AWMSG Secretariat Assessment Report – Limited submission

Darunavir/cobicistat (Rezolsta®) 800mg/150mg film coated tablet

Company: Janssen-Cilag Ltd

Licensed indication under consideration: in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus 1 (HIV 1) infection in adolescents 12 to <18 years of age, weighing at least 40 kg.

Date of licence extension: 9 March 2020

Comparator(s)

The comparator included in the company's submission was single agent darunavir with ritonavir booster as separate pills.

Limited submission details

- The limited submission criteria were met based on a minor licence extension and anticipated minimal budgetary impact in NHS Wales

Clinical effectiveness

- In 2015, Rezolsta® a once daily fixed dose combination (FDC) tablet of darunavir/cobicistat was recommended by the All Wales Medicines Strategy Group (AWMSG) as an option for use in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years or older.
- This limited submission criteria covers the license extension to include use in adolescents 12 years to <18 years of age, weighing at least 40 kg.
- Cobicistat, a pharmacokinetic enhancer, is an analogue of the protease inhibitor ritonavir which, unlike ritonavir, has no anti-retroviral activity. AWMSG has previously recommended cobicistat as an option for use as part of other fixed dose combinations.
- This submission includes evidence from an ongoing, open-label, Phase II/III study (GS-US-216-0128) conducted to assess the the efficacy, safety, and pharmacokinetics of darunavir 800 mg and cobicistat 150 mg administered as separate tablets in combination with two nucleoside reverse transcriptase inhibitors (NRTIs) in seven HIV-1 infected, treatment-experienced, virologically suppressed adolescents (weighing at least 40 kg).
- The primary end-point was met: virologic success (HIV-1 RNA < 50 copies/ml) at Week 48 (a standard measure of HIV-1 control) was achieved in six out of seven patients.
- The Committee for Medicinal Products for Human Use (CHMP) concluded that pharmacokinetic data for the different components of Rezolsta® indicated that darunavir levels in adolescents were within the overall range of those observed in adults treated with darunavir and cobicistat. The difference observed for cobicistat was not considered clinically relevant.

- The safety profile of the individual components of Rezolsta® is well-established. Study GS-US-216-0128 is considered too small to draw meaningful conclusions regarding safety. However, the study did not reveal any new safety concerns. The CHMP concluded that overall the safety profile in adolescents was similar to that observed in adults for the same dosage and consistent with the known safety profiles of darunavir and cobicistat.
- Rezolsta® provides an alternative to ritonavir boosted darunavir for patients who do not tolerate ritonavir. The company suggest that a darunavir/cobicistat FDC tablet may improve compliance and reduce pill burden.

Budget impact

- The company estimates that the eligible number of patients in Wales would be five per year. Assuming an uptake of 10-20% approximately one patient per year would receive Rezolsta® in each of the next five years. The company based these estimates on annual incidence figures from the 2019 Collaborative HIV Paediatric Study (CHIPS) data. CHIPS is an ongoing multi-centre cohort study of HIV infected children in the UK and Ireland and includes Welsh patients. The company assumed that Rezolsta® will only be used in patients currently taking darunavir plus ritonavir as separate tablets.
- Rezolsta® would have an additional cost of £579 per patient annually if it displaces darunavir plus ritonavir.
- The budget impact analysis is limited to the comparator included in the company's submission. The company estimate does not consider displacement of any other protease inhibitor regimens such as those containing atazanavir.
- Whilst there are some limitations in the company's estimate, the overall budgetary impact is anticipated to be minimal.

Additional information

- AWTTC is of the opinion that, if recommended, darunavir/cobicistat (Rezolsta ®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.
- The company anticipates that darunavir/cobicistat (Rezolsta®) may be supplied by a home healthcare provider.

Evidence search

Date of evidence search: 03 August 2020
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.

References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Darunavir/cobicistat (Rezolsta®) 800mg/150mg film coated tablet. Reference number: 3779. October 2020

Appendix: Previous AWMSG secretariat assessment report (published June 2015)

In July 2015, AWMSG appraised Darunavir/cobicistat (Rezolsta®▼) in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus 1 (HIV 1) infection in adults aged 18 years or older (AWTTC reference number 2193). This advice is now incorporated into the Final Appraisal Recommendation (FAR) of Darunavir/cobicistat (Rezolsta®▼) in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus 1 (HIV 1) infection in adults and in adolescents (aged 12 years and older, weighing at least 40 kg) (AWTTC reference number 3779).

The original report for AWTTC reference number 2193 is included below for completeness.

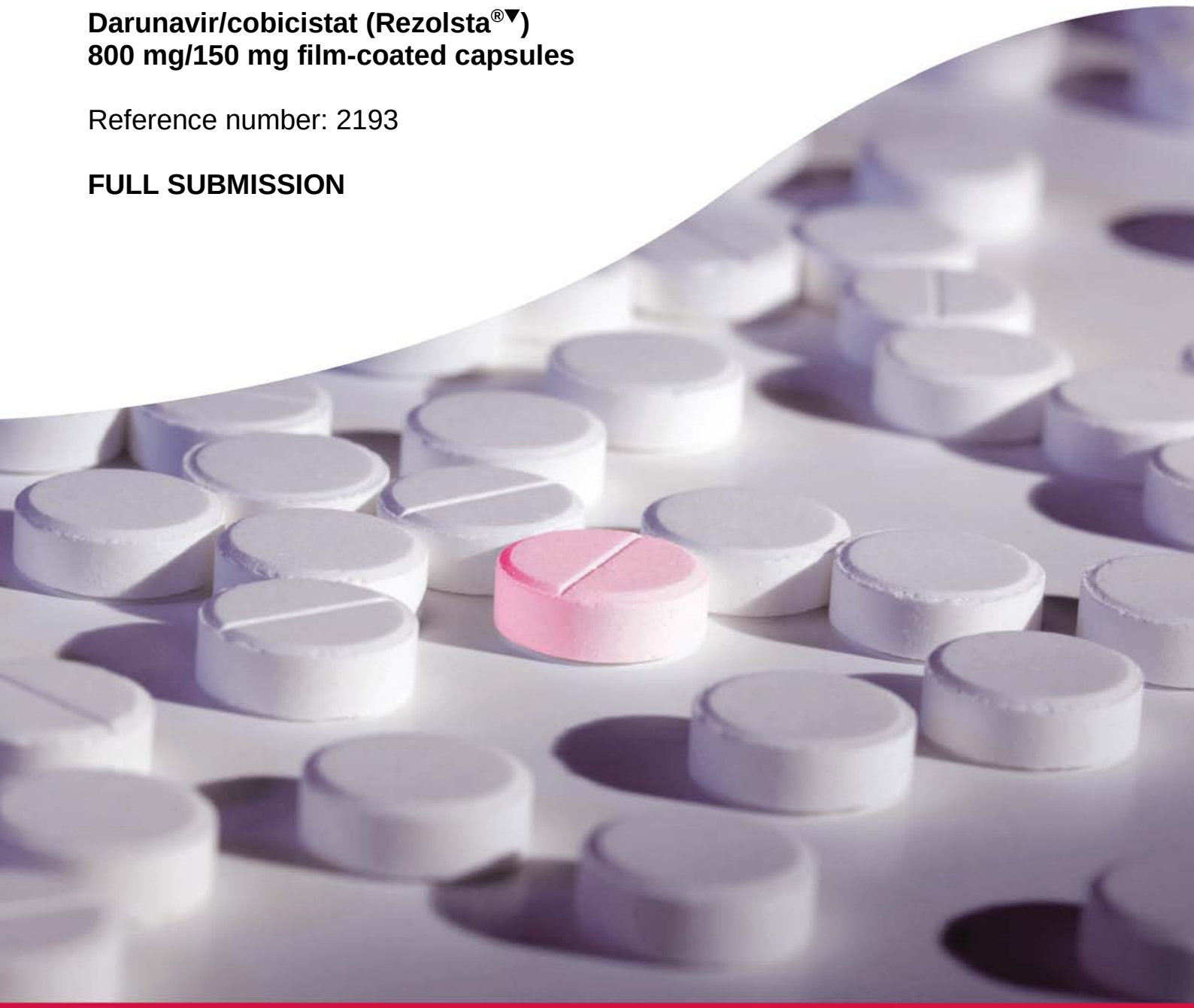
All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG SECRETARIAT ASSESSMENT REPORT

Darunavir/cobicistat (Rezolsta®▼)
800 mg/150 mg film-coated capsules

Reference number: 2193

FULL SUBMISSION



This report has been prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC), in collaboration with the Centre for Health Economics and Medicines Evaluation, Bangor University.

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This report should be cited as:
All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Darunavir/cobicistat (Rezolsta®▼) 800 mg/150 mg film-coated capsules. Reference number: 2193. June 2015.

AWMSG Secretariat Assessment Report
Darunavir/cobicistat (Rezolsta®▼) 800 mg/150 mg film-coated capsules

This assessment report is based on evidence submitted by Janssen-Cilag Ltd on 27 February 2015[1].

1.0 PRODUCT DETAILS

Licensed indication under consideration	Darunavir/cobicistat (Rezolsta®▼) in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years or older. Genotypic testing should guide the use of darunavir/cobicistat[2].
Dosing	Antiretroviral therapy (ART)-naive patients: One tablet once daily with food. ART-experienced patients: One tablet once daily with food in patients without darunavir resistance associated mutations (DRV-RAMs) and who have plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥ 100 cells x 10^6/L. In all other ART-experienced patients or if HIV-1 genotype testing is not available the use of darunavir/cobicistat is not appropriate. Refer to the Summary of Product Characteristics for further information regarding darunavir resistance, missed doses and special populations[2].
Marketing authorisation date	19 November 2014[3]

2.0 DECISION CONTEXT

2.1 Background

Human immunodeficiency virus (HIV) is a retrovirus that infects cells in the human immune system, such as $CD4^+$ lymphocytes, causing their destruction which results in the progressive suppression of the host immune system. Untreated HIV is a progressive disease leading to the development of acquired immunodeficiency syndrome (AIDS)[4]. In 2013, there were 1,661 patients with HIV resident in Wales (75% male, 75% white), of whom 1,404 were receiving antiretroviral therapy (ART)[5].

Current British HIV Association guidelines for the treatment of HIV recommend a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one ritonavir-boosted protease inhibitor (PI) or non-nucleoside reverse transcriptase inhibitor (NNRTI) or an integrase inhibitor (INI) in anti-retroviral therapy-naive patients[6]. The choice of ART should take into consideration drug interactions, co-morbidities, pregnancy and cardiovascular risk factors. Over time HIV mutations resistant to ART can develop, particularly if adherence is suboptimal, resulting in virological failure (viral load > 50 copies/ml)[4,6]. If therapy starts to fail, resistance testing is performed and the results reviewed along with any archived mutations. The ART regimen should be changed as quickly as possible to avoid the accumulation of resistant mutations[6].

Cobicistat is an analogue of the PI ritonavir which, unlike ritonavir, has no anti-retroviral activity[7]. Cobicistat is a potent inhibitor of cytochrome CYP3A which increases the absorption and slows down metabolism of darunavir with the net effect of enhanced plasma levels and prolonged half-life[7,8].

Rezolsta®▼ is a fixed dose combination (FDC) of the PI darunavir with cobicistat, a PI booster.

2.2 Comparators

The comparators included in the company submission were:

- Darunavir (Prezista®) with ritonavir (Norvir®)
- Atazanavir (Reyataz®) with ritonavir (Norvir®)

2.3 Guidance and related advice

- British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2012 (Updated November 2013)[6].
- European AIDS Clinical Society. European guidelines for the treatment of HIV-infected adults in Europe. Version 7.02 (2014)[9].

The All Wales Medicines Strategy Group (AWMSG) has previously issued recommendations for darunavir (Prezista®) in combination with ritonavir (Norvir®)[10–12] and elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (Stribild®▼) fixed dose combination (FDC) tablet[13].

Statements of advice (SOA) have been issued for:

- Darunavir (Prezista®) for use in combination with cobicistat[14]
- Cobicistat (Tybost®▼)[15]

These medicines cannot be endorsed for use within NHS Wales.

3.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

The applicant company provided evidence from a phase I crossover study (GS-US-216-0115) comparing the pharmacokinetics (PK) of darunavir co-administered with ritonavir or with cobicistat, and a PK bridging programme of two phase I crossover studies (TMC114IFD1001 and TMC114IFD1003) comparing the darunavir/cobicistat FDC with darunavir co-administered with cobicistat and with ritonavir as single agents[1,16–18]. The company submission also included a phase IIIb single-arm, open-label study (GS-US-216-0130) investigating the efficacy, safety and PK of darunavir co-administered with cobicistat as single entities[1,19]. An indirect comparative analysis of pooled phase III study data was included to address the lack of head-to-head comparative data[1,20].

3.1 GS-US-216-0115 crossover study

GS-US-216-0115 was a phase I open-label, multiple-dose, two period crossover study in healthy volunteers, with treatment A: darunavir 800 mg plus cobicistat 150 mg (as single agents) once daily and treatment B: darunavir 800 mg plus ritonavir 100 mg (as single agents) once daily over a ten day period, followed by a five day washout period between treatments[1,18]. Plasma PK was performed over 24 hours measuring darunavir concentration predose (C_0), maximum plasma concentration (C_{max}), area under the concentration–time curve at 24 hours (AUC_{24}) and concentration at 24 hours (C_{24}). Darunavir co-administered with cobicistat was demonstrated to be bioequivalent to darunavir co-administered with ritonavir, with the 90% confidence intervals (CIs) for AUC_{24}, C_{max} and C_0 lying within the predefined 80–125% range[1,7].

3.2 Phase I bridging studies

Two phase I open-label, randomised, crossover studies in healthy volunteers, TMC114IFD1001 (IFD1001) and TMC114IFD1003 (IFD1003), investigated the PK of the darunavir/cobicistat FDC[16,17].

Study IFD1001 compared the bioavailability of the darunavir/cobicistat FDC with that of darunavir co-administered with ritonavir as single entities. Volunteers (n=36) received: three treatments: darunavir 800 mg and ritonavir 100 mg co-administered as single agents

once-daily or darunavir/cobicistat 800/150 mg FDC once-daily (as formulation GOO3 and as formulation GOO4)[16]. Treatments were administered over three, randomised 10-day sequences under fed conditions. Plasma concentrations of darunavir, cobicistat and ritonavir were taken over 24 hours once steady state conditions for darunavir were achieved on day ten. The C_{max} and AUC_{24} were within the limits of bioequivalence between the two FDC formulations of darunavir/cobicistat and darunavir plus ritonavir[16].

In study IFD1003 the primary outcome was the PK and bioequivalence of darunavir administered with cobicistat as a FDC versus co-administration as single agents under fasted and fed conditions[1,17]. The least square means ratios of the key PK parameters for darunavir exposure as the FDC versus the single agents showed no significant difference under both fasted and fed conditions. The presence of food increased the exposure to darunavir while having no effect on cobicistat pharmacokinectics. The 90% confidence intervals of the least square means ratio for each PK parameter fell within the pre-defined limits of 80–125% established for bioequivalence[7,17].

3.3 GS-US-216-0130 study

GS-US-216-0130 was an open-label, single arm, multicentre study in HIV-1 infected, ART-naive adults or ART-experienced adults with no darunavir resistance associated mutations (DRV RAMs)[1,19]. The primary efficacy endpoint was the proportion of patients with HIV RNA < 50 copies/ml at weeks 24 and 48. The primary safety endpoint was adverse events and laboratory tests up to 24 weeks of treatment. Patients (n = 313) received darunavir 800 mg and cobicistat 150 mg co-administered as single agents once daily plus two investigator-selected NRTIs for at least 48 weeks. Of the 313 patients who received at least one dose of treatment medicine 295 were ART-naive and and 18 were ART-experienced[1,19].

At 24 weeks 83.7% (95% CI 79.0–87.6) of ART-naive and 61.1% (95% CI 35.7–82.7) of ART-experienced patients had HIV-RNA < 50 copies/ml (virologic success). At 48 weeks 82.7% and 50.0% of ART-naive and ART-experienced patients respectively achieved virologic success[7,19]. Resistance development to darunavir, other PIs or the NRTI backbone was rare at the 24 week analysis[7].

3.4 Adjusted indirect treatment comparison

In the absence of head-to-head studies the company have provided comparative analyses of pooled phase III data from three studies (GS-216-0130[19], ARTEMIS[21] and ODIN[22]). ARTEMIS and ODIN studies had two arms, in this analysis the darunavir 800 mg plus ritonavir 100 mg once-daily arms were included as comparator arms to the darunavir 800 mg plus cobicistat 150 mg single arm of study GS-US-216-0130 to investigate non-inferiority[20]. Snapshot analysis of virologic response at week 48 was taken as the common time point for comparison.

A total of 313 patients (297 ART-naive and 18 ART-experienced) treated with darunavir plus cobicistat and 637 patients (343 ART-naive and 294 ART-experienced) treated with darunavir plus ritonavir were included in the analysis. Odds ratios were adjusted for the following sources of confounding bias: darunavir treatment adherence; age; gender; race; baseline CDD4+ T-cell counts; baseline HIV-1 RNA; HIV disease status and previous retroviral use. The snapshot analysis at 48 weeks resulted in an estimated odds ratio for the comparison of darunavir plus cobicistat versus darunavir plus ritonavir of 0.878 (95% CI 0.576–1.339). The lower 95% CI boundary was within the pre-defined margin for inferiority of 0.531[20]. Overall this suggests that the response to darunavir plus cobicistat is comparable to darunavir plus ritonavir[1,20].

3.5 Comparative safety

No serious adverse events were reported across any of the treatment groups in the phase I studies[16,17]. Over all studies reported, the incidence rates of grade 3 and 4 AEs, were small and non severe. Rash, nausea and diarrhoea were the most frequent AEs reported, with two discontinuations as a result of rash. CHMP have not identified any safety concerns associated with either the darunavir/cobicistat FDC or the separate entities[7].

3.6 AWTTC critique

- There are no efficacy or safety studies for the darunavir/cobicistat FDC. The clinical development programme for darunavir/cobicistat FDC was based on the development programmes of the single agents, a pharmacokinectic bridging programme and a phase IIIb single arm study. CHMP concluded that the bridging studies were acceptable for demonstrating efficacy of darunavir/cobicistat FDC[1].
- The only efficacy and safety data for darunavir plus cobicistat currently available is from a single-arm open-label study (GS-US-216-0130) investigating the separate tablets[19]. There are no long–term safety data on darunavir with cobicistat either as the FDC or single entities. Currently 48 week data are available for darunavir with cobicistat as single entities[7].
- Direct comparative data for the darunavir/cobicistat FDC is limited to the bioavailability study (IFD1001) which demonstrated bioequivalence of darunavir in the FDC compared to co-administration with ritonavir in healthy subjects[16]. There is no direct comparative efficacy or safety data in HIV patients included in the submission.
- There is limited data on patients switched from other regimens, in study GS-US-216-0130 only 18 participants were ART-experienced[7,19]**.**
- Indirect analysis of pooled data provided by the company demonstrated non-inferiority of darunavir plus cobicistat as separate tablets to ritonavir-boosted darunavir[20]. Potential sources of confounding bias in baseline characteristics were adjusted for in the model, however, as with all indirect comparisons results should be interpreted with caution.
- None of the studies presented in the company submission collected health-related quality of life (HRQoL) data which would be of value in assessing the comparative merits of the FDC.
- Rezolsta®▼ is currently the only once-daily single tablet PI booster FDC product licensed in the UK. The company suggest that a darunavir/cobicistat FDC tablet may improve compliance and reduce bill burden.
- The company state that the low rate of resistance development confirms a high genetic barrier to resistance of darunavir boosted with cobicistat[1]. It is unclear if this barrier to resistance when darunavir is boosted with cobicistat is comparable to that of darunavir co-administered with an alternative PI booster such as ritonavir.
- The darunavir/cobicistat FDC provides an alternative to ritonavir boosted darunavir for patients who do not tolerate ritonavir[1].

4.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

4.1 Cost-effectiveness evidence

4.1.1 Context

The company submission includes a cost minimisation analysis (CMA) of the antiretroviral PI darunavir 800 mg plus cobicistat 150 mg as a once-daily oral FDC indicated for use in combination with other antiretroviral medicinal products for the treatment of HIV-1 infection in treatment naive adults (aged 18 years or older) compared against darunavir 800 mg and atazanavir 300 mg both taken once-daily and boosted with once-daily ritonavir 100 mg[1].

No direct comparative data are available for darunavir/cobicistat FDC and these comparators. The company has described an open-label, single-arm study of darunavir 800 mg boosted with cobicistat 150 mg (GS-US-216-0130)[19] and provides a pooled, adjusted comparative analysis of patient-level data from this study and trials investigating darunavir 800 mg boosted with ritonavir 100 mg[20]. Evidence is also provided on an open-label, randomised bioavailability study comparing darunavir/cobicistat FDC and darunavir boosted with ritonavir (IFD1001)[16] and an open-label, randomised study (IFD1003) investigating bioequivalence of darunavir/cobicistat FDC and darunavir plus cobicistat taken as three individual tablets (two 400 milligrams darunavir and one 150 milligrams cobicistat tablets)[17].

The economic evaluation is based on a Markov model comprising three health states (on treatment, off treatment and death) and the analysis is limited to consider acquisition costs of darunavir/cobicistat FDC and the chosen comparators only. The model assumes equal efficacy, safety, discontinuation rates and nucleoside reverse transcriptase inhibitor backbone for all three treatments and does not include subsequent lines of treatment. Mortality data are taken from the Office of National statistics (Welsh population all-cause mortality)[23] and Public Health England (HIV-specific mortality rates)[24] and a 10-year time horizon was chosen based on the assumption that the majority of patients will have switched to subsequent lines of treatment after ten years. Medicine acquisition costs were obtained from the British National Formulary[25] and a discount rate of 3.5% per annum was applied after the first year.

One-way sensitivity analyses were used to investigate the effect of changing the discount rate to 0% and 6%, and increasing the time horizon to 20 years. The impact of changes in the discontinuation rate to values reported by the studies used for the pooled adjusted comparison was also investigated[19,21,22].

4.1.2 Results

The results of the base case analysis are presented in Table 1. Darunavir/cobicistat FDC is reported to produce cost savings compared to atazanavir boosted with ritonavir and to be cost-neutral compared to darunavir boosted with ritonavir.

Table 1. Cost and cost difference of darunavir/cobicistat FDC compared to comparator treatments over ten years

	Total costs over 10 years*	Difference over 10 years
Darunavir/cobicistat 800 mg/150 mg FDC	£15,614†	-
Atazanavir 300 mg plus ritonavir 100 mg	£15,889	-£275
Darunavir 800 mg plus ritonavir 100 mg	£15,614	-£0

FDC: fixed dose combination
*Costs are based on British National Formulary list prices[25].
†Discount rate of 3.5% applied after one year.

Sensitivity analyses investigated the effect of changes in the discount rate, time horizon and discontinuation rate on results. Cost savings only changed marginally within the ranges tested and darunavir/cobicistat FDC remained cost-neutral compared to darunavir plus cobicistat as single entities and cost-saving compared to atazanavir plus ritonavir in all analyses.

4.1.3 AWTTC critique

The reliability of the CMA presented in the company submission is dependent on the extent to which darunavir/cobicistat FDC is considered to be therapeutically equivalent to the comparator therapies. There is a lack of direct comparative data, but the company has provided evidence supporting the bioequivalence of darunavir/cobicistat FDC to darunavir plus ritonavir under fasted and fed conditions[16,17].

Strengths and limitations of the economic analysis are as follows:

- The use of CMA in the comparison of darunavir/cobicistat FDC compared to darunavir plus ritonavir appears justifiable based on the bioequivalence data presented by the company. However, bioequivalence is established only between darunavir/cobicistat FDC and darunavir plus cobicistat (separate tablets). As a consequence of the bioequivalence between these two agents, the company applies the efficacy and safety results of the study investigating the separate tablets to the FDC directly. Furthermore, based on a published pooled adjusted comparative analysis which suggested that cobicistat 150 mg was non-inferior to ritonavir 100 mg as a booster for darunavir 800 mg and similar bioavailability[20], the CMA compares darunavir/cobicistat FDC to darunavir plus ritonavir without any direct or indirect comparative data on efficacy and safety which could introduce bias.

- No data on the effect of darunavir/cobicistat FDC on patient health-related quality of life are available as none of the studies presented by the company collected such data. The company argues that equivalence in safety and efficacy supports the assumption of equal quality of life compared to darunavir plus ritonavir. However, a lack of quality of life data and direct comparison between the two treatments means the appropriateness of CMA cannot be assured with certainty.
- The company's analysis assumes equal efficacy and safety between darunavir plus ritonavir (and hence darunavir/cobicistat FDC) and atazanavir plus ritonavir. However, darunavir plus ritonavir was superior to atazanavir plus ritonavir in the combined tolerability and virologic efficacy endpoints and discontinuation rates due to toxicity were found to be higher with atazanavir[26]. The company suggest this is a conservative approach as patients receiving atazanavir plus ritonavir are more likely to switch treatment earlier and would therefore incur higher costs with subsequent lines of treatment.
- The economic model includes the health state of "off treatment" although no costs for second-line treatments were included. The company propose that the costs associated with subsequent treatment would be the same in both arms. The discontinuation rates were assumed to be same in the model however this may be considered a conservative approach as atazanavir plus ritonavir demonstrated an inferior tolerability profile. Due to differences in tolerability, discontinuation rates and costs, the use of CMA appears inappropriate.
- The company presents one-way sensitivity analyses which show that within the ranges selected, cost-effectiveness is not sensitive to changes in parameter estimates. The superiority of darunavir/cobicistat FDC was not compared to atazanavir plus ritonavir. The company reported this was due to no direct clinical evidence being available.

5.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

5.1 Budget impact evidence

5.1.1 Context and methods

Prevalence and incidence data for HIV infection in Wales were obtained from Public Health Wales reports for the years 2007 to 2012[27] but the budget impact analysis does not consider mortality. Based on the average number of new cases per year between 2007 and 2012, it is estimated that the yearly incidence of HIV in Wales is 152 new patients per year assuming incidence to be constant over the first five years after introduction of darunavir/cobicistat FDC and prevalence is assumed to increase at a rate of 8.94% per year. The company assumes that all diagnosed patients are treated for HIV and that in 2015, 29.93% of patients receive a PI and are therefore eligible for treatment with darunavir/cobicistat FDC. This proportion is expected to decrease to 20.93% by 2019. Expected uptake rate is assumed to be 9.92% in year one rising to 49.92% in year five which translates into 58 patients receiving darunavir/cobicistat FDC in year one increasing to 289 patients in year five.

5.1.2 Results

The estimated net budget impact is presented in Table 2. The company assumes that darunavir/cobicistat FDC will displace darunavir plus ritonavir. Given the fact that darunavir/cobicistat FDC is priced at parity with darunavir plus ritonavir the budget impact would be £0.

Table 2. Company-reported costs associated with use of darunavir/ cobicistat FDC for the treatment of HIV-1 infection

	Year 1 (2015)	Year 2 (2016)	Year 3 (2017)	Year 4 (2018)	Year 5 (2019)
Number of eligible patients currently receiving PIs	588	534	535	557	580
Uptake (%)	9.92%	21.76%	31.50%	41.40%	49.92%
Treated patients	58	116	169	231	289
Total cost of treatment introduced	£225,474	£448,789	£650,973	£891,405	£1,117,552
Total cost of treatment being replaced	£225,474	£448,789	£650,973	£891,405	£1,117,552
Overall net cost	**£0**	**£0**	**£0**	**£0**	**£0**
Derived from the number of Welsh residents treated minus patients aged 15 or less[27] Market shares of darunavir/cobicistat FDC and PIs extrapolated from recent market research data[28]					

Varying the market share of darunavir 800 mg plus cobicistat 150 mg FDC by 10% did not change the results.

5.1.3 AWTTC critique

Due to the fact that the budget impact analysis as presented by the company is based on medicine acquisition cost only, the uncertainties regarding therapeutic equivalence as noted above for the CMA apply. Other limitations are as follows:

- The displacement of atazanavir plus ritonavir by darunavir/cobicistat FDC has not been considered in the budget impact analysis however atazanavir plus ritonavir is more expensive, and inclusion would most likely result in cost-savings.

5.2 Comparative unit costs

Acquisition costs for darunavir/cobicistat FDC (Rezolsta®▼) and alternative PI options for the use in combination with other antiretroviral medicinal products for the treatment of HIV-1 infection in treatment naive adults are presented in Table 3.

Table 3. Examples of acquisition costs of antiretroviral PIs and PI boosters

Regimens	Example doses	Approximate monthly costs per patient*
Darunavir 300mg plus cobicistat 150mg (Rezolsta®) 30 tablets	Once daily as a fixed dose combination	£317.24
Atazanavir (Reyataz®) 300mg capsules (30 pack)	Once daily (to be taken in combination with cobicistat or low-dose ritonavir)	£303.38
Darunavir (Prezista®) 800mg tablets (30 pack)	Once daily (to be taken in combination with cobicistat or low-dose ritonavir)	£297.80
Fosamprenavir (Telzir®) 700mg tablets (60 pack)	Twice daily (to be taken in combination with low-dose ritonavir)	£220.13
Lopinavir + ritonavir (Kaletra®) 200mg + 50mg tablets (120 pack)	Two tablets twice daily	£285.41
Saquinavir (Invirase®) 500mg tablets (120 pack)	Two tablets twice daily (to be taken in combination with low-dose ritonavir)	£251.26
Tipranavir (Aptivus®) 250mg capsules (120 pack)	Two tablets twice daily (to be taken in combination with low-dose ritonavir)	£441.00
Ritonavir (Norvir®) 100mg tablets (30 pack)	Once or twice daily as low-dose booster for other PIs	£19.44
Cobicistat (Tybost®) 150mg tablets (30 pack)	Once daily as low-dose booster for other PI	£21.38
This table does not imply therapeutic equivalence of drugs or the stated doses and not all regimens may be licensed for use in this patient population. See relevant Summaries of Product Characteristics for full licensed indications and dosing details[29–36]. *Costs are based on BNF list prices assuming vial wastage[25]. Costs of administration are not included.		

6.0 ADDITIONAL INFORMATION

6.1 Prescribing and supply

AWTTC is of the opinion that, if recommended, darunavir/cobicistat (Rezolsta®▼) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

The company anticipate that darunavir/cobicistat (Rezolsta®▼) may be supplied by a home healthcare provider.

6.2 Ongoing studies

The company states that study GS-US-216-130 (see Section 3.3) is ongoing however timelines for the final analysis are presently unknown[1].

6.3 AWMSG review

This assessment report will be considered for review three years from the date of the Final Appraisal Recommendation.

6.4 Evidence search

Date of evidence search: 20 March 2015
Date range of evidence search: No date limits were applied to database searches.

References

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