

An update on treatment of FIP using antiviral drugs in 2024: growing experience but more to learn

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Introduction

In the UK, antivirals with high efficacy in the treatment of FIP have been legally available since 2021 (initially remdesivir, and subsequently its active form GS-441524). In that time, we have gained experience in managing the disease and monitoring treatment, and we have seen excellent outcomes. Legally available sources of antivirals effective for FIP now exist in many other countries, although in some parts of the world there remains, sadly, no quality assured, legally available supply. This article summarizes the current advice on treatment of FIP to aid practitioners managing these cases and is based on current available information; however the information will likely change as more experience and publications become available. It includes information on the recently available additional antiviral EIDD-1931 (the active form of molnupiravir). Treatment needs to be tailored to the individual cat based on response, compliance, and client finances. For further information on making a diagnosis of FIP, please see further reading at the end of this document.

Treatment protocols (updated May 2024)

Legally available antivirals in the UK and other countries via import now include remdesivir

(injectable), GS-441524 (oral suspension and oral tablets), and EIDD-1931 (oral tablets). The following advice is based on published and unpublished data and experience. Treatment of individual cases remains the responsibility of the attending veterinarian. The dosages below are based on experience using reputable preparations of known antiviral content. Extrapolation is not applicable to other oral preparations where the active component and/or its content are not known or provided by the manufacturer.

Use of oral GS-441524 for the whole treatment course, including at the start

Oral GS-441524 (available as a suspension of 50 mg/mL and tablets of 50 mg (quad scored)) can be used from the start of FIP treatment for the entire treatment course (e.g., 12-week/84-days; see later regarding the duration of treatment courses). It is important to support owners in medicating their cats, which can be challenging. Oral GS-441524 suspension or tablets can be given with a small treat (tablets can be crushed for this) or directly into the cat's mouth. Further study is needed to review the effect of food on absorption, but it is recommended to give in a small treat or on an empty stomach, leaving a

gap of an hour or more before feeding a larger meal. Fasting cats overnight can increase their hunger to facilitate medicating in the morning, and similarly for an evening dose. However, starving kittens is never recommended as they cannot cope with this. Any withholding of food needs to be tailored to the age of the cat.

Injectable remdesivir is reserved for cats that cannot be medicated orally

Injectable remdesivir (10 mg/ml) is effective in the treatment of FIP but is associated with some side effects (see below); particularly pain on subcutaneous injection which is seen in 50% of cats. Previous FIP treatment protocols suggested this be used at the start of treatment before transitioning to oral GS-441254. However, we now know that FIP cats can be treated successfully with oral GS-441524 from their first day of treatment. This avoids pain on injections and reduces the costs of the treatment (the dose for the weight of the cat using GS-441524 is cheaper than remdesivir). Use of injectable remdesivir should be reserved for the following situations:

- Severe neurological signs and inability to swallow or tolerate oral medication;
- Extremely dehydrated/unwell cats;
- Cats that cannot be orally medicated for other reasons.

In some circumstances, if a cat is hospitalized and has a poor appetite, which is affecting the ability to medicate it, 48 hours of remdesivir (given intravenously not subcutaneously) can result in significant clinical improvements which may facilitate subsequent oral medication with GS-441524. The remainder of the treatment course can then be given as an oral GS-441524. The transition between remdesivir and oral GS-441524 can be immediate, i.e., from one treatment to the next.

Duration of antiviral treatment is still a minimum of 84-days

Recommendations have usually been to treat for 84-days/12-weeks minimum and most of the authors' experience is with 12-week courses. However, we know that cats have been successfully treated with shorter courses of oral GS-441524 (at 15 mg/kg PO SID) for 42-days/6-weeks duration (personal communication K. Hartmann, R. Hofmann-Lehmann, D. Gunn-Moore). Publications are in preparation for these shorter courses, but the knowledge of these studies, and the reduced costs associated with 6-weeks, compared to 12-weeks, of treatment, means that we should also consider them if appropriate for the patient. Further study is needed to learn about the experience and reported outcomes for different durations of treatment. If treated cats respond rapidly, with resolution of clinical signs (including effusions), normalization of biochemistry abnormalities (and if available normalized serum alpha-1 acid glycoprotein (AGP) levels at 4 and 6 weeks), the attending clinicians could consider stopping and monitoring the cat carefully for possible relapse. This would include (if available) checking AGP and/or biochemistry 4 weeks after stopping treatment, increasing confidence of remission if results remain normal. AGP is not available in many countries and it may be that serum amyloid A (SAA) can be used similarly, but further studies are needed. Communication with owners should discuss that, currently, most published response rates and outcomes are for cats treated for 12 weeks.

Dosage recommendations

With experience, and as yet unpublished data on therapeutic drug monitoring (TDM), dosage recommendations have increased from previous FIP treatment protocols. However, one must remember that published evidence shows that over 85% of cats respond to the previously recommended drug dosages, which is still a great response. Based on TDM studies, we also now know that individual cats vary in their absorption of oral GS-441524, with those absorbing poorly likely



requiring higher dosages to achieve clinical and biochemical remission.

It is important that dosage of oral GS-441524 is adjusted according to clinical response, given these variations in absorption and the limited availability of TDM to guide treatment.

Based on our collective experience, our current dosage recommendations are:

- The daily dosage of oral GS-441524 can be given once daily (every 24 hrs) or divided twice daily (every 12 hrs); some cats may benefit from twice daily treatment to optimize serum levels of GS-441524;
- For cats challenging to medicate, and responding well, once daily treatment is acceptable;
- Higher dosages may overcome issues with poor absorption in some cats and have a better chance of crossing the blood brain barrier and the blood eye barrier;
- Dosage should be adjusted according to response (and TDM if measured and available).

Table 1

PO, per os (orally); IV, intravenous; SQ, subcutaneous; q, every; hours

Clinical presentation	GS-441524 PO dosage	Remdesivir IV or SQ Injection dosage
Effusion(s) and <u>without</u> ocular or neurological signs	15 mg/kg q 24 hrs or split q 12 hrs	10-15 mg/kg q 24 hrs
No effusion and without ocular or neurological signs	15 mg/kg q 24 hrs or split q 12 hrs	12-15 mg/kg q 24 hrs
Ocular signs present (±effusion)	15-20 mg/kg q 24 hrs or split q 12 hrs	15 mg/kg q 24 hrs
Neurological signs present (±effusion)	10 mg/kg q 12 hours	20 mg/kg q 24 hours

Cats should be re-examined after 1-2 weeks (sooner if not improving or deteriorating) and dosage adjusted depending on monitoring at this point (see ‘Monitoring’).

Notes on weighing cats

It is very important to weigh cats weekly during treatment, using accurate scales e.g., cat or baby scales. Weight gain and/or growth in kittens will occur with successful treatment necessitating an increase in dose to ensure that the dosage of antiviral administered is still appropriate for the type of FIP being treated as in Table 1.

Not increasing the dose as the kitten grows appears to be one of the most common causes for a poor response to treatment, and treatment failure.



Medicating cats is challenging for owners. Advise them on techniques to hide antiviral medication in small treats.

What to expect during treatment

- In the first 2-5 days you should see an improvement in demeanor, appetite, resolution of pyrexia, and reduction in abdominal or pleural fluid (if present).

- NB: More clinical signs attributable to FIP may be seen during the initial few days of treatment, i.e., before the medication has had time to take effect. This can include the development or recurrence of pleural fluid which may require drainage (if the cat is at home, advise the owner to measure resting respiratory rate and respiratory effort). Neurological signs or uveitis may also develop (e.g., owners may notice a change in iris color). If neurological or ocular changes are noted, the drug dosage should be reviewed in case an increase is indicated.
 - Effusions usually resolve by 2 weeks. If an effusion is still present at 2 weeks, consider increasing the dosage (by 5-10 mg/kg/day and consider splitting into twice daily doses if treated orally once daily).
 - Serum albumin increases and globulin decreases (i.e., they normalize) may take several weeks, but note that globulins can initially increase when a large volume effusion is absorbed. In some cases, globulins may remain mildly increased even at the end of a successful treatment course, and this mild hyperglobulinaemia has not been associated with relapse in our experience, if all other parameters have normalized.
 - Lymphopenia and anemia may take longer to resolve, up to 10 weeks. A lymphocytosis (and eosinophilia) can also occur during successful treatment.
 - Enlarged lymph nodes typically reduce in size over a few weeks of treatment, but in some cases, they do not return to normal size nor normal ultrasonographic echogenicity, even by the end of treatment. However, this does not seem to signify FIP relapse if all other parameters have returned to normal, treatment can be stopped as planned and the patient monitored.
 - If progress is not as expected, consider reviewing the diagnosis (see below) and/or increasing dosage; occasionally other antivirals can be considered.

Prognosis

Response rates are around 85%, with cats that respond rapidly (e.g., returning to completely normal within 30 days) having a better overall response. Some cats fail to respond to antiviral treatment, often deteriorating in the first 2 weeks; some cats may be too sick for the antivirals to work (although consider intravenous remdesivir in sick cats that cannot be medicated otherwise). Relapse is uncommon (<10%) but tends to occur in the first few weeks after stopping treatment. Using TDM to inform dosing, and/or higher dosages, may result in higher response rates. Survival times are long (although we are all still learning about this) with late relapses (or reinfections) rarely reported. Since the drugs have only been available since late 2021, we don't yet know if cats that appear to be cured stay that way lifelong, although results so far are very encouraging.

Note on using antiviral treatment trials as an aid to diagnosis

In some situations, it is not possible to achieve a definitive diagnosis of FIP due to cost constraints, availability of testing, or instability of the patient precluding invasive testing. Antiviral treatment trials can be considered using an appropriate dosage and objective measures to identify improvement e.g., serial neurological or ocular examinations. Improvements in demeanor and return of normothermia are expected within 48 hours, and add weight to the diagnosis. Note that effusions can take longer to resolve (see 'What to expect during treatment') and improvements in hematology and biochemistry abnormalities can also take weeks. Failure to improve on an adequate dosage of antivirals (preferably with TDM if available) should prompt investigation for an alternative diagnosis. Most cats are notably better by 2-5 days, however, a small number of cats can take up to 10 days; however, there have usually been some positive signs before then.

Monitoring during treatment

Clinical response is most important to monitor; a failure to improve may necessitate an increase in dosage. Monitoring should be adequate to assess response but, particularly when the cat is doing well, repetition of costly tests that are unlikely to alter treatment (e.g., limiting testing to previously abnormal parameters and basic screen) and multiple, potentially stressful, clinic visits should be limited. Owners should be encouraged to weigh their cat at home (e.g., using inexpensive baby scales) and keep a diary of appetite and demeanor, respiratory rate and other parameters as indicated. The recommendations below will change depending on the cat's response to treatment:

- **After 48 hours** an improvement in demeanor and normothermia is expected. A verbal report of progress and ease of medicating the cat should be obtained around this time.
- **After 2 weeks** weight, demeanor, effusions (in- house scanning, abdominal girth measurement) should be reviewed. Additionally, serum biochemistry and hematology can be assessed, adapting to cost constraints as needed (e.g., consider whether measurement of total protein, PCV, and plasma color assessment, using a spun micro-hematocrit tube, could be used as a cost-effective and rapid initial screen to indicate whether additional testing is indicated). Normalization of serum AGP (if elevated before treatment) may be useful to predict remission.
- **After 6 weeks** the cat should be re-examined and the above assessments repeated.
- **After 12 weeks** the cat should be examined before stopping treatment and all assessments should ideally be normal. Mild persistent hyperglobulinemia and mild abdominal lymphadenomegaly are sometimes reported and not associated with relapse. If all other parameters are normal (including AGP) then treatment can still be stopped.
- Point-of-care ultrasonography (POCUS) to monitor for effusion resolution and/or lymph node size is useful if available and affordable (see below image).



Monitoring after treatment

Once treatment is completed (usually 12 weeks' duration), cats should be monitored for relapse by their owners; loss of appetite, weight changes, or other clinical signs. The clinical signs of relapse may differ from those at initial diagnosis (e.g., neurological signs in cats that previously had effusions). Ideally, the cat is examined ~4 weeks after stopping treatment. Monitoring AGP may provide reassurance if it remains normal. Any clinical signs should be promptly investigated.



Side effects of remdesivir and GS-441524

- Remdesivir may cause pain on subcutaneous injection in 50% of cats so pre-treatment with analgesics (e.g., gabapentin, pregabalin, buprenorphine) is recommended;
- Cats may seem depressed or nauseated for a few hours after IV remdesivir administration;
- Remdesivir and GS-441524 may result in mild increases in ALT enzyme activity that do not require specific treatment (seen in ~30% of cats). Although some vets prescribe hepatoprotectants such as S- adenosylmethionine (SAME) supplements, the need for these has not been confirmed and so their use should be balanced with funds and ease of administering oral medication;
- Mild eosinophilia and lymphocytosis are also reported and do not require treatment;
- Uroliths of GS-441524 have been rarely described, although not with the legally available GS-441524 or remdesivir preparations, so it may be that they occur when illegal or unlicensed preparations

containing higher (often unknown) levels of antivirals are used. It may be prudent, when using high dosages of antivirals, to increase water intake and investigate any urinary signs that develop. Urine can be assessed for crystals that could represent GS-441524.

Supportive care for FIP cats

Cats with FIP may benefit from various types of supportive care. No specific supplements have been studied alongside antivirals, and multiple oral medications may not be optimal due to compliance (as well as additional costs). However, sick and dehydrated cats may require intravenous fluid therapy. The following interventions can be considered depending on the case:

- Affected cats may be painful e.g., from pleural and peritoneal inflammation, distension from masses, uveitis, and neurological lesions. Treatment with opioids, such as buprenorphine, may be of benefit and other drugs such as NSAIDs (if hydration status and renal parameters are normal and the cat is eating) as part of multimodal analgesia;
 - Repeat drainage of pleural effusions may be required during the initial treatment period if associated with dyspnea.
 - Abdominal effusions are not normally drained, unless they are causing respiratory compromise due to pressure;
 - Cats with FIP have often lost weight and body condition so nutrition is a priority. Appetite stimulants such as mirtazapine (and/or capromorelin oral solution) may be useful and some sick cats benefit from feeding tube placement short-term and this can also facilitate medicating. Since nasal tubes are poorly tolerated by cats and may cause depression,

cats with profound anorexia that cannot be alleviated by the drugs above may benefit from an oesophagostomy (O-)tube being placed;

- Drugs such as maropitant may benefit cats feeling nauseous and encourage eating;
- Occasionally, FIP can cause severe (sometimes hemolytic, see below) anemia and blood transfusion can be considered alongside antivirals;
 - Hepatoprotectants e.g., SAME, with or without silybin are not usually required, even in cats with ALT enzyme activity increases;
 - Generally, corticosteroids are contraindicated in the treatment of FIP with antivirals to avoid adverse effects and immunosuppression. If an anti-inflammatory agent is required in cats undergoing FIP treatment, consider using a NSAID (if hydration status and renal parameters are normal and the cat is eating). However, cats with uveitis may need topical corticosteroids and cats with severe neurological signs occasionally require short-term systemic corticosteroids (1-5 days) to reduce inflammation. Rarely, cats with FIP develop immune-mediated hemolytic anemia (IMHA) and these often require systemic corticosteroid treatment for more than a few days to help resolve the anemia alongside the antiviral treatment.

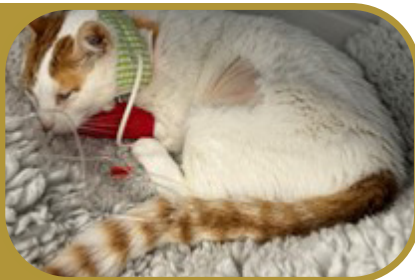


In the event of a poor response during treatment or relapse

e.g., recurrence or lack of resolution of effusion, pyrexia, development of new ocular or neurological signs, or persistent clinical pathology abnormalities:

- Ensure that you are still confident that the cat has FIP; review diagnosis, look for additional pathology, consider repeat sampling (e.g., external laboratory analysis and culture of any fluid; cytology or biopsy of lymph nodes ± feline coronavirus antigen or RNA detection, but bear-in-mind that finding the virus is more difficult when on treatment), AGP;
 - **If relapse occurs during treatment;** increase the dosage of GS-441524 (or remdesivir) by 5-10

A cat with FIP being treated with antivirals but also fluid therapy and with an O-tube in place for nutrition.



mg/kg/day and consider spitting into twice daily doses (if treated orally once daily) and monitor as above, ensuring treatment is not stopped before the cat has been normal clinically and on clinical pathology for at least 2 weeks. The increased dosage used will depend on the dosage the cat is on at the time of the relapse, the nature of the relapse and finances, but can be up to that recommended for neurological FIP (see dosage table above) or even higher (please seek guidance when considering this);

- **If relapse occurs after completion of treatment;** restart GS-441524 (or remdesivir) course at a higher dosage (by 5-10 mg/kg/day and consider splitting into twice daily doses if treated orally once daily previously); the optimum duration for repeat treatment is not known but 12-weeks repeat treatment has been used successfully. The increased dosage used will depend on the dosage the cat was previously treated with and the nature of the relapse, but can be up to that recommended for neurological FIP (see dosage table 1 above);

- Consider TDM, if available, to check serum GS-441524 levels to inform dosing;
- If the cat is already receiving a high dosage of GS-441524 and/or TDM serum levels are adequate, consider switching to EIDD-1931 (see below) and seeking guidance as adjunct treatments such as mefloquine, feline interferon or polyprenyl immunostimulant may be options (see below).

EIDD-1931

This drug (the active form of molnupiravir) is another antiviral effective for the treatment of FIP in cats, although our knowledge on its usage is much less than for GS-441524. The recommended dosage is 15 mg/kg every 12 hours, and it is available in 60 mg tablets for oral use. Potential adverse effects include cytopenia, especially neutropenia, rarely pancytopenia, reduced appetite/nausea, increased ALT enzyme activity and, potentially, renal compromise. Use of EIDD-1931 should thus be reserved for:

- Cats failing to respond to treatment with GS- 441524 or remdesivir despite adequate dosage (ideally assessed with TDM if possible and available);
- Cats relapsing after treatment with GS-441524 or remdesivir at adequate dosages.

Neutering, parasiticide treatment, and vaccination during or after treatment for FIP

- Neutering is ideally performed from a month after treatment is completed if the cat has responded well. However, if leaving the cat unneutered is causing stress (e.g. attempts to escape or distress for queens on heat) then neutering during treatment can be considered if the cat is doing well on treatment with at least another 2-4 weeks of treatment remaining if possible. Measuring AGP (if available) to confirm it is normal before neutering can be reassuring;
- There is no contraindication to routine worming or flea treatment for cats on GS-441524 or remdesivir;
- No information is available on response to vaccination of cats receiving treatment for FIP. Prospective studies are needed but analysis of treated cases suggests that cats can be safely vaccinated after or during successful treatment without causing relapse of FIP. Vaccine should be given as recommended for the cat depending on its environment and risk (see WSAVA or ABCD Vaccination Guidelines). If urgent vaccination is needed during treatment, due to risk of infectious disease, then they should only be given if the cat is clinically well;
- If veterinary visits and procedures are necessary, clinic stays should be minimized and Cat Friendly Clinic protocols and handling implemented to reduce stress to the cat.

Treatment with feline interferon (IFN), polyprenyl immunostimulant, or mefloquine

- Combinations of IFN omega, polyprenyl immunostimulant, and mefloquine have been used in the period following the end of treatment with GS-441524 (or remdesivir) in some cats; however, currently there is no evidence to suggest they are needed as high response rates of over 85% have been seen without these adjunct treatments;
- Mefloquine has also been used to treat cats with FIP when cost constraints absolutely prohibit the use of a full course of, or increased dosage of, more effective antivirals such as GS-441524. Studies are needed to evaluate its effectiveness but it should only be used when absolutely no alternatives are available as GS-441524 is known to be very effective.

Further reading

Diagnosis of FIP

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Information on feline coronavirus and FIP - link to unabridged pdf is at bottom of this webpage

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