions. Gilead acknowledged the conclusions made in the GS-1489 manuscript, but re-iterated that statistically significant differences in all grade treatment related adverse events were also observed in study 1490 (Sax *et al*), which compared Biktarvy with DTG + F/TAF. Thus, across the three studies which compared Biktarvy with DTG plus either ABC/3TC or F/TAF, where DTG was the common agent used in all comparator regimens, significant differences favouring Biktarvy were observed in all grade treatment-related adverse events.

When on therapy with combination agents the sum effect of all components of the regimen would drive the outcome (whether efficacy, tolerability or safety), and therefore the only benefit in apportioning an (adverse) outcome to one (or more) of the components of a regimen in a setting where the patient was required to take all components, was to help inform subsequent patient management. More specifically, as an example, even in a hypothetical situation where all grade treatment related adverse events was solely driven by ABC/3TC when combined with DTG (which was clearly not the case given the finding in GS-1490 that significant differences in that measure were observed when Biktarvy was compared against DTG + F/TAF), the fact was that the combination of DTG + ABC/3TC was still associated with significantly greater all grade treatment-related adverse events compared with Biktarvy. Thus, a physician armed with the conclusion from Gallant *et al* might consider removal of ABC/3TC from the regimen of DTG + ABC/3TC in a patient that experienced a treatment-related adverse event, but knowledge of this conclusion in itself did not reduce the potential incidence of treatment-related adverse events if a patient were to remain on a combination of DTG + ABC/3TC. Given the same outcome was observed when DTG was combined with F/TAF, Gilead maintained that it was appropriate to summarise the data as being vs 'DTG-containing regimens', particularly given that the items in question clearly stated that this claim was restricted to 'DTG plus ABC/3TC or F/TAF'.

Gilead noted that ViiV had also asserted that the highly selective use of adverse event data for study GS-1490 gave a misleading overall impression of the study results and an exaggerated claim. ViiV acknowledged that Sax *et al* stated that 'study drug-related adverse events were less common in the bictegravir group than in the dolutegravir group (57 [18%] of 320 vs 83 [26%] of 325, p=0·022)' but that the authors also stated that 'Adverse events leading to study drug discontinuation were uncommon, occurring in five (2%) of 320 participants in the

bictegravir group and one (<1%) of the 325 in the dolutegravir group'. ViiV identified that the authors concluded that 'Discontinuations due to adverse effects ascribed to study medications occurred rarely in both groups and none occurred in more than one participant, indicating a lack of a pattern to these events'. In doing so, ViiV conceded that there were significantly fewer all grade treatment related adverse events for Biktarvy vs DTG + F/TAF in study GS-1490, which undermined its argument regarding the conclusions of Gallant *et al*. The discussion around discontinuation data due to adverse events and other measures of adverse events, had been addressed multiple times above.

Finally, Gilead noted ViiV's assertion that the claim was too broad as it referred to all DTG-based regimens, yet, the supporting data only included comparisons between Biktarvy and two DTG-containing regimens: Triumeq and DTG plus F/TAF. On this basis, ViiV claimed that such an all-embracing, misleading claim was exaggerated and could not be substantiated. Gilead emphatically disagreed with this assertion. The relevant claim clearly specified that the comparator in this case was DTG in combination with ABC/3TC (Triumeq) or F/TAF.

Gilead noted ViiV's allegation that the deliberate use of highly selected data from a larger dataset to qualify the headline claim was a breach of Clause 7 (7.2, 7.3, 7.4) (which ViiV cited without application to the facts) and did not maintain high standards (breach of Clause 9.1). For the reasons outlined above, Gilead maintained that it had not breached any of these clauses of the Code and that it had maintained high standards in its promotion of Biktarvy.

In response to a request from the case preparation manager for Gilead to respond in relation to Clause 7.10, Gilead noted that the full context in which the claim was made was 'In Phase 3 clinical trials: Better tolerated than DTG-containing regimens' and this was prominently and immediately accompanied by the qualifying statement, '*Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF (secondary endpoint)'*. Gilead noted ViiV's allegation of a breach of Clause 7.10 in relation to this claim and could identify two elements of ViiV's complaint which were relevant to a breach of this clause.

First, ViiV assert that the highly selective use of adverse event data for study GS-1490 (Sax *et al*) gave a misleading overall impression of the study results and an exaggerated claim.

Gilead explained that the claim made clearly cross referenced three studies - GS-1489 (Galant *et al*), GS-1490 (Sax *et al*) and GS-1844 (Molina *et al*) – and clearly indicated that the claim related to all grade treatment-related AEs. Gilead submitted that it had explained why the claim was accurate and capable of substantiation. By being clear on the basis for the claim being made, with clear references, Gilead disagreed that an exaggerated claim was made and as such the claim did not breach Clause 7.10 of the Code.

Second, ViiV asserted that the claim was too broad as it referred to DTG-based regimens, yet, the supporting data only included comparisons between Biktarvy and two DTG-containing regimens: Triumeq (DTG/ABC/3TC) and DTG plus F/TAF. On this basis ViiV claimed that such an all-embracing, misleading claim was exaggerated and could not be substantiated.

Gilead disagreed with this assertion. The relevant claim clearly specified that the comparator in the claim was DTG in combination with ABC/3TC or F/TAF. In doing so, an accurate claim was made which was not an exaggerated claim in relation to other dolutegravir regimens that were not within the scope of the claim, and the claim did not breach Clause 7.10 of the Code.

PANEL RULING

The Panel noted that the claim 'Better tolerated than DTG-containing regimens' which appeared on the stand panel (BIK\IHQ\18-09\\1177b) and in the revised video (BIK\IHQ\18-09\\1177a(1)) specifically referred to by ViiV was referenced to Gilead Data on File, Gallant *et al*, Sax *et al*, and contrary to ViiV's submission, Molina *et al*. In both materials, directly above the claim, it stated 'In Phase 3 clinical trials' and directly below the claim was the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)'. The Panel noted that although the statement appeared within the same visual field as the claim, it was in much smaller, less prominent font than the claim 'Better tolerated than DTG-containing regimens'.

The Panel noted that study GS-1489 (Gallant *et al)*, a double-blind, multicentre, phase 3, randomised, controlled, non-inferiority trial comparing bictegravir/emtricitabine/tenofovir alafenamide vs dolutegravir/abacavir/lamivudine for initial treatment of HIV-1 infection, stated that adverse events related to study drug were less common with bictegravir/emtricitabine/tenofovir alafenamide than with dolutegravir/abacavir/lamivudine (26% vs 40%; p-value provided in Gilead data on file ($p<0.001$)), the difference being driven by a higher incidence of drug-related nausea in the dolutegravir/abacavir/lamivudine group (5% vs 17%; $p<0.0001$). The study authors stated that the incidence and severity of adverse events was mostly similar between groups except for nausea, which occurred less frequently in patients given bictegravir/emtricitabine/tenofovir alafenamide than in those given dolutegravir/abacavir/lamivudine. The study authors further stated that both regimens were well tolerated; adverse events leading to study discontinuation were noted in no participants in the bictegravir/emtricitabine/tenofovir alafenamide group and 1% of participants in the dolutegravir/ abacavir/lamivudine group.

The Panel noted that study GS-1490 (Sax *et al* (2017)), a Phase III non-inferiority trial of bictegravir/emtricitabine/tenofovir alafenamide [bictegravir group] vs dolutegravir/emtricitabine /tenofovir alafenamide [dolutegravir group] stated that study-drug related adverse events were less common in the bictegravir group than in the dolutegravir group (18% vs 26%, $p = 0.022$). However, the Panel noted statements in Sax *et al* that incidence and severity of adverse events were similar between groups and few participants discontinued treatment due to adverse events (2% in the bictegravir group and <1% in the dolutegravir group).

The Panel noted that study GS-1844 (Molina *et al* (2018) was a Phase III non-inferiority study which evaluated switching to fixed dose bictegravir/emtricitabine/tenofovir alafenamide from dolutegravir/abacavir/lamivudine; treatment related adverse events were recorded in 8% of the bictegravir group and 16% of the dolutegravir group ($p=0.006$). Treatment was discontinued due to adverse events in 2% of the bictegravir group vs 1% of the dolutegravir group. The Panel noted the statement in Molina *et al* that the findings suggest that the tolerability profile for bictegravir/emtricitabine/tenofovir alafenamide was similar to that of dolutegravir/abacavir/lamivudine.

The Panel further noted ViiV's submission that the Biktarvy European Medicines Agency assessment report stated that as expected, the safety profile of B/F/TAF (Biktarvy) was similar to DTG+FTC/TAF. The Panel also noted Gilead's submission that the claim in question was a tolerability claim rather than a safety claim and both companies' comments about the assessment of tolerability.

The Panel noted ViiV's allegation that that the claim 'Better tolerated than DTG-containing regimens' was too broad as it referred to all DTG-based regimens, yet, the supporting data only included comparisons between Biktarvy and two DTG-containing regimens: Triumeq and DTG plus emtricitabine/tenofovir alafenamide. The Panel further noted ViiV's allegation that the claim also overstated the differences in tolerability profiles when comparing Biktarvy with DTG-containing regimens. The Panel noted that the statement, which appeared in smaller, less prominent font below the claim in question, only referred to all-grade treatment-related adverse events with Biktarvy compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint).

The Panel noted that although the statement appeared to reflect the information in studies GS-1489, GS1490 and GS1844 with regard to all-grade treatment-related adverse events, it did not reflect the results with regards to the other factors within these studies which might contribute to the tolerability profiles of the medicines or the overall conclusions of the studies with regard to tolerability. The Panel considered that the immediate impression of the claim 'Better tolerated than DTG-containing regimens' to readers, would be that Biktarvy was better tolerated than all DTG-containing regimens which was misleading and could not be substantiated by the referenced studies and the statement immediately beneath did not negate this misleading impression. Further, in the Panel's view, better tolerability might imply statistically significant differences in measures other than all grade treatment-related adverse events eg rates of discontinuation. In this regard, the Panel noted Gilead's submission that the rates of discontinuation between the treatment groups in GS-1489, GS-1490 and GS-1844 were not statistically significantly different. The Panel considered therefore that the claim 'Better tolerated than DTG-containing regimens' was misleading, exaggerated Biktarvy's properties, was not capable of substantiation and was not qualified by the statement that followed. A breach of Clauses 7.2, 7.3, 7.4 and 7.10 of the Code was ruled with regard to the claim in question as it appeared on both the stand panel (ref BIK\IHQ\\1177b) and within the revised video (BIK\IHQ\\1177a(1)).

Overall, the Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled.

APPEAL BY GILEAD

Gilead appealed the Panel's rulings in the following 2 general areas:

- that the statement, 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' was not sufficiently prominent on the materials; and

- that the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' did not adequately qualify the claim 'better tolerated' as it did not reflect the results with regards to other factors within these studies which might contribute to the tolerability profiles of the medicines or the overall conclusions of the studies with regards to tolerability.

Gilead submitted that the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' was sufficiently prominent on the materials and so should be read as part of the claim.

Gilead noted that the Panel had considered the words 'Better Tolerated than DTG-containing regimens' as a claim in isolation from the words above and below that statement. Gilead submitted that the Panel's approach here was incorrect, that this wording should be considered in the context in which it was put, and that the full claim 'In Phase 3 clinical trials: Better tolerated than DTG-containing Regimens. Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' should be assessed in considering whether the material met the requirements of the Code.

Gilead submitted that as the Panel noted, the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' appeared in the same visual field as the rest of the claim. The stand panel was a large panel, with the wording 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' being in 100 point font some 2.5 cm high (based on the lower case 'i'). An example of the actual font was provided. In addition, the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' was approximately 5 feet and 10 inches above floor level, meaning it was at eye level for the majority of visitors to the stand. This statement was clearly not a footnote added in small print at the bottom of the stand, but an integral part of the claim, was prominently displayed and was immediately apparent to the reader.

Gilead submitted that the claim 'Better tolerated than DTG-containing regimens' was prominently preceded by 'In Phase 3 Clinical Trials'. This qualification immediately narrowed down the scope of the rest of the claim, considering that the HIV specialist conference delegates were experienced in the management of HIV and the associated latest research in this field, and would have been intimately familiar with the comparators that were used in the Phase 3 Biktarvy studies, GS-1489, GS-1490 and GS-1844 (DTG/ABC/3TC and DTG + F/TAF). The re-iteration of the comparators in the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' adjacent to the claim 'Better Tolerated than DTG-containing regimens' would have further reinforced this knowledge.

Gilead submitted that Clause 7.2 required that 'Material must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine'. Gilead submitted that in this circumstance, it was not probable that experienced HIV specialists reading this claim would have been unclear as to the comparators in which Biktarvy was studied and the basis upon which the claim 'better-tolerated' was made.

Gilead submitted that Clause 7.3 required that medicines or services for the same needs or intended for the same purpose were compared. Gilead submitted that in this instance, the claim was drawn from double blind randomised Phase 3 clinical trials in the same treatment populations across all 3 studies, thereby clearly fulfilling the requirements of this clause.

Gilead submitted that the supplementary information to Clause 7 clarified that 'In general claims should not be qualified by the use of footnotes and the like'. Whilst, for the reasons set out above, the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' was not 'footnotes and the like'. In any event it was clear from the supplementary information (and the words 'in general') that this did not automatically mean the adjacent wording should be disregarded and that the material as a whole should be considered when assessing whether the wording used was clear or not. There were inconsistencies in the Panel's ruling here, as on one hand the Panel ruled that this

statement was not sufficiently prominent on the materials despite being in the same frame, while also ruling below that it was reasonable to make a connection between the video and other imagery shown elsewhere on the stand.

Gilead submitted that of note was the Panel's ruling on complaints raised in relation to the complainant's stand at the same conference. In Case AUTH/3165/2/19 the Panel deemed it was sufficient for the audience to click through an interactive display panel to obtain the necessary information to qualify the parent claim of 'Unbeaten in head to head clinical trials' and to identify in what respects the product had been unbeaten. In that case, the Panel noted that the screen in question contained no details of the patient populations in the studies and a user would have to click on the screen to access such information. The Panel also stated that this was not necessarily unacceptable, in part because the promotion was tailored to physicians experienced in the management of HIV infection. This was particularly relevant as the audience across both cases was the same, and the SPC for Biktarvy similarly outlined that it should be prescribed by physicians experienced in the management of HIV infection.

Consequently, Gilead maintained that if a qualification found only through 'tapping through' screens on an interactive display could be ruled to be acceptable in one instance, a sentence that was presented in the same frame as the accompanying claim with 100 size font must also be regarded as sufficiently prominent to be taken into account when assessing the claim, especially when the audience was the same. Gilead recognised that another consideration of the Panel in Case AUTH/3137/12/18 was whether any standalone material in itself could be considered misleading; this point was addressed in more detail below, but Gilead pointed out that any assessment on whether or not the overall claim was misleading must be judged against the full statement as written, 'In Phase 3 clinical trials: Better tolerated than DTG-containing Regimens. Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)'. In addition to the points above, the statement 'Better tolerated than DTG-containing regimens' and the statement regarding treatment related adverse events were both linked via a dagger symbol, leaving any of the remaining audience beyond doubt that the two claims were intrinsically linked and designed to be read together.

In conclusion Gilead submitted that the statement, 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' was sufficiently prominent to support the claim 'Better Tolerated than DTG-containing regimens', and that the full claim 'In Phase 3 clinical trials: Better tolerated than DTG-containing Regimens. Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' was what should be assessed by the Panel in considering whether the material met the requirements of the Code.

Gilead submitted that the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' adequately qualified the claim 'better tolerated' and, therefore, the claim 'Better-tolerated than DTG-containing regimens' was not misleading, did not exaggerate Biktarvy's properties and was capable of substantiation.

Gilead submitted that the Panel considered that the immediate impression of the claim 'Better tolerated than DTG-containing regimens' to readers would be that Biktarvy was better tolerated than all DTG-containing regimens which was misleading and could not be substantiated by the referenced studies and the statement immediately beneath did not negate this misleading impression. For the reasons outlined above, the use of the phrase 'In Phase 3 Clinical trials', the prominent mention of DTG/3TC/ABC and DTG + F/TAF (ie the font size of claim, the fact

that it was at eye level, and accompanied with a dagger symbol), and the experience of the conference delegates made it inconceivable that this comparison could have been misinterpreted to mean all DTG-containing regimens.

The Panel also noted the claim 'Better tolerated than DTG-containing Regimens. Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' only referred to all grade treatment-related adverse events with Biktarvy compared to DTG plus ABC/3TC or FTC/TAF and did not reflect the results with regards to other factors within these studies which might contribute to the tolerability profiles of the medicines or the overall conclusions of the studies with regards to tolerability. Gilead submitted that in doing so, the Panel noted Gilead's submission that the rates of discontinuation between the treatment groups in GS-1489, GS-1490 and GS-1844 were not statistically significantly different. The Panel therefore considered the claim 'Better tolerated than DTG-containing regimens' was misleading, exaggerated Biktarvy's properties, was not capable of substantiation and was not qualified by the statement that followed.

Gilead submitted that the full claim made was not misleading, was a fair comparison, was capable of substantiation and did not exaggerate the properties of Biktarvy.

Gilead submitted that a critical underlying consideration was that this must be considered in a backdrop of the claim being made in a setting where the audience was experienced in the management of HIV and was best placed to assess the relevance of the claim in the context of managing HIV patients.

Gilead submitted that the Panel appeared to determine that because there were no significant differences in discontinuation rates across the cited clinical studies, it was misleading to solely make claims about differences in all grade treatment related adverse events to support the claim 'better tolerated'. However, there was no regulatory or clinical guidance that stated that 'rates of discontinuations' was a more relevant measure of tolerability than 'treatment related adverse events'. When assessing tolerability or safety, all relevant measures from clinical trials should be considered, and a determination of the overall profile should be appropriately characterised. For the Panel to have ruled that Gilead was being misleading by not disclosing rates of discontinuation (especially considering that no significant differences were observed between arms on this measure), there must be firm evidence to support that this measure must always be disclosed when making a claim about tolerability – no evidence was provided to support this.

Gilead submitted that the measure 'All grade treatment-related adverse events' was a pre-specified secondary endpoint across all the studies cited and disclosed as such. As a measure of tolerability, Gilead argued that 'all grade treatment-related adverse events' held potentially more relevance than other measures of tolerability, not just because it was, by definition, linked back to the drug/regimens in question, but the audience would already be aware that rates of discontinuation due to AEs was (fortunately) relatively rare in the management of HIV in 2018, when using guidelines-recommended regimens.

Gilead submitted that it interpreted the Panel's comments about the claim not reflecting the results with regards to other factors within these studies which might contribute to the tolerability profiles of the medicines, as asserting that the claim is not fair and balanced. 'Balance' was defined as 'to offset or compare the value of (one thing) with another'. Thus, if other measures of tolerability significantly favoured any of the comparator arms across any of the three relevant

clinical studies, Gilead would clearly have been obliged to disclose this information. However, as no significant differences were observed in any other measures of tolerability across these studies, there was effectively no relevant information for Gilead to balance this claim against. The Panel also noted the overall conclusions of the studies (manuscripts) with regard to tolerability did not necessarily reflect the claims made by Gilead. The Panel also made reference to regulatory documents such as the EPAR.

Gilead submitted that firstly, in relation to the EPAR, the Panel noted the conclusion made by the EPAR that 'the safety profile of B/F/TAF was similar to DTG+FTC/TAF' as a reason to support that the claim 'better tolerated' was incapable of substantiation. However, Gilead made no claim about safety within the piece and according to ICH guidance the terms safety and tolerability were clearly not interchangeable (EMEA CPMP/ICH/363/96, 1998). Therefore, the statement in the EPAR did not contradict any of the tolerability claims made by Gilead. It was clearly possible to have two medicines or regimens with similar safety but differences in tolerability. While the EPAR was silent around characterising the tolerability of Biktarvy, Table 27 of the EPAR illustrated the differences Study Drug Related AEs which Gilead used to support the claim 'better tolerated'.

Gilead submitted that when considering the conclusions from the respective peer reviewed manuscripts, further context was required. In the setting of peer-reviewed publications, the findings from Phase 3 studies were expected to be discussed within the broader context of the HIV field, a requirement that clearly did not apply in a promotional setting. To this end, it was relevant to understand how the management of HIV had evolved. Living with HIV in the 80s and early 90s was a death sentence; early clinical trials in HIV were focused on prolonging life. Over time, as antiretroviral agents were used in combination, it became increasingly possible to suppress HIV for longer periods of time, leading to increasing life expectancy (Cohen *et al* 2006). However, in the pursuit of virological control, many medicines in the late 1990s and throughout the 2000s were associated with high rates of poor tolerability and safety. For example, the pivotal ACTG 5142 study (Riddler *et al* 2008) conducted throughout 2006 and published in 2008 demonstrated that 131 of 753 HIV patients (17%) had a new grade 3 or 4 sign or symptom, and 259 of 753 patients (34%) had a new grade 3 or 4 laboratory abnormality. In this study, toxicity leading to discontinuation of one or more medicines in the initial regimen occurred in 134 of 753 patients (18%) at a median follow-up of 112 weeks. In a publication as recently as 2012, regimens containing efavirenz, a medicine which had been a HIV Treatment Guidelines preferred regimen for many years, was associated with 31% >Grade 2 treatment-related AEs, and 8% of patients discontinuing due to AEs at 48 weeks (Cohen *et al* 2012). These were just examples for the sake of brevity.

Gilead submitted that thus, when reviewing the results of the Biktarvy clinical studies in the context of other studies in the field of HIV, it was not unexpected that authors would conclude that Biktarvy and comparator were both 'well-tolerated'. That both regimens were well-tolerated did not preclude the observation that one regimen still had some significant advantages on some aspects of tolerability. And in consideration of this context, Gallant *et al* still concluded that, 'dolutegravir, abacavir, and lamivudine was associated with more adverse events in total than bictegravir, emtricitabine, and tenofovir alafenamide', while Molina *et al* also concluded that '… the tolerability … finding is particularly notable within the context of a switch study, in which the enrolled participants are presumably already tolerating their original regimen and, in many switch studies, more adverse events are reported in the switch group than in the group that receives baseline treatment' (whereas, by contrast, in this study there were significantly fewer treatment-related adverse events for the switch regimen [Gilead's addition for clarity]).

Therefore, Gilead submitted that the claim 'Better-tolerated' as substantiated by the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' was not inconsistent with how the tolerability profiles had been characterised in the context of these peer-reviewed manuscripts. Rather, the key consideration was that the claims were capable of substantiation, were sufficiently complete to enable the recipient (comprised of physicians experienced in the management of HIV) to form their own opinion of the therapeutic value of the medicine and were appropriately tailored to the right audience.

MHRA and Irish Pharmaceutical Healthcare Association (IPHA) Code of Practice Council

Gilead submitted that in addition to the points raised above, the Panel did not acknowledge in its ruling that these materials, (except the revised version of the video), and this claim, were reviewed by the MHRA as part of their pre-vetting of Biktarvy promotional materials and that the MHRA confirmed that it did not object to the items submitted.

Gilead submitted that whilst it recognised that the Code extended beyond the relevant UK legal requirements for pharmaceutical promotional materials, and that the Panel had to consider the material in the context of a complaint, given that part of the function of the MHRA's pre-vetting was to ensure that the materials were not likely to mislead (in particular in relation to claims about the tolerability of a medicine) then Gilead submitted that in the context of this complaint, the MHRA's views here were relevant. This was particularly the case when subjective decisions were being made on the balance of probabilities.

Further, Gilead submitted that the fact that the MHRA approved the stand materials in pre-vetting was particularly pertinent when considering whether high standards had been maintained (Clause 9.1). Gilead submitted that the materials were of a high standard and the approval of the materials on the stand by the MHRA supported this.

Gilead submitted that also relevant in connection with the subjective assessment to be made on the balance of probabilities was that ViiV raised a similar complaint regarding the claim 'Better Tolerated than DTG-containing regimens' to the Irish Pharmaceutical Healthcare Association (IPHA) Code of Practice Council. The material that was the subject of the complaint contained some similarities and some differences to the materials under discussion in this complaint. Where the materials were similar – qualification of 'better tolerated than DTG-containing regimens' by 'significantly fewer all grade treatment-related adverse events' – the IPHA Code of Practice Council ruled no breach, even in a setting where the claim wasn't further qualified by the pre-emptive phrase 'In Phase 3 clinical trials'. For completeness, the IPHA Code of Practice Council ruled breaches insofar as the nature of the comparators was deemed not to be sufficiently prominent, however the Irish material differed from the current material under discussion as it did not specify 'DTG+ ABC/3TC or F/TAF' immediately under the 'Better Tolerated' claim, unlike materials (ref BIK\IHQ\\1177b and BIK\IHQ\\1177a(1)).

In conclusion, Gilead submitted that the claim in question, and as laid out, was sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine, that medicines for the same needs or intended for the same purpose were being appropriately compared, the claim was capable of substantiation, and did not exaggerate the properties of Biktarvy.

Therefore, Gilead appealed against the ruling that this claim was in breach of Clauses 7.2, 7.3, 7.4 and 7.10 as it appeared on both the stand panel (ref BIK\IHQ\\1177b) and within the revised video (ref BIK\IHQ\\1177a(1)). Gilead also submitted that it had maintained high standards in relation to this material and that the Panel's ruling of a breach of Clause 9.1 should not be upheld.

RESPONSE FROM VIIV

ViiV alleged that Gilead's appeal merely restated arguments that the Panel had rejected, and ViiV considered the rulings of the Panel should be upheld.

ViiV noted that in November 2018 when the Glasgow conference took place, Biktarvy was a newly licensed fixed-dose combination product for HIV (25 June 2018). It was not yet commissioned by NHS England and was not yet included in the BHIVA guidelines, so most UK health professionals attending the congress would have limited experience of it.

ViiV alleged that Gilead's clinical trial program had shown Biktarvy had non-inferior efficacy when compared to two dolutegravir-containing regimens, Triumeq (DTG/ABC/3TC) and dolutegravir plus TAF/FTC. Adverse event profiles (including overall AEs, Serious AEs, AEs leading to discontinuation) were also comparable apart from lower levels of nausea than Triumeq in the treatment-related AEs analysis. From the study where this difference was most marked, authors suggested that this difference was due to the abacavir (ABC) component of Triumeq, not DTG.

ViiV alleged that the claim 'Better tolerated than DTG-containing regimens' appeared prominently on large panels at the conference booth, with an inadequate qualifying footnote in much smaller size that was legible only on closer inspection. Conference booths were built for high impact to attract delegates' attention and convey messages quickly to passers-by even if they did not read the whole detail of the stand. The Gilead booth stand panels were around 15 feet high, with the main claims being able to be read from across the hall, but any other text indecipherable at that distance.

ViiV alleged that the claim 'Better tolerated than DTG-containing regimens' appeared in enormous font, dwarfing other information on panels and was clearly the intended take-home message. The information immediately above it ('In Phase 3 clinical trials') was in bold and underlined, yet the qualifying footnote (unacceptable in the view of the Code) was in even smaller font, not in bold and not underlined – clearly indicating that Gilead were happy for readers to be left with the misleading impression that however it was looked at, Biktarvy was better tolerated that all DTG-containing regimens. As the Panel agreed, this was exaggerated, misleading, not capable of substantiation and not qualified by the statement that followed.

ViiV alleged that the claim 'Better tolerated than DTG-containing regimens' did not reflect a balanced view of the data overall. Firstly, the claim was all-embracing as it implied Biktarvy was better tolerated than all DTG-containing regimens. DTG (unlike bictegravir) could be combined with any number of antiretrovirals to make a regimen. Biktarvy had only been tested against two DTG-containing regimens. The footnote made the comparators clear but was too small in comparison to the size of the claim which was bold, capitalised and huge.

Secondly, ViiV alleged that the claim was exaggerated and misleading as it was an unbalanced interpretation of the data which clearly showed Biktarvy and the DTG-containing regimens it had

been compared to have comparable AE profiles. This was the finding of various independent regulatory bodies that had assessed the data:

- The EMA had concluded the following in the Biktarvy EPAR for Biktarvy and its comparator regimens (DTG/ABC/3TC or DTG + TAF/FTC): 'The adverse event (AE) profile was generally similar in ART-naive and virologically suppressed adults, with similar rates of any AEs, Grade 3 or 4 AEs, SAEs, SAEs considered related to study drugs, and AEs leading to study drug discontinuation across the different treatment groups' (Biktarvy EPAR).
- The NHS Clinical Commissioning Policy Proposition for B/F/TAF stated that 'results suggest that B/F/TAF has a similar safety tolerability profile to both DTG/ABC/3TC and DTG/F/TAF' with respect to treatment-naïve studies, and with respect to the study in virologically suppressed patients, 'results suggest that B/F/TAF has a similar safety and tolerability profile to both DTG/ABC/3TC and boosted protease inhibitor-based regimens'.
- The FDA also made a similar assessment for each of the studies 1489, 1490 and 1844 (NDA 210251 Uni-Review, Section 7.3): 'The reasons for discontinuation of study drugs were comparable between the two groups'.

ViiV alleged that to cherry pick one sub-analysis that showed a difference in treatment-related adverse events was misleading, did not reflect the data fairly and was inconsistent with the overall safety conclusions of the study. ViiV agreed that one DTG regimen (DTG/ABC/3TC) had shown a difference in tolerability (GI effects) but that was attributable to the ABC component of the regimen (Gallant *et al* and Molina *et al*), and this was known because when that component was not included (in the study comparing Biktarvy vs DTG + TAF/FTC (Sax *et al*)) there was no difference in GI effects. Gilead had known this but despite this had used this evidence vs one regimen to suggest issues with all DTG-containing regimens, denigrating not only DTG but all the regimens that included it. This was misleading. ViiV also agreed with the Panel's ruling that 'better tolerability' might imply statistically significant differences in measures other than all grade treatment-related adverse events eg rates of discontinuation', but there were no other differences in tolerability seen in any of the studies as agreed by Gilead.

Thirdly, ViiV alleged that contrary to Gilead's assertion that there was no guidance on adverse events reporting, a recent joint industry and journal recommendation on reporting adverse events in clinical trials considered the three most important measures of adverse events as being deaths, serious adverse events and discontinuations due to adverse events. All of which were comparable when looking at Biktarvy vs the two DTG-containing regimens. On the topic of treated related adverse events, the authors noted '... Given the inherent subjectivity in such attribution, it has limited value in the context of randomized, double blind clinical trials and was considered less important than the other adverse event reporting …' (Lineberry *et al* 2016).

Thus, although ViiV agreed the fact that these studies found a difference in this one parameter against one specific regimen (DTG/ABC/3TC), it alleged that this did not support the broad claim that Biktarvy was better tolerated than all DTG-containing regimens as it did not reflect the balance of evidence.

ViiV alleged that Gilead reasserted that it had not made a safety claim; however, ICH stated, 'The safety of a medical product concerns the medical risk to the subject …' and 'The tolerability of the medical product represents the degree to which overt adverse effects can be tolerated by

the subject'. Thus, it could be seen that tolerability was part of the safety profile of a medicine and determined by the individual's response to adverse effects.

ViiV alleged that fourthly, Gilead claimed that Clause 7.3 was not relevant as it 'requires medicines or services for the same needs or intended for the same purpose are compared' and it submitted the fact the data from clinical trials with the same treatment populations satisfied this. Clause 7.3 required that comparisons were not misleading, which was addressed above. However, it was also misleading in another way – by implying that Biktarvy could be used in the same populations as all DTG-containing regimens which it could not. Even if ViiV looked at only the two regimens which Gilead cited in its inadequate qualifying footnote it could be seen Biktarvy had a much more limited indication than any DTG-containing regimen. Biktarvy was for adults only and those without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir, whereas DTG as Tivicay had a much broader indication including children over 6 years, adolescents, and those with resistance; Triumeq too could be used in adolescents and those with resistance (Biktarvy, Tivicay and Triumeq SPCs). Broadening the claim to 'DTG-containing regimens' as if they were all comparable and that Biktarvy could be used in the same populations clearly risks confusing prescribers and putting patients at risk. It was paramount that medicines advertising was clear, unambiguous and not misleading to avoid putting patients at risk, and that the impression created was true and able to be proven. None of that was the case here.

ViiV alleged that Gilead claimed in its appeal that the delegates would already know which comparators were used in all their studies and the preceding statement, 'In Phase 3 Clinical trials' narrowed the scope of the rest of the claim but this logic would imply there was no need to make the comparators clear. At the time of the conference Biktarvy was a newly licensed medicine, and it would be unreasonable to assume that all readers had intimate knowledge of all study comparator arms and not be misled by the large claim that Biktarvy was 'Better tolerated than DTG-containing regimens' and interpreted that to mean better than *all* DTG-containing regimens.

With regard to Gilead's points about ViiV's claim 'Unbeaten in head to head clinical trials' (Case AUTH/3165/2/19) ViiV noted that the key difference here was that the claim stood alone, was correct and was without need of any further information to be true. There were no details that potentially misled readers. As such, the Panel's rulings on this case were inappropriate as a comparison. The Panel ruled no breaches of Clauses 7.2, 7.3, 7.4, 9.1 as alleged by Gilead and it was notable that Gilead had not appealed this ruling.

In conclusion, ViiV alleged that for Gilead to qualify the overarching, all-embracing claim of better tolerability with a cherry-picked focus on treatment-related AEs versus one specific regimen (DTG/ABC/3TC) did not negate the misleading impression or give readers enough information to form their own opinion of the therapeutic value of the medicine and encourage rational use of the medicine.

ViiV alleged that the footnote 'significantly fewer all grade treatment related AEs compared to DTG plus ABC/3TC or FTC/TAF' was insufficient to substantiate the broad claim and this claim therefore misled by exaggeration. The use of both a smaller font size and the superscript dagger (†) indicator adjacent to the references and the claim clearly indicated this was a footnote, and was disingenuous to imply otherwise. Cherry-picking of data to qualify, as a footnote, a much broader unsubstantiated claim was a clear breach of Clauses 7.2, 7.3, 7.4, 7.10 and did not maintain high standards in breach of Clause 9.1.

Finally, when reaching its decision in this case ViiV asked the Appeal Board to reflect on the significantly overstating nature of the 'Better tolerated than DTG-containing regimens' claim that Gilead was making. There was over 1,000,000 patient years of experience of DTG and it was licensed in over 100 countries. The WHO recommended dolutegravir as preferred HIV treatment option in all populations. By contrast Gilead was making a broad and misleading claim based on the results of a handful of studies and the implications of such a false claim could extend far beyond a Glasgow booth.

APPEAL BOARD RULING

The Appeal Board noted Gilead's submission that the materials at issue, (except the revised version of the video), and the claim were reviewed by the MHRA as part of its pre-vetting of Biktarvy promotional materials. The Appeal Board noted that it judged the material at issue based on the evidence provided in this case and in relation to the requirements of the Code. These comments also applied to points 2 and 3 below.

The Appeal Board noted that the claim 'Better tolerated than DTG-containing regimens' which appeared in very large font on the stand panel (BIK\IHQ\18-09\\1177b) and in the revised video (BIK\IHQ\18-09\\1177a(1)) was referenced to Gilead Data on File, Gallant *et al*, Sax *et al*, and Molina *et al*. Directly above the claim in smaller bold underlined font, the material at issue stated 'In Phase 3 clinical trials' and directly below the claim was the statement 'Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)' in the smallest of the three fonts used and this was neither bold nor underlined. The Appeal Board noted that although the statement below the claim appeared within the same visual field as the claim it was clearly far less prominent. The Appeal Board noted that the main claim was linked to the qualifying statement by a superscript dagger (†). The Appeal Board noted that the supplementary information to Clause 7 stated that 'In general claims should not be qualified by the use of footnotes *and the like*.' (Emphasis added)

The Appeal Board noted Molina *et al* which evaluated switching to fixed dose bictegravir/emtricitabine/tenofovir alafenamide [bictegravir group] from dolutegravir/abacavir/lamivudine [dolutegravir group]; treatment related adverse events were recorded in 8% of the bictegravir group and 16% of the dolutegravir group (p=0.006). Treatment was discontinued due to adverse events in 2% of the bictegravir group vs 1% of the dolutegravir group. Molina *et al* stated that the findings suggest that the tolerability profile for bictegravir/emtricitabine/tenofovir alafenamide was similar to that of dolutegravir/abacavir/lamivudine.

The Appeal Board noted that Sax *et al* which evaluated bictegravir/emtricitabine/tenofovir alafenamide [bictegravir group] vs dolutegravir/emtricitabine/tenofovir alafenamide [dolutegravir group] stated that study-drug related adverse events were less common in the bictegravir group than in the dolutegravir group (18% vs 26%, p = 0.022). However, incidence and severity of adverse events were similar between groups and few participants discontinued treatment due to adverse events (2% in the bictegravir group and <1% in the dolutegravir group).

The Appeal Board noted that Gallant *et al* stated that adverse events related to study drug were less common with bictegravir/emtricitabine/tenofovir alafenamide than with dolutegravir/abacavir/lamivudine (26% vs 40%; p-value provided in Gilead data on file (p<0.001)), the difference being driven by a higher incidence of drug-related nausea in the

dolutegravir/abacavir/lamivudine group (5% vs 17%; p<0.0001). The study authors stated that the incidence and severity of adverse events was mostly similar between groups except for nausea, which occurred less frequently in patients given bictegravir/emtricitabine/tenofovir alafenamide than in those given dolutegravir/abacavir/lamivudine. The authors further stated that both regimens were well tolerated; adverse events leading to study discontinuation were noted in no participants in the bictegravir/emtricitabine/tenofovir alafenamide group and 1% of participants in the dolutegravir/abacavir/lamivudine group. The study authors suggested that the difference in incidence of nausea between groups was most likely because of differences between tenofovir alafenamide and abacavir.

The Appeal Board noted that the Biktarvy European Medicines Agency assessment report stated that as expected, the safety profile of B/F/TAF (Biktarvy) was similar to DTG+FTC/TAF.

Whilst the Appeal Board noted from Gilead's submission that the audience at the conference were experienced HIV specialists familiar with the Biktarvy Phase 3 clinical trials and the comparator regimens used, it questioned if all attendees would be so knowledgeable given at the time of the conference Biktarvy was not available to prescribe on the NHS in England and had only briefly been available in Scotland.

The Appeal Board noted that although all-grade treatment-related adverse events was used to support the main claim 'Better tolerated than DTG-containing regimens' this did not reflect the results with regard to the other factors within these studies, eg rates of discontinuation, which might contribute to the tolerability profiles of the medicines or the overall conclusions of the studies with regards to tolerability. In addition, the Appeal Board noted that there were DTG-based regimens not included in the cited studies.

Furthermore, the Appeal Board considered that the large difference in font size between the main claim and the statement beneath it was such that the take-home message was the main claim 'Better tolerated than DTG-containing regimens'. The Appeal Board noted that in response to a direct question Gilead acknowledged that Biktarvy was not better tolerated than DTG containing regimens.

The Appeal Board considered that the claim 'Better tolerated than DTG-containing regimens' on its own implied that Biktarvy was better tolerated than all DTG-containing regimens and was thus misleading, exaggerated Biktarvy's properties and could not be substantiated by the referenced studies and the statement immediately beneath did not negate this misleading impression. The Appeal Board upheld the Panel's rulings of a breach of Clauses 7.2, 7.3, 7.4 and 7.10 of the Code with regard to the claim in question as it appeared on both the stand panel (ref BIK\IHQ\\1177b) and within the revised video (BIK\IHQ\\1177a(1)). The appeal on this point was unsuccessful.

The Appeal Board considered that high standards had not been maintained and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

2 Use of imagery showing a rose which had shed many of its thorns

This imagery described by ViiV appeared on the stand panel (ref BIK\IHQ\18-09\\1177c) which was not specifically referred to by ViiV and only the image of a rose head appeared in the revised video referred to by ViiV (BIK\IHQ\18-09\\1177a(1)).

The stand panel included an image of a rose which had shed a number of thorns which lay beside it. Above it stated 'The beauty of what is possible' followed by 'Biktarvy (BIC/FTC/TAF) combines bictegravir – a novel INSTI – with DESCOVY▼ (FTC/TAF), a durable guideline-preferred dual-NRTI backbone'.

The video (BIK\IHQ\18-09\\1177a(1)) consisted of three separate videos looping simultaneously in different areas of the stand and contained a number of claims including the claim at Point 1 (The Panel noted that the video provided by Gilead bore the reference BIK\IHQ\18-09\\1177a.

COMPLAINT

ViiV asserted that the depiction of a rose with most of its thorns shed, immediately after the contested claim suggested an overstated tolerability and safety profile improvement with Biktarvy compared with DTG-containing therapy. This could not be substantiated by the body of evidence from studies GS-1489, GS-1490, and GS-1844, as outlined above. The imagery implied that Biktarvy was 'safe' or 'safer'. ViiV alleged that 'safe' was in breach of Clauses 7.4 and 7.9 and 'safer' was in breach of Clause 7.2 because it was a hanging comparison; it was also disparaging (Clause 8.1).

ViiV asserted that Gilead's editing of the video (ref BIK/IHQ/18-09/1177a) to remove the segment with the thorns falling off the rose stem was insufficient. Associations between the rose, loss of thorns and the claim appeared throughout the booth. The general themes of the rose and thorn imagery together with the prominent disputed claim 'Better tolerated than DTG-containing regimens' were clearly meant to imply that Biktarvy had a superior tolerability profile (dropping of thorns) and that DTG-containing regimens might cause pain or harm to HIV patients. ViiV alleged that if the campaign misrepresented safety and disparaged a competitor then it also brought the industry into disrepute in breach of Clauses 9.1 and 2.

ViiV noted that Gilead stated the image of rose and thorns was illustrative of the three attributes claimed for Biktarvy (>90% efficacy and 0 resistance, better tolerated than DTG-containing regimens and small single tablet regimen with flexible daily dosing), all of which the company asserted could be substantiated. Gilead maintained that the imagery did not imply that Biktarvy was safe because some thorns remained on the rose, nor did imply that Biktarvy was 'safer' because no safety claims were made in association with the rose. ViiV submitted that by the same argument if fewer remaining thorns implied that the product was not inherently 'safe', then the dropping of some of the thorns must imply some relative improvement which, as described earlier, could not be substantiated.

RESPONSE

Gilead explained that the image of the rose and thorns was designed to encompass the totality of claims made for Biktarvy across the items available on the exhibition stand, all of which were appropriately qualified and capable of substantiation, specifically:

- 'Biktarvy (BIC/FTC/TAF) combines bictegravir- a novel INSTI- with DESCOVY (FTC/TAF), a durable guideline-preferred dual NRTI-backbone'
- In Phase 3 clinical trials:
    - >90% efficacy and 0 resistance (Non-inferior vs comparator in all registrational studies)

- Better tolerated than DTG-containing regimens; Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF (secondary endpoint)
- Small, single tablet regimen with flexible daily dosing.

The image of the rose and thorns, coupled with these claims, was designed to show that Biktarvy possessed a favourable profile on multiple attributes that were considered important in the management of HIV, as supported by treatment guidelines and had addressed a number of limitations seen with other treatments, including in relation to efficacy, resistance, tolerability, number of tablets and dosing flexibility. In fact, this sum total of attributes, plus others not mentioned as part of this campaign, was clearly considered to be sufficiently relevant to result in Biktarvy receiving the highest level of recommendation in 3 international HIV treatment guidelines within 3-6 months of its licensing.

Importantly, whilst the dropped thorns were intended to show that Biktarvy had addressed some of the limitations seen with other treatment regimens, some thorns remained on the rose to recognise that Biktarvy was not totally devoid of limitations (contraindications or warnings).

Gilead noted that ViiV argued that the video shown on the stand relating to the 'Better tolerated than DTG-containing regimens' claim (BIK\IHQ\18-09\\1177a (revised)) created an association between the rose and the claim, and in doing so also with the thorns. ViiV's assertions were based on a view that the image focused only on a comparison of Biktarvy vs DTG + ABC/3TC or F/TAF, and the claim itself 'better tolerated than DTG-containing regimens'. As outlined above, the intent of the rose and thorns was to depict the sum attributes claimed for Biktarvy, not restricted to a comparison vs DTG + ABC/3TC or F/TAF, and this was the way in which the Gilead stand was set out and how and where the imagery was displayed. The thorns imagery was not used alongside the DTG comparative claim and similar imagery of the rose flower was used across all the videos that fell under item 'BIK\IHQ\18-09\\1177a – revised', even though these other videos did not mention DTG-containing regimens. The only image of a rose with loose thorns appeared on the main stand panel alongside the headline statement 'The Beauty of What is Possible' followed by the claim, 'Biktarvy (BIC/FTC/TAF) combines bictegravir- a novel INSTI- with DESCOVY (FTC/TAF), a durable guideline-preferred dual NRTI-backbone'.

Gilead submitted that to the extent that the main rose and thorns image represented, in part, each of the individual Biktarvy claims, it did so fairly and in a balanced way – thorns remained on the rose and a limited number of loose thorns were shown. Each of the individual claims were accurate, fair, balanced and capable of substantiation, including the comparative claim relating to tolerability of DTG-containing regimens as discussed at Point 1 above, and the way the imagery was presented did not overstate the comparative differences in limitations as a whole between Biktarvy and other treatments, or the tolerability differences between Biktarvy and the DTG-containing regimens referenced in the claim (particularly as the imagery did not represent this claim in isolation but all limitations highlighted across the stand).

Gilead submitted that the imagery was not intended to, and did not, imply that other HIV treatment regimens (DTG-containing or otherwise) might cause harm or pain to people living with HIV; rather the thorns represented treatment limitations only. Furthermore, the imagery did not imply that Biktarvy was 'safe' or 'safer'. Some thorns remained on the rose and Gilead did not make any promotional claims about safety in any of the items in question; the claim Gilead made on its stand in connection with DTG-containing regimens related to tolerability only and not safety. To the extent that the imagery implied a comparison, again it did so clearly by

reference to the claims made across the stand and in relation to the sum total of attributes identified in the claims.

Gilead noted that the rose and thorn imagery used on the stand was included in the materials reviewed and approved by the Medicines and Healthcare products Regulatory Agency (MHRA) as part of its pre-vetting of Biktarvy promotional material. If the MHRA had considered that the imagery suggested anything other than the clear meaning intended by Gilead as outlined above, Gilead was certain that it would not have approved any material with this imagery. Further, Gilead did not accept that, in displaying materials and imagery, that had been reviewed and approved by the MHRA, it had acted such a way as to bring discredit upon, or reduce confidence in, the pharmaceutical industry or in a way that had not maintained high standards. Gilead strongly rejected the assertion that it had acted in breach of Clause 9.1 or Clause 2.

PANEL RULING

The Panel noted ViiV's concern with regard to the visual of a rose which appeared to have lost a number of its thorns. The Panel noted that it appeared that the only image of a rose with both thorns on it and thorns beside it appeared on the main stand panel (ref BIK/IHQ18-09//1177c) alongside the headline statement 'The Beauty of What is Possible' followed by the claim, 'Biktarvy (BIC/FTC/TAF) combines bictegravir- a novel INSTI- with DESCOVY (FTC/TAF), a durable guideline-preferred dual NRTI-backbone'. The Panel noted that ViiV had not specifically referred to this item, however it had referred to associations between the rose and loss of thorns appearing throughout the booth. The Panel noted that whilst it was an established principle that items should be capable of standing alone, each stand panel was an integral part of a circular formation such that delegates within the circular formation would, on the balance of probabilities, be exposed to images from more than one stand panel. In the exceptional circumstances of this case, the Panel considered that when considering the acceptability of each stand panel context was particularly important and thus each should also be read within the context of the other materials on the stand.

In the Panel's view, although the stand panel (ref BIK/IHQ18-09//1177c) was not cited by ViiV and thus did not come within the scope of the complaint, ViiV had referred to the image on the stand panel and, noting its comments above about context, the Panel considered that it was relevant to the Panel's consideration of the allegations raised with regard to the revised video (ref BIK\IHQ\18-09\\1177a(1)).

The Panel further noted Gilead's submission that the image of the rose and thorns was designed to encompass the totality of claims made for Biktarvy across the items available on the exhibition stand, all of which Gilead claimed were appropriately qualified and capable of substantiation, specifically:

- 'Biktarvy (BIC/FTC/TAF) combines bictegravir- a novel INSTI- with DESCOVY (FTC/TAF), a durable guideline-preferred dual NRTI-backbone'
- In Phase 3 clinical trials:
    - >90% efficacy and 0 resistance (Non-inferior vs comparator in all registrational studies)
    - Better tolerated than DTG-containing regimens; Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF (secondary endpoint)
    - Small, single tablet regimen with flexible daily dosing.

The Panel noted Gilead's submission that the image of the rose and thorns, coupled with these claims, was designed to show that Biktarvy possessed a favourable profile on multiple attributes that were considered important in the management of HIV and to the extent that the imagery implied a comparison, it did so clearly by reference to the claims made across the stand and in relation to the sum total of attributes identified in the claims.

In the Panel's view, on the balance of probabilities, most readers would associate the picture of the rose as representing Biktarvy. The Panel considered that thorns on a rose stem would be seen as something injurious rather than representing different attributes as described by Gilead; the imagery implied that Biktarvy might cause less injury in comparison with a 'rose' with more thorns. The Panel considered that within the context of the stand and noting its comments above about the stand's circular formation, it appeared that Biktarvy was being compared to DTG-containing regimens as acknowledged by Gilead.

The Panel noted ViiV's allegation that the general theme of the rose and thorn imagery across the stand together with the claim 'Better tolerated than DTG-containing regimens' implied that Biktarvy had a superior tolerability profile compared with DTG-containing therapy. The Panel noted that the revised video which was provided by Gilead included a number of images of the rose head within the video loops with no images of thorns.

The Panel noted its comments above with regard to the context in which each item on the stand appeared.

The Panel noted that although only the rose head appeared throughout the revised video, the video was displayed within the context of the stand and, in the Panel's view, visitors to the stand would make a connection between the rose with thorns beside it on the stand panel (ref BIK/IHQ18-09//1177c) and the rose head in the revised video. The Panel noted that the revised video was made up of three separate videos looping simultaneously in different areas of the stand.

The Panel noted that within the three video loops, an image of the rose head appeared directly before and/or directly after the following claims, which all included the caveat 'In Phase 3 clinical trials': Better tolerated than DTG-containing regimens; Small STR with flexible daily dosing; >90% efficacy and 0 resistance. In the Panel's view, ViiV had not established that the flower head image within the three video loops was a hanging comparison and therefore no breach of Clause 7.2 was ruled.

The Panel noted its comments above with regard to the stand panel and context and considered that they were relevant here. The Panel considered, on the balance of probabilities, that visitors to the stand would associate the image of the rose head in the videos (ref BIK/IHQ18-09//1177a(1)) appearing before and after the claims including 'Better tolerated than DTG-containing regimens' with the image of the rose with some dropped thorns on the stand panel (ref BIK/IHQ18-09//1177c). The Panel considered, therefore, that the video, by association with the imagery and claim on the stand panel and the claim 'Better tolerated than DTG-containing regimens' within the video loops, implied that Biktarvy was less hazardous than DTG-containing regimens and it considered that this implication could not be substantiated and a breach of Clause 7.4 was ruled in relation to the video and it disparaged DTG-containing regimens in breach of Clause 8.1.

The Panel did not consider that the rose head depicted in the video implied that Biktarvy was safe as alleged; no breach of Clause 7.9 was ruled.

The Panel considered that Gilead had failed to maintain high standards and a breach of Clause 9.1 was ruled.

On balance, the Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use.

APPEAL BY GILEAD

Gilead noted that the Panel ruled that the video (BIK/IHQ 18-09//1177a(1)) implied that Biktarvy was less hazardous than DTG-containing regimens, due to the claim 'Better tolerated than DTG-containing regimens' within the video loops and an association with the imagery on another panel on the stand, and it considered that this implication could not be substantiated and ruled a breach of Clause 7.4. Further, the Panel ruled that the video disparaged DTG-containing regimens in breach of Clause 8.1.

Gilead submitted that the material (ref BIK/IHQ 18-09//1177a(1)) was comprised of three individual videos that were shown on three equally prominent panels. The videos each contained an image of a rose head and this image was shown consistently across each of three videos displayed on the stand, as well as the wording 'The Beauty of What is Possible' statement. Each of the videos also contained a different claim highlighting different treatment limitations that Biktarvy had at least in part overcome, one of:

- In Phase 3 clinical trials: >90% efficacy and 0 resistance
- In Phase 3 clinical trials: Better tolerated than DTG-containing regimens. Significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or FTC/TAF (secondary endpoint)
- In Phase 3 clinical trials: Small STR with flexible daily dosing.

Gilead submitted that the Panel had decided that, on the balance of probabilities, a connection was created between the video and imagery shown elsewhere on the stand (in material which was not specifically within the scope of ViiV's complaint) due to the inclusion of the image of the rose head (without any thorns).

If the stand was to be considered as a whole (and so a link was to be created between the rose head in the video and the rose and thorn image on a separate panel), then it was appropriate to consider all the stand panels and all the videos and apportion equal connection to them when deciding what it was probable that the specialist HIV clinician considered was being represented. There was no reasonable basis to assert that the claim regarding DTG-containing regimens held more prominence in this context than the other equally prominent claims on the stand.

Gilead submitted that the image of the rose and thorns was designed to illustrate that the Biktarvy data and clinical profile went some way to achieving high efficacy, reduced (no) resistance, improved aspects of tolerability (as qualified), and dosing convenience. The video that included the claim 'Better tolerated … etc.' was only one of the three videos, and therefore only made a claim on one of the aforementioned attributes.

Whilst Gilead set out in its original response to the complaint the intention of the rose and thorns imagery to show that Biktarvy had addressed some key treatment limitations, the Panel did not clearly outline in its ruling why the other attributes listed on the stand could not be equally considered as contributing to the overall image and feel of the promotion, and why instead it was considered that the image was simply representing the relative hazardous nature of Biktarvy in comparison to DTG-containing regimens.

Gilead submitted that accordingly, it did not agree that it was probable that the audience would interpret the presence of the rose head in the videos as intended to connect them with the rose and thorns imagery on the main stand panel in a way that was intended to specifically link the dropped thorns with the 'Better tolerated than DTG-containing regimens … etc.' claim, as opposed to any of the other claims in the videos. The rose heads were displayed as a consistent image across the campaign, not as a tool to subtly link the one claim in dispute to dropped thorns displayed centrally. The Panel's position here contrasted with its position on the claim assessed in point 1 where it decided that wording adjacent to a claim should not be taken in to account when assessing the acceptability of that claim.

Gilead submitted that further, it did not agree that it was probable that the specialist HIV physician audience visiting the stand would view the videos and consider that the small number of loose thorns on the central stand panel were implying that DTG-containing regimens were, in fact, hazardous or injurious. Not only was this just too remote and indirect a connection, but the audience exposed to the imagery were all experts in the management of HIV, with significant (up to 4 years) experience of prescribing DTG in clinical practice at the time of the Glasgow 2018 conference. To suggest that such an experienced audience would take a literal interpretation of this image and conclude that DTG was instead hazardous did not give them due credit. The video did not disparage DTG-containing regimens in breach of Clause 8.1. Gilead submitted this not just because it considered this to be the correct position but also because of the context in which the Biktarvy campaign shown on the HIV Glasgow stand was in fact developed. The rose and thorn imagery in the campaign was developed by Gilead's US based global marketing team to demonstrate the qualities of Biktarvy vis a vis some of the limitations seen with other HIV treatments. The imagery was not developed to be used in the context of any specific comparative claim relating to DTG-containing regimens and this was not how it had been used by the Gilead US team. An example of an advertisement used by the US team during the period prior to the Glasgow conference was provided. The imagery came first, and the addition of the 'Better tolerated claim' was a later step in the UK Biktarvy material shown at the Glasgow conference. The rose and thorns imagery was never intended to indicate any safety or hazard message, and Gilead did not agree that it was probable that the intended audience would view it in that way. To the contrary, the imagery was designed to show a positive image to represent Biktarvy, to show the features and benefits of the product, hence the headline statement 'The Beauty of what is Possible'. After all, roses were mostly associated with positive intent, as a flower given as a positive and caring gesture, and not with an intent to cause injury.

MHRA and IPHA Code of Practice Council

Gilead submitted that, again, in the context of indicating alternative views to the decision reached by the Panel, it highlighted that both the MHRA and the IPHA Code of Practice Council had reviewed the rose and thorns imagery in connection with the Biktarvy material.

The rose and thorn imagery used on the stand was included in the materials that were reviewed and approved by the MHRA as part of its pre-vetting of Biktarvy promotional material. If the MHRA had considered that this imagery suggested anything other than the clear meaning intended by Gilead as outlined above, Gilead considered that it would have objected to the material. Further, Gilead did not accept that, in displaying materials and imagery on its stand that had been reviewed and approved by the MHRA, it had not maintained high standards and so appealed the ruling of a breach of Clause 9.1.

Gilead submitted that the rose and thorns imagery was also considered by the IPHA Code of Practice Council in the case brought before them, and they ruled no breach in response to a similar complaint raised.

Material that was not the subject of complaint

Gilead submitted that as a separate point of appeal, and in the alternative and without prejudice to the arguments raised above which it considered adequately established that the Appeal Board should overturn the breaches ruled, it noted that in making a ruling on this complaint the Panel had recognised the exceptional circumstances of this case where the Panel was making a ruling on material that was specifically identified as being the subject of the complaint but had found it was in breach of the Code only due to associations identified with images contained in other material on the stand that was not specifically the subject of the complaint. Given these unusual circumstances, Gilead asked the Appeal Board to consider whether the Panel's approach here was correct or whether the Panel had gone beyond its remit in identifying a breach in the complained about material that primarily arose due to content in a material that was not specifically the subject of the complaint submitted. Whilst Gilead recognized that context was important, the situation here went beyond that and required an assessment and judgment on the specific detail of the context in deciding whether the complained about material was acceptable. As no specific complaint was made against the material that contained the image of a rose which had shed thorns (ref BIK/IHQ18-09//1177c), it was fair to assume that the main rose imagery including the dropped thorns was accepted to fairly represent Biktarvy in terms of addressing existing HIV treatment limitations. If this was the case, was it appropriate to take that imagery and place it in a different context and rule the combined piece in breach? Gilead specifically did not include images of a rose and dropped thorns in the video containing only the 'Better tolerated claim' as this would imply that the imagery was specific to that claim and it was not as explained above.

Finally, Gilead submitted, for completeness, that if the appeal was successful at Point 1, then it followed that Gilead's appeal against the breaches ruled in relation to this section of the complaint relating to the rose and thorns should be upheld too. The breaches ruled by the Panel in relation to this complaint, namely that (a) the material was in breach of Clause 7.4 as the video by association with the imagery and claim on the stand panel and the claim 'Better tolerated than DTG-containing regimens' within the video loops implied that Biktarvy was less hazardous than DTG-containing regimens and that this implication could not be substantiated and (b) that the video disparaged DTG-containing regimens in breach of Clause 8.1, should not be upheld.

Further Gilead submitted that it had maintained high standards in relation to this material and that the Panel's ruling of a breach of Clause 9.1 should again not be upheld.

RESPONSE FROM VIIV

ViiV alleged that imagery was hugely powerful in conveying meaning and making it memorable which was why advertisers in all industries focussed so heavily upon it. It was also why the meaning it conveyed must be clear and accurate.

ViiV alleged that roses were cultivated for their flowers as medicines were developed for their benefits and any reasonable viewer would assume that the flower here was intended to represent the benefits of Biktarvy, which Gilead confirmed in its appeal. ViiV acknowledged that roses were mostly associated with positive intent, however, any rational person would also be wary of the injurious nature of the thorns on a rose stem.

ViiV alleged that the imagery implied that Biktarvy might cause less injury in comparison with another regimen with more thorns. As the Panel agreed, viewers would, on the balance of probabilities, associate the image of a rose head in the looping video with the claim 'Better tolerated than DTG-containing regimens' with the prominent image of a rose with dropped thorns on the large booth panel. This created the impression that Biktarvy had a superior tolerability profile compared to DTG-containing regimens which was further reinforced by the repetition of this imagery across the booth along with the aforementioned claim.

ViiV noted that, initially, it and Gilead had entered into inter-company dialogue face-to-face to discuss ViiV's concerns with regard to Gilead's booth in Glasgow, the outcome of which was an amendment to its initial video to remove imagery of thorns dropping from a rose stem, although the rose and thorn imagery remained across the conference booth along with the disputed claim 'Better tolerated than DTG-containing regimens' on the booth panels and in the video. Despite numerous emails and written letter exchanges, inter-company dialogue was unsuccessful to address ViiV's concerns and clearly highlighted Gilead's intent to show the rose and thorn imagery alongside the disputed claim.

ViiV alleged that the use of the rose and thorn imagery to represent Biktarvy, was misleading at best, and dangerously complacent with respect to risk management of a new medicine at worst. Imagery was always open to interpretation, but ViiV alleged that there was no reasonable interpretation of this imagery that made it acceptable as it created an unjustified impression of the safety profile of Biktarvy and implied superior tolerability compared to DTG-containing regimens by use in association with the aforementioned claims.

ViiV noted that it was of concern that Gilead was conveying through this imagery a sense that Biktarvy had a better safety profile because Biktarvy was a new medicine for which the full real-world safety profile was as yet unknown. This was clear from the black triangle the promotional material carried. This overstatement of safety at the Glasgow conference was particularly concerning given the lack of real world experience at that time, and considering newer data now showed emerging safety signals with regard to weight gain associated with INSTIs and TAF, and an absence of data in pregnancy and paediatrics.

ViiV alleged that Gilead asserted that the addition of tolerability claims was a later addition at the HIV Glasgow conference booth to the rose and thorn imagery initially developed by the US-based marketing team. This was disingenuous as ViiV noted that Gilead had used the rose and thorn imagery in conjunction with tolerability claims from as early as September 2018 in Australia. Gilead continued to use the rose and thorn imagery along with tolerability claims in promotional materials in Australia, most notably at the recent Australasian HIV & AIDS (ASHM) conference where large 3D thorns were seen to be hanging off a rose stem above the booth.

The same campaign had been seen across promotional materials in several other countries. ViiV acknowledged that promotional materials in countries outside of the UK were outside of the scope of the Code, but considered these materials pertinent to demonstrate that Gilead's intentions to link the rose and thorn imagery with claims of improved tolerability were different from what it stated in its appeal.

ViiV alleged that by Gilead's own admission, the rose and thorn imagery was created to demonstrate the treatment limitations Biktarvy had overcome with other regimens, and as such was disparaging in intent. Biktarvy had not 'overcome', and in fact the characteristics of Biktarvy which Gilead highlighted were achieved with other regimens prior to its authorisation; >90% efficacy at Week 48 was now a standard in HIV clinical trials, as stated above the claim of better tolerability did not reflect the totality of the data, there were other small single-tablet regimens available (Juluca, a DTG-based regimen was the smallest) and did not have flexible daily dosing ie Biktarvy had only once daily dosing with or without food, while Tivicay could be taken once or twice a day with or without food.

ViiV agreed with the Panel that most viewers would see the rose as representing Biktarvy and the thorns as something injurious rather than representing three random 'benefits' as described by Gilead. Consequently, ViiV alleged that the rose and thorn imagery, by association with the imagery and aforementioned disputed claim implied that Biktarvy was less hazardous than DTG-containing regimens, was not capable of substantiation and was disparaging of DTG-containing regimens, as ruled by the Panel, in breach of Clauses 7.4, 8.1 and 9.1.

APPEAL BOARD RULING

The Appeal Board noted its comments above at point 1 with regard to prevetting by the MHRA and considered that they were relevant here. The Appeal Board also noted its rulings in point 1 above.

Context was a very important consideration particularly for images such as that of the red rose. The Appeal Board considered, on the balance of probabilities, that visitors who saw the Gilead stand would associate the image of the rose head in the videos (ref BIK/IHQ18-09//1177a(1)) appearing before and after the claims including 'Better tolerated than DTG-containing regimens' with the large image of the rose with some dropped thorns on the main stand panel (ref BIK/IHQ18-09//1177c). The Appeal Board noted that although this stand panel had not been specifically cited in the complaint ViiV had referred to associations between the rose and loss of thorns appearing throughout the booth. The Appeal Board considered, therefore, that the video, by association with the imagery and claim on the stand panel and the claim 'Better tolerated than DTG-containing regimens' within the video loops, implied that Biktarvy was less hazardous than DTG-containing regimens. The Appeal Board considered that this implication could not be substantiated and it disparaged DTG-containing regimens. The Appeal Board upheld the Panel's rulings of a breach of Clauses 7.4 and 8.1 in relation to the video. The appeal on this point was unsuccessful.

The Appeal Board considered that Gilead had failed to maintain high standards and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

3 Claim 'The beauty of what is possible … Biktarvy … is now a reality'

This claim appeared within a standalone looping video available on the stand (ref BIK\IHQ\18-09\\1177d) which was not referred to by ViiV and within the revised video (ref BIK\IHQ\18-09\\1177a(1)) specifically referred to by ViiV.

COMPLAINT

ViiV alleged that the claim could not be substantiated; it promised a brighter future, even a utopian state of antiretroviral treatment beyond what other regimens delivered. At best, this was ambiguous and at worst it overstated the benefits of Biktarvy. ViiV alleged breaches of Clauses 7.2, 7.3 and 7.10.

ViiV noted that Gilead had asserted that the claim was not a specific claim about Biktarvy and was always accompanied by a number of other claims (>90% efficacy and 0 resistance, better tolerated than DTG-containing regimens and small single tablet regimen with flexible daily dosing) which were all appropriately qualified and substantiated. Gilead had submitted that the headline gave readers an opportunity to reflect and draw their own conclusions.

ViiV noted that it had previously alleged that the claim 'Better tolerated than DTG-containing regimens' was in breach of Clause 7. Clause 7.10 stated that promotion must encourage rational prescribing and claims should not imply that a medicine or an active ingredient had some special merit quality or property. ViiV asserted that by stating 'the beauty of Biktarvy is now a reality' Gilead implied no other antiretroviral product had those qualities and that Biktarvy has some special merit.

RESPONSE

Gilead noted ViiV's assertion that this claim could not be substantiated and made a promise of a brighter future, even a utopian state of antiretroviral treatment beyond what other regimens delivered and that the claim was, at best, ambiguous and, at worst, an overstatement of any benefit of Biktarvy. ViiV had alleged breaches of Clauses 7.2, 7.3 and 7.10.

Gilead noted that ViiV had changed the claim 'The beauty of what is possible … Biktarvy … is now a reality', by altering it to 'the beauty of Biktarvy is now a reality', a claim with a different meaning, to support its allegation that the claim was intended to imply that Biktarvy had some special merit.

Gilead stated that its clear intention was to state the 'beauty of what is possible' as a simple means to introduce the subsequent claims (>90% efficacy and 0 resistance, better tolerated than DTG-containing regimens (significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF) and small, single tablet regimen with flexible daily dosing), and add to this that Biktarvy was now available. Within the header, no specific claims were made about Biktarvy, ie no features or benefits were described, either in isolation or vs any other relevant medicines. The intention was simply to encourage the reader to reflect on each of the subsequent claims that were made, each of which were appropriately qualified and substantiated.

There was no intention from this claim – deliberate or otherwise – to suggest that Biktarvy possessed some special merit and the claim did not do so. To the extent that any attribute was asserted for Biktarvy by the claim, it was that it had addressed, to some extent, all of the limitations identified in the claims made on the stand. It was unclear to Gilead how this

overstated any benefit of Biktarvy. Where there might also be a claim, it was that Biktarvy was now a reality, which was substantiated by the fact it had been granted a marketing authorization. Gilead therefore submitted that the series of statements, 'The beauty of what is possible … Biktarvy … is now a reality', complied with the Code including Clauses 7.2, 7.3 and 7.10.

In summary, Gilead reiterated that the claims made for Biktarvy were based on data from a comprehensive Phase 3 clinical study programme where Biktarvy was compared against the DTG based regimens (DTG plus ABC/3TC or F/TAF), hence the comparative nature of the Biktarvy messages. Gilead submitted that all of its claims were clearly and sufficiently substantiated to aid in the decision making of the health professionals who read them. Accordingly, Gilead strongly defended any suggestion that the activities and claims were in breach of the Code as alleged.

PANEL RULING

The Panel noted that from Gilead's description of the materials it appeared that the claim only appeared in the video (ref BIK\IHQ\18-09\\1177d) which was not referred to by ViiV.

The Panel noted, however, that the statement flow 'The beauty of what is possible … Biktarvy … is now a reality' also appeared in the revised video (ref BIK\IHQ\18-09\\1177a(1)) referred to by ViiV and was referenced to the Biktarvy SPC.

The Panel noted Gilead's submission that the claim at issue was meant to introduce the subsequent claims (>90% efficacy and 0 resistance (Non-inferior vs comparator in all registrational studies), better tolerated than DTG-containing regimens (significantly fewer all grade treatment-related AEs compared to DTG plus ABC/3TC or F/TAF) and small, single tablet regimen with flexible daily dosing), and add to this that Biktarvy was now available.

The Panel considered that the claim 'The beauty of what is possible … Biktarvy … is now a reality' when considered in isolation was not necessarily unreasonable. However, the context of the claim within the material and in relation to all the materials on the stand was relevant. The Panel noted its comments and rulings above at Points 1 and 2 and considered that they were relevant here. The Panel considered that linking the claim 'The beauty of what is possible … Biktarvy … is now a reality' in the video (ref BIK\IHQ\18-09\\1177a(1)) which also included the claim 'Better tolerated than DTG-containing regimens' and the rose imagery was misleading and exaggerated the properties of Biktarvy. The Panel therefore ruled a breach of Clauses 7.2, 7.3 and 7.10.

The Panel noted that whilst the claim also appeared within a standalone video available on the stand (ref BIK\IHQ\18-09\\1177d), which looped through to repeatedly show the Biktarvy logo and intermittently included the statement flow 'The beauty of what is possible … Biktarvy … is now a reality', this item was not specifically referred to by ViiV and therefore the Panel made no rulings with regard to this item.

APPEAL BY GILEAD

Gilead agreed with the Panel's view that the claim 'The beauty of what is possible … Biktarvy … is now a reality', when considered in isolation, was not necessarily unreasonable. However, the Panel considered the context of the claim within the material and in relation to all the materials

on the stand was relevant. The Panel considered that linking the claim in the video (ref BIK\IHQ\18-09\\1177a (1)) which also included the claim 'Better tolerated than DTG-containing regimens' and the rose imagery, was misleading and exaggerated the properties of Biktarvy. The Panel therefore ruled a breach of Clauses 7.2, 7.3 and 7.10.

Gilead did not agree with the Panel's ruling. In line with its prior response, Gilead submitted that the Panel had not identified why the other claims made on the panel (efficacy, resistance, single tablet regimen, small pill, flexible dosing) might not also be relevant to the assessment of this claim which again clearly showed that 'The Beauty of What is Possible' was intended to represent the total attributes of Biktarvy and not one specific element.

Gilead submitted that in addition, logically, as the Panel's view was that the claim when considered in isolation was not necessarily unreasonable, Gilead requested that if its appeal was successful in relation to Point 1 above, then it considered that the Panel's decision on this point would necessarily change and its appeal on this point should also be successful.

Gilead submitted that the claim did not suggest any special properties or use any superlative to describe Biktarvy and if considered acceptable if used in isolation, Gilead did not consider that the claim was any less acceptable within the context in which it was used, and so not in breach of Clause 7.10.

MHRA and IPHA Code of Practice Council

Gilead submitted that, again, in the context of indicating alternative views to the decision reached by the Panel, it highlighted that both the MHRA and the IPHA Code of Practice Council had reviewed the 'Beauty of What is Possible' claim in connection with Biktarvy material.

Gilead submitted that the claim was used in the materials that were reviewed and approved by the MHRA as part of its pre-vetting of Biktarvy promotional material and they did not object to the material. The claim was also considered by the IPHA Code of Practice Council which ruled no breach in response to a similar complaint raised.

In summary, Gilead reiterated that for the reasons set out above, it did not consider that the materials it displayed on the HIV Glasgow conference stand breached the clauses of the Code as ruled by the Panel and accordingly it appealed the Panel's rulings.

RESPONSE FROM VIIV

ViiV alleged that the claim 'The Beauty of what is possible … Biktarvy … is now a reality' was, at best, ambiguous and at worst an overstatement of Biktarvy's benefit compared to other antiretroviral regimens. It could not be substantiated and made a promise of a brighter future and suggested a significant advance of antiretroviral treatment beyond what other regimens delivered. Gilead used the phrase the 'The beauty of what is possible' prominently in promotion, alongside the image of the rose stripped of most of its thorns, in its portrayal of Biktarvy as in some way a significant advance in the management of HIV infection that was not achievable prior to the availability of Biktarvy. Clause 7.10 stated promotion must encourage rational prescribing and claims should not imply that a medicine or an active ingredient has some special merit quality or property. By stating 'the beauty of what is possible … Biktarvy … is now a reality', Gilead implied that no other antiretroviral product had these qualities and that Biktarvy had some special merit. Given the context of the phrase, used as it was in close

proximity to inaccurate and misleading claims of superiority with respect to the tolerability of DTG-based regimens, ViiV alleged that the phrase exaggerated, was misleading and implied special merit as ruled by the Panel (in breach of Clauses 7.2, 7.3 and 7.10).

MHRA pre-vetting and IPHA ruling

ViiV noted that the PMCPA had, on various occasions, judged materials that had been through vetting in breach of the Code. The PMCPA was an independent industry body that responded to complaints whereas the MHRA pre-vetting system did not consider the material in light of complaints. The IPHA findings were not relevant as materials, arguments and regulations varied by jurisdiction. In summary, ViiV alleged that the promotion of Biktarvy by Gilead, as represented by the items found in breach by the Panel, were highly misleading to health professionals. The claim 'Better tolerated than DTG-containing regimens' was fundamentally flawed for the reasons explained above, and this, coupled with the rose and thorn imagery and 'the beauty of what is possible … Biktarvy …. Is now a reality' claim, was misleading and disparaging of DTG-containing regimens.

APPEAL BOARD RULING

The Appeal Board noted its comments at point 1 with regard to prevetting by the MHRA and considered that they were relevant here. The Appeal Board also noted its comments and rulings in points 1 and 2 above.

The Appeal Board considered that linking the claim 'The beauty of what is possible … Biktarvy … is now a reality' in the video (ref BIK\IHQ\18-09\\1177a(1)) which also included the claim 'Better tolerated than DTG-containing regimens' and the rose imagery was misleading and exaggerated the properties of Biktarvy. The Appeal Board therefore upheld the Panel's rulings of breaches of Clauses 7.2, 7.3 and 7.10. The appeal on this point was unsuccessful.

Complaint received **20 December 2018**

Case completed **18 November 2019**