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Clinical Expert Summary

Fidaxomicin (Dificlir®▼) is indicated in adults for the treatment of *Clostridium difficile* infections (CDI) also known as *C. difficile*-associated diarrhoea (CDAD)

1. Existing guidelines

Experts cited UK national guidelines, such as those issued by the Department of Health, on the management of *Clostridium difficile* infection (CDI) that were issued prior to fidaxomicin (Dificlir®▼) availability and so do not provide advice on its use. It was noted that these guidelines were adapted for local use. One expert stated that if fidaxomicin was approved for use, local guidelines would need to be updated to ensure it was prescribed appropriately.

2. Disease prevalence/incidence

It was stated that there were 1,300 proven cases of CDI in Wales in 2011–2012, with one expert estimating that 75% of cases occur in hospital inpatients. An expert suggested that the number treated is likely to be higher than this as some patients will be treated empirically. Experts indicated that the number of cases that would be treated with fidaxomicin would depend on the strategy employed.

One expert noted there are only a small number of patients at their hospital-based geriatrics practice that would be eligible, such as those with recurrent episodes and those with severe CDI that did not respond to the predominant treatment. Based on current CDI incidence at their hospital, another expert estimated they would treat 1–2 patients per month with fidaxomicin.

3. Current treatment options

Oral formulations of metronidazole and vancomycin were stated to be current first line treatments of CDI, dependent on clinical severity etc. Experts stated that metronidazole (three times daily) would be used for non severe disease, while vancomycin (125 mg four times daily, increasing to 250 mg or 500 mg based on severity) is used for severe disease; for the most severe cases, it was stated that oral/rectal vancomycin 500 mg and intravenous metronidazole were used, with intravenous immunoglobulin also added if there is no response. One expert suggested that rifampicin is sometimes used in refractory cases, while other treatment options include faecal transplantation or, in patients with complications, surgical intervention. Another expert noted that refractory cases are still extremely difficult to treat, with a relatively low evidence base for other treatments. Reference to treating CDI according to guidelines was made.

The predominant treatment in use was suggested to be oral vancomycin.

4. Unmet needs

One expert stated that recurrent and refractory CDI is a significant problem and patients often take a long time to recover and have prolonged hospital admissions. The expert welcomed any medication that could reduce the risk of recurrence and suggested that another proven medication to use in refractory cases would be very useful. Another expert stated that some elderly patients have a partial clinical response to oral vancomycin treatment and remain on treatment for several weeks. Further, it was noted that some groups of elderly patients suffer multiple relapses/recurrences of infection and that fidaxomicin may offer an alternative treatment. It was additionally suggested that fidaxomicin could be considered in cases unresponsive to oral vancomycin.

It was also suggested that there is a need for better translation of data from recent studies in the form of guidelines for clinical management of CDI. One expert also stated that there was currently very little evidence based guidance on the management of CDI patients who do not respond to standard therapy with metronidazole or vancomycin.

5. Knowledge of product in given indication

An expert suggested that a treatment plan would need to be developed according to the cost of the product, but suggested that, if made available, it would be with restricted access (such as for a specific indication or approved by microbiology). The expert suggested that the cost would influence the place of fidaxomicin in therapy (first line or refractory/recurrent cases) and the level of restrictions on use.

Another expert considered that fidaxomicin should be used after oral vancomycin had failed to produce a clinical cure, particularly in elderly patients with partial clinical response or suffering multiple relapses/recurrences of infection. An expert suggested that it could have a selective use on certain hospital units (such as Intensive Care Units or Renal Units) to treat cases of CDI where the use of vancomycin may cause selective pressure for glycopeptide-resistant enterococci, but considered this theoretical at this stage.

An expert suggested that in current practice patients who fail to respond to the 125 mg dose of vancomycin will have the dose increased, up to 500 mg four times daily, with an improvement in clinical cure rates, so that existing practice is likely to generate an improved cure rate with vancomycin than that obtained in the clinical trials. The expert noted claims that fidaxomicin is associated with a lower rate of disease recurrence compared to oral vancomycin, but highlighted that this has only been documented for non-ribotype 27 strains of *C difficile*. As ribotype 27 represents the predominant strain in a number of hospitals, the expert suggested that this would negate any potential advantage of fidaxomicin in such hospitals, although it may still be beneficial in those hospitals in which ribotype 27 strains are uncommon.

Experts were in agreement that there are currently limited therapeutic options for the treatment of CDI and fidaxomicin provides a potentially valuable option for those who fail to respond to vancomycin, and in those with recurrent disease.