
Supplementary Online Content

van Engen A, Casamayor M, Loftus F, et al. Economic evaluation of fidaxomicin for the treatment of Clostridium difficile infection (C. difficile-associated diarrhoea) in Ireland. *JHEOR* 2015;2(2):192-206

Appendix: Overview Model Input Parameters and Ranges used

This supplementary material has been provided by the authors to give readers additional information about their work.

Appendix: Overview Model Input Parameters and Ranges used

| Variable Name | Variable Description | Base Case Input* | Distribution | Range for SA | | Source |
|---------------------|---|------------------|------------------------------------|------------------|------------------|----------------------------|
| | | | | Min | Max | |
| OR_cure_fdx_non_sev | Odds ratio for clinical cure in non-severe CDI treated with FDX | 1.45 | Log Normal (mean= 1.48; SD=0.248) | 0.630 | 3.360 | FDX studies ^{1,2} |
| OR_cure_fdx_sev | Odds ratio for clinical cure in severe CDI treated with FDX | 0.86 | Log Normal (mean= 0.86; SD=0.273) | 0.502 | 1.465 | FDX studies ^{1,2} |
| OR_cure_fdx_rec | Odds ratio for clinical cure in CDI recurrence treated with FDX | 1.08 | Log Normal (mean= 1.08; SD=0.488) | 0.415 | 2.808 | FDX studies ^{1,2} |
| OR_cure_mtz | Odds ratio for clinical cure in non-severe CDI (first recurrence) treated with metronidazole | 0.24 | Log Normal (mean=0.24; SD=1.10) | 0.030 | 2.220 | Zar et al ³ |
| p_cure_van_non_sev | Clinical cure in non-severe CDI treated with VAN | 0.878 | Beta (n=346; N=394) | 0.802 | 0.897 | FDX studies ^{1,2} |
| p_cure_van_sev | Clinical cure in severe CDI treated with VAN | 0.853 | Beta (n=180; N=211) | 0.802 | 0.897 | FDX studies ^{1,2} |
| p_cure_van_rec | Clinical cure in CDI recurrence treated with VAN | 0.889 | Beta (n=80; N=90) | 0.817 | 0.945 | FDX studies ^{1,2} |
| OR_rec_fdx_non_sev | Odds ratio for recurrence rate in non-severe CDI treated with FDX | 0.490 | Log Normal (mean=0.49; SD = 0.214) | 0.320 | 0.740 | FDX studies ^{1,2} |
| OR_rec_fdx_sev | Odds ratio for recurrence rate in severe CDI treated with FDX | 0.456 | Log Normal (mean=0.46; SD = 0.279) | 0.264 | 0.788 | FDX studies ^{1,2} |
| OR_rec_fdx_rec | Odds ratio for recurrence rate in any CDI recurrence treated with FDX. This is the same OR as for patients with their 1st recurrence at study entry | 0.528 | Log Normal (mean=0.53; SD = 0.368) | 0.256 | 1.086 | FDX studies ^{1,2} |
| OR_rec_mtz | Odds ratio for recurrence rate in any CDI recurrence treated with metronidazole | 1.37 | Log Normal (mean=0.49; SD = 0.94) | 0.264 | 10.37 | Zar et al ³ |
| OR_rec_fdx_mult_rec | Odds ratio recurrence fidaxomicin compared to vancomycin for CDI patients with ≥ 2 recurrences | 0.528 | None | 0.256 | 1.00 | FDX studies ^{1,2} |
| OR_history_mult_rec | Odds ratio recurrence in patients with ≥ 2 previous recurrences | 3.87 | Log Normal (mean=1.35; SD = 0.63) | 1.12 | 13.34 | Fekety et al ⁴ |
| p_rec_van_non_sev | Recurrence rate in non-severe CDI treated with VAN | 0.231 (0.084) | Beta (n=80; N=346) | 0.188 (0.067) | 0.277 (0.102) | FDX studies ^{1,2} |
| p_rec_van_sev | Recurrence rate in severe CDI treated with VAN | 0.267 (0.098) | Beta (n=48; N=180) | 0.205 (0.073) | 0.333 (0.126) | FDX studies ^{1,2} |

Appendix: Overview Model Input Parameters and Ranges used - cont'd

| Variable Name | Variable Description | Base Case Input* | Distribution | Range for SA | | Source |
|------------------|---|---------------------|-------------------------|------------------|----------------------------|--|
| | | | | Min | Max | |
| p_rec_van_rec | Recurrence rate in patients with a recurrence treated with VAN | 0.325 (0.123) | Beta (n=26; N=80) | 0.227 (0.082) | 0.431 (0.171) | |
| p_rec_after 30 | Recurrence rate after 30 days of EOT | 0.084 (0.029) | Beta (n=33; N=394) | 0.059 (0.000) | 0.113 (0.392) | FDX studies ^{1,2} |
| p_complication | Probability of a complication with FDX or VAN (all CDI subgroups) | 0.003 | Beta (n=4; N=1,147) | 0.001 | 0.024 | FDX studies ^{1,2} , Perras et al ⁵ |
| p_die_CDI | CDI mortality (30-day) | 0.060 (0.020) | Beta (n=657/10,975) | 0.056 (0.002) | 0.064 [†] (0.002) | Karas et al ⁶ |
| p_die_background | Annual all-cause mortality | 0.013 (0.0004) | None | 0.000 (0.000) | 0.090 (0.033) | Irish Decennial Life Tables ⁷ |
| _CommunityUse | Percentage of community use | 0.25 | Beta (n=473.5; N=1,894) | 0 | 0.5 | Questionnaire feedback by Irish microbiologists ⁸ |
| _Wastage | Percentage wastage | 0.10 | Beta (n=10; N=100) | 0.05 | 0.15 | Barry et al, 2009 ⁹ |
| c_complication | Cost (EURO) of severe CDI complication | 19,180 [‡] | None | 0 | 16,170 | CASEMIX Ready-reckoner (2012) |
| c_GP | Cost GP visit (EURO); clinic visit | 28 | Gamma | 22 | 34 | NCPE |
| c_GP_home | Cost GP visit (EURO); home visit | 28 | None | 22 | 34 | NCPE |
| c_GW | Cost per day in general ward (EURO) | 871.74 | Gamma | 697 | 1,046 | Questionnaire feedback by Irish microbiologists ⁸ |
| c_IW | Cost per day in an infectious ward (EURO) | 1,026 | Gamma | 820 | 1,231 | Questionnaire feedback by Irish microbiologists ⁸ |
| c_med_fdx | Medication cost of fidaxomicin for 10 days \ | 1,682 | None | Not varied | | Astellas, data on file ⁸ |
| c_med_met | Medication cost metronidazole for 10 days | 4.47 | None | Not varied | | MIMs Ireland (October 2011) |
| c_med_van250 | Vancomycin 250mg QID medication cost for 10 days | 211 | None | Not varied | | MIMs Ireland (October 2011) |
| c_med_van500 | Vancomycin 500mg QID medication cost for 10 days | 405 | None | Not varied | | MIMs Ireland (October 2011) |

Appendix: Overview Model Input Parameters and Ranges used - cont'd

| Variable Name | Variable Description | Base Case Input* | Distribution | Range for SA | | Source |
|-------------------------|---|------------------|--------------------|--------------|--------|---|
| | | | | Min | Max | |
| c_med_van500mtz | Vancomycin 500mg QID + IV metronidazole medication cost for 10 days (weighted average price of hospital and community use plus dispensing fee and assuming 10% wastage) | 552 | None | Not varied | | MIMs Ireland (October 2011) |
| c_pharm_dispensing | Dispensing fee per item (GMS scheme) in Euro | 4.50 | None | Not varied | | NCPE |
| c_pharm_pt_care_fee | Pharmacist monthly patient care fee (community use under HTD scheme) in Euro | 62.03 | None | Not varied | | NCPE |
| c_van_taper | Cost of vancomycin taper regimen cost for 5 weeks | 192 | None | Not varied | | MIMs Ireland (October 2011) |
| c_last_resort | Cost last resort therapy (rifampicin + immunoglobulin) in case vancomycin taper regimen fails (EURO) | 966 | None | 397 | 11,101 | MIMs Ireland (October 2011); Flynn (30th July 2012) |
| LOS_CDI_non_sev | Length of stay due to CDI (in days); non-severe CDI | 10.00 | Gamma (SD=1.42) | 16.64 | 22.20 | Assumption |
| LOS_CDI_sev | Length of stay due to CDI (in days); severe CDI | 16.34 | Gamma (SD=1.30) | 9.83 | 14.91 | Derived from data from St James's Hospital, Dublin, Ireland provided by NCPE (2012) |
| p_hosp_IW_non_sev | Percentage of patients with non-severe CDI hospitalised on isolated infectious disease ward | 0.98 | None | 0 | 1 | Questionnaire feedback by Irish microbiologists ⁸ |
| p_hosp_IW_sev | Percentage of patients with severe CDI hospitalised on isolated infectious disease ward | 0.98 | Beta (n=98; N=100) | 0 | 1 | Questionnaire feedback by Irish microbiologists ⁸ |
| p_hosp_rec_non_sev | Probability that a non-severe recurrence within 30 days of the previous episode is treated in hospital | 0.75 | Beta (n=75; N=100) | 0.50 | 1 | Questionnaire feedback by Irish microbiologists ⁸ |
| p_hosp_rec_sev | Probability that a severe recurrence within 30 days of the previous episode is treated in hospital | 0.90 | Beta (n=90; N=100) | 0.50 | 1 | Assumed to be >75% for non-severe recurrences |
| p_hosp_rec_late_non_sev | Probability that a non-severe recurrence after 30 days of the previous episode is treated in hospital | 0 | None | 0 | 0.05 | Questionnaire feedback by Irish microbiologists ⁸ |

Appendix: Overview Model Input Parameters and Ranges used - cont'd

| Variable Name | Variable Description | Base Case Input* | Distribution | Range for SA | | Source |
|---------------------|---|---------------------|------------------|--------------|------|--|
| | | | | Min | Max | |
| p_hosp_rec_late_sev | Probability that a severe recurrence after 30 days of the previous episode is treated in hospital | 1 | None | 0.8 | 1 | Questionnaire feedback by Irish microbiologists ⁸ |
| u_CDI | Utility while being on CDI | 0.30 | Normal (SD=0.1) | 0.10 | 0.50 | Slobogean ¹⁰ |
| u_CDI_2 | Utility during the first 10 days of cure after severe CDI | 0.34 | Normal (SD=0.1) | 0.14 | 0.54 | Slobogean ¹⁰ |
| u_no_CDI | Utility during the first 10 days of cure after non-severe CDI | 0.78 | Normal (SD=0.1) | 0.58 | 0.98 | Slobogean ¹⁰ |
| u_complication | Utility decrement for patients experiencing a serious complication | 0.10 | Normal (SD=0.05) | 0 | 0.15 | Assumption |

*Number in brackets refers to the calculated 10-day probability where applicable.

†For the sensitivity analysis the maximum 30-day mortality rate for severe CDI was considered to be 0.42 (0.105).

‡Inflator equals 2.56% (increased from December 2010 to December 2011 for health costs; CSO 2012).

MIMS Ireland = Monthly Index of Medical Specialties Ireland; NCPE = National Centre for Pharmacoeconomics Ireland

¹ Report of Study 101.1.C.003: A multi-national, multi-center, double-blind, randomized, parallel group study to compare the safety and efficacy of 200 mg PAR-101 taken q12h with 125 mg vancomycin taken q6h for ten days in subjects with *Clostridium difficile*-associated diarrhea.

² Report of Study 101.1.C.004: A multi-national, multi-center, double-blind, randomized, parallel group study to compare the safety and efficacy of 200 mg PAR-101 taken q12h with 125 mg vancomycin taken q6h for ten days in subjects With *Clostridium difficile*-associated diarrhea.

³ Zar FA, Bakkanagari SR, Moorthi KM, Davis MB: A comparison of vancomycin and metronidazole for the treatment of *Clostridium difficile*-associated diarrhea, stratified by disease severity. *Clin Infect Dis* 2007;45:302-7.

⁴ Fekety R, McFarland LV, Surawicz CM, Greenberg RN, Elmer GW, Mulligan ME: Recurrent *Clostridium difficile* diarrhea: characteristics of and risk factors for patients enrolled in a prospective, randomized, double-blinded trial. *Clin Infect Dis* 1997;24:324-33.

⁵ Perras C, Tsakonas E, Ndegwa S, Conly J, Valiquette L, Farrah K: Vancomycin or metronidazole for treatment of *Clostridium difficile* infection: clinical and economic analyses. Canadian Agency for Drugs and Technologies in Health, Ottawa 2011.

⁶ Karas JA, Enoch DA, Aliyu SH: A review of mortality due to *Clostridium difficile* infection. *J Infect* 2010;61:1-8.

⁷ Central Statistics Office Ireland: Irish life tables, no. 15: 2005-2007. <http://www.cso.ie/en/media/duplicatocsomedia/newmedia/releasespublications/documents/birthsdm/current/irishlife.pdf>. Accessed October 29, 2014.

⁸ Astellas, data on file.

⁹ Barry M, et al. Economies in drug usage in the Irish healthcare setting. Department of Health report 2009. Available at http://www.dohc.ie/publications/economies_drug_usage.html. Accessed October 2014.

¹⁰ Slobogean GP, O'Brien PJ, Brauer CA: Single-dose versus multiple-dose antibiotic prophylaxis for the surgical treatment of closed fractures. *Acta Orthop* 2010;81:256-62.