Prescribing Points

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This newsletter is written by the Medicines Optimisation Team, Oxfordshire CCG (OCCG), Jubilee House, Oxford Business Park South, Oxford, OX4 2LH. It is for all health professionals in Oxfordshire and is uploaded to the OCCG website. For queries, contact OCCG.medicines@nhs.net .
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Updated Public Health England Antibiotic Guidelines

Urinary Tract Infections

Public Health England have updated their UTI prescribing guidance in response to the increasing resistance seen to trimethoprim and the increasing number of E.coli bacteraemias seen in secondary care. These are, in part, thought to be linked to inappropriately treated UTI infections.

The guidance now recommends:

- **nitrofurantoin** (100mg mr caps bd) as **first line** treatment in all adults where eGFR allows; unless a patient is particularly at low risk of resistance (e.g. younger women with an acute UTI and no risk factors as below). If nitrofurantoin is not an option in patients with risk factors for resistance, please consider using pivmecillinam

URINARY TRACT INFECTIONS – refer to PHE UTI guidance for diagnosis information

Note: As antimicrobial resistance and *Escherichia coli* bacteraemia is increasing, use nitrofurantoin first line,[16B-] always give safety net and self-care advice, and consider risks for resistance.[1D] Give TARGET UTI leaflet.

UTI in adults (lower) PHE URINE SIGN CKS women CKS men RCGP UTI clinical module SAPG UTI	**Treat women** with severe/or ≥3 symptoms.[1A+,3D] **All patients first line antibiotic:** nitrofurantoin if GFR >45mls/min; if GFR30-45,[22B+,24B+] only use if resistance and no alternative. **Women (mild/≤ 2 symptoms):**[1A+] Pain relief,[42A-,43A-] and consider back-up/ delayed antibiotic.[19A+] If urine not cloudy, 97% NPV of no UTI.[4A-] If urine cloudy, use dipstick to guide treatment: nitrite, leucocytes, blood all negative 76% NPV; nitrite plus blood or leucocytes 92% PPV of UTI.[4A-] **Men:** Consider prostatitis and send MSU[1A+] OR if symptoms mild/non-specific, use negative dipstick to exclude UTI. **>65 years:** treat if fever ≥38°C or 1.5°C above base twice in 12h AND dysuria OR ≥2 other symptoms.[40] **If treatment failure:** always perform culture.[1A+]	*1st line:* **nitrofurantoin** *If low risk of resistance:* trimethoprim ***If 1st line options unsuitable:*** *If GFR<45mls/min:* pivmecillinam[10A+,12A-,30A+] *If high risk of resistance:* fosfomycin[15B-,16B-,17A-] *If organism susceptible:* amoxicillin[30A+]	100mg m/r BD[7A-,9D,31D,32B-,33B+,35A-] 200mg BD[12A+,30A+] 400mg stat then 200mg TDS[12A+,36B+,37A+,38B+] 3g stat in women; men: 2nd 3g dose 3d later (unlicensed)[1A+,15B-,16B-,17A-] 500mg TDS	3 days Men: 7 days
	Low risk of resistance: younger women with acute UTI and no resistance risks. **Risk factors for increased resistance include:** care home resident,[41B-] recurrent UTI (2 in 6 months; ≥3 in 12 months), hospitalisation for >7d in the last 6 months, unresolving urinary symptoms, recent travel to a country with increased resistance, previous UTI resistant to trimethoprim, cephalosporins, or quinolones.[18B-] **If risk of resistance:** send urine for culture & susceptibilities, & always safety net.			

- In recurrent UTIs (see overleaf), reinforce the use of simple measures where possible, with a 3-6 month course of nitrofurantoin to be used if a daily prophylactic antibiotic is thought to be appropriate. Response to this should be reviewed regularly. Pivmecillinam can be considered as second line option for recurrent UTIs ,with trimethoprim to be reserved only for recent culture sensitive cases.

Updated Public Health England Antibiotic Guidelines - continued

Recurrent UTI in non-pregnant women: 2 in 6mths or ≥ 3 UTIs/year	**First line:** Advise simple measures, incl. hydration & analgesia.[7D] Cranberry products work for some women, but good evidence is lacking.[4D,5A+,6A+] **Second line:** Standby or post-coital antibiotics.[1A,3B+] **Third line:** Antibiotic prophylaxis.[1A+,2A-] Consider methenamine if no renal or hepatic impairment.[8A,9A]	*First line:* nitrofurantoin *Second line:* pivmecillinam *If recent culture sensitive:* trimethoprim Methenamine hippurate[9A+]	100mg 200mg 200mg 1g BD[10D]	At night OR *post-coital* stat (off- label)[1A+,3B]	3-6 months; then review recurrence rate and need[3C] 6 months[9A+]

So What?
Prescribers should be aware that nitrofurantoin is now recommended as the first line treatment option in UTI. Trimethoprim should only be used in low resistance risk patients or where cultures show sensitivity. Local guidance will be updated shortly to reflect this change

Antibiotics in Pregnancy
New evidence has been published showing an increased risk of spontaneous abortion associated with the use of particular antibiotics in pregnancy. Results indicated that azithromycin (OR 1.65; 95% CI 1.34 to 2.02), clarithromycin (OR 2.35; 95% CI 1.90 to 2.91), metronidazole (OR 1.70; 95% CI 1.27 to 2.26), sulphonamides (OR 2.01; 95% CI 1.36 to 2.97), and tetracyclines (OR 2.59; 95% CI 1.97 to 3.41) were associated with the increased risk. Public Health England antibiotic prescribing guidance now recommends:
'In pregnancy, take specimens to inform treatment, use this guidance for alternatives or seek expert advice. **Penicillins, cephalosporins and erythromycin are not associated with increased risks**.If possible, **avoid tetracyclines, quinolones, aminoglycosides, azithromycin,clarithromycin, high dose metronidazole(2g stat)** unless the benefits outweigh the risks. Short-term use of nitrofurantoin is not expected to cause foetal problems (theoretical risk of neonatal haemolysis). Trimethoprim is also unlikely to cause problems unless poor dietary folate intake, or taking another folate antagonist.'

So What?
Previous guidance did not include azithromycin and clarithromycin as antibiotics to avoid in pregnancy, however it is now recommended that erythromycin is the only macrolide used based on the new evidenc e. Local guidance will be updated shortly to reflect this change.

Nystatin – Change of Recommended Dosage

Following discussions with the Medicines and Healthcare products Regulatory Agency (MHRA), the British National Formulary (BNF) has updated the dosage recommendations for nystatin suspension for the treatment of oral candidiasis, to reflect the Summary of Product Characteristics (SPC) for generic nystatin products. Previous BNF dosage recommendations for nystatin were in line with those in the SPC for Nystan® Oral Suspension. The BNF statement can be found here.

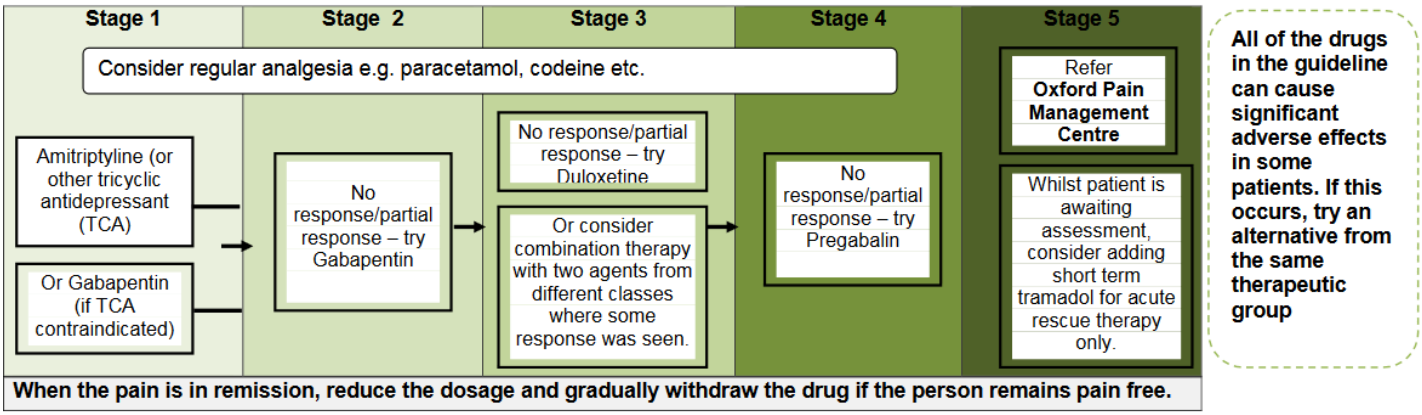
Recent confusion about the dose of nystatin arose as a result of different dosage recommendations in the respective SPCs. The Nystan® SPC was updated in 2015 to recommend a higher dose for children over 2 years old and adults, whilst the generic nystatin SPC was not. The change was in alignment with recommendations from a European Public Assessment Report that looked at paediatric studies, and the higher doses used in the US. The Nystan® SPC has now reverted back to the lower dose.
The BNF dosage recommendation has reverted back to the lower dose and is as follows:

- Adults and children — 100,000 units (1 ml) 4 times a day.

So What?
Ensure that the correct dosage instructions are given on prescriptions for nystatin suspension.
Please note that the paper BNF 72 Sept 16- Mar 17 entry on Nystatin is now out of date. The online BNF has been updated to reflect the most recent change.
The default directions on EMIS have not been updated to reflect this change, so continue to default to 4-6ml QDS.
Prescribers will need to free type in the dose until this update has taken place (hopefully within the next few weeks).

Guideline for the Management of Neuropathic Pain in Primary Care

A local Guideline for the Management of Neuropathic Pain was approved by APCO in March 2017. The guideline summarises the treatment options along with information on titration and practical prescribing advice. The flow chart below illustrates the treatment pathway:



It is important to discuss with the patient at an early stage that complete elimination of neuropathic pain is often impossible. A reduction of pain to allow increased function would be a more realistic target and trials of analgesics consider a 30-50% reduction in pain score to be a success. Patient expectation can be a lot higher than this, so it is important to manage the patient's expectations from the start of treatment.

Each drug should be tried for at least 4 weeks at the maximum tolerated dose before deciding on the success of the treatment. When altering patient's medication, make only one change at a time in order to assess which medication is working. If the patient is not finding the treatment beneficial, titrate down, stop and remove from repeat before starting a new drug.

The natural history of painful neuropathy is only poorly understood and some patients may even see some spontaneous resolution of pain, enabling reduction of tablets and dosages. Therefore, it is important to review on a regular basis. When pain has been in remission for 6 months, consider reducing the dosage and withdraw if the patient remains pain free.

So What?

Prescribers should be aware of the updated guideline and use when considering the options for new patients, when reviewing the treatment of existing patients and when considering a referral to secondary care.

When to Prescribe Buprenorphine Patches

There has been a minor amendment in the Opioid Prescribing Guidelines for Non Cancer Pain in regard to buprenorphine patches. Previously, there was confusion over whether the patient had to have swallowing difficulties, or whether it was also appropriate to prescribe buprenorphine patches for patients who could not tolerate any of the other options. The guideline now states buprenorphine patches should be prescribed:

On specialist recommendation only. Only for patients with stable persistent pain who have swallowing difficulties or cannot tolerate other options. Not to be used for any other patient group.

Therefore, if the Oxford Pain Management Centre advises that the only suitable option for the patient is buprenorphine patches, then it would be appropriate to initiate the prescribing in primary care.

SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation

The MHRA released an update in March 2017 on the increased risk of lower –limb amputation (mainly toes) with use of canagliflozin.
The canagliflozin trials, CANVAS and CANVAS-R, are ongoing and involve patients at high risk of cardiovascular disease. As of September 2016, the incidence of lower-limb amputation (mostly affecting the toes) in the CANVAS study was 7 in 1,000 patient-years with canagliflozin 100 mg daily and 5 in 1,000 patient-years with canagliflozin 300 mg daily, compared with 3 in 1,000 patient-years with placebo. The study enrolled around 4,300 patients.
An increased risk of amputation was not seen in studies of dapagliflozin and empagliflozin. However, data is limited and the risk could also be a class effect. The Summary of Product Characteristics (SPC) for canagliflozin, dapagliflozin, and empagliflozin is being revised to include a warning on the potential increased risk of lower-limb amputation, mostly affecting the toes. For canagliflozin, the prescribing information will also list lower-limb amputation as an uncommon side effect (occurring in fewer than 10 patients in 1,000).

So What?

Advice for healthcare professionals:

- carefully monitor patients receiving canagliflozin who have risk factors for amputation, such as poor control of diabetes and problems with the heart and blood vessels
- consider stopping canagliflozin if patients develop foot complications such as infection, skin ulcers, osteomyelitis, or gangrene
- advise patients receiving any sodium-glucose co-transporter 2 (SGLT2) inhibitor about the importance of routine preventive foot care and adequate hydration
- continue to follow standard treatment guidelines for routine preventive foot care for people with diabetes. **Preventative foot care is important for all patients with diabetes.** See local guidelines.
- For patients with active foot ulceration please refer to appropriate podiatry service as per Oxfordshire Diabetic Foot Pathway.
- report any suspected side effect with SGLT2 inhibitors or any other medicine on a Yellow Card

In Oxfordshire, **SGLT2 inhibitors are classified as AMBER** on the Oxfordshire Formulary and therefore should only be **initiated on recommendation of a diabetes specialist** (e.g. nurse or doctor from OCDEM or the Community Diabetes Service). Empagliflozin is the first line SGLT2 inhibitor in Oxfordshire.

Toujeo® 300units/ml (glargine) Insulin Safety Update

Toujeo® is a high strength basal insulin for once-daily administration. High strength insulin products have been developed for patients with large daily insulin requirements to reduce the number and volume of injections.

Toujeo is AMBER on the Oxfordshire Formulary, so should only be prescribed on recommendation of the diabetes specialist team (OCDEM or Community Diabetes Service).

Therefore, the specialist team will advise on converting the patient's dose from standard insulin glargine or other insulins. Close metabolic monitoring is recommended during the switch and in the initial weeks thereafter. Further information on dose conversion can be found in the SPC, however dose conversion should only take place following advice from a specialist.

Change in Glucose Content in Lucozade

Lucozade is often recommended as treatment for hypoglycaemia. Therefore, it is important to note that Lucozade have reduced the glucose content in their drinks by almost 50%. Until stocks run out of the old product, both the old and new formulations will be available in shops. **Patients should be advised to check the label of any product purchased** to ensure that they are aware of the correct quantity to consume.
Currently, 100ml of Lucozade Original contains 17g of carbohydrate; this was reduced to 8.9g in April. In Oxfordshire, we follow the advice in the TREND Sick Day Rules, which recommend treating hypoglycaemia with 10g of carbohydrate. In the old formulation this would be roughly 50ml of Lucozade Original, but with the new formulation 100ml would have to be used. Alternatively, some other options are included in the table below.

Type of food Alternative	Amount (Each serving provides approximately 10 g of carbohydrate)
Fruit juice*	100mL or ½ glass
Cola (NOT diet)*	100 mL or ½ glass
Lemonade (NOT diet)*	150–200 mL or ¾–1 glass
Milk	200 mL or 1 glass
Soup*	200 mL or 1 mug
Ice cream*	50 g or 1 large scoop
Complan®	3 level teaspoons (as a drink)
Drinking chocolate*	2 level teaspoons (as a drink)
Ovaltine® or Horlicks®	2 level teaspoons (as a drink)

*Sugar quantities may vary according to brand. Keep sugary drinks at home for emergencies.

So what?
When giving a patient the appropriate TREND Sick Day Rule leaflet, it is important to make them aware of the potential differences in Lucozade products. The leaflet will be updated in the near future to reflect the change. Additionally, clinicians should be aware of the change in glucose content in instances where Lucozade Original is used for Oral Glucose Tolerance Tests (OGTT). In primary care OGTT are carried out infrequently, other than perhaps in pregnancy. Polycal is one option that can be used as an alternative to Lucozade (113 mL = 75g of anhydrous glucose, 1 x 200ml bottle costs £1.75).

Drugs in short supply - Price Concessions and NCSO

Each month the DoH publishes a list of drugs in short supply which have a NCSO (No Cheaper Stock Obtainable) price assigned to them. Significant items will be communicated via Prescribing Points and Scriptswitch each month. Please be aware the Scriptswitch price is not a true reflection of the actual NCSO price and therefore a negative saving could be displayed. Negative savings of this nature will be excluded from PIS achievement by OCCG.

Drug	NCSO Price	Original Price	Further Information
Sumatriptan 50mg tablets	£28.65 (6)	£1.34 (6)	Consider switch to alternative 1st line option – zolmitriptan 2.5mg (£5.06 per 6)
Mefenamic acid 500mg tablets	£59.99 (28)	£5.80 (28)	Consider switch to Ponstan Forte 500mg (£15.72 per 100)

NHS Improvement and MHRA Patient Safety Alert: Valproate and developmental disorders

On 6 April 2017, NHS Improvement and MHRA issued a Patient Safety Alert to further highlight risks to the unborn child and support the safety of girls and women taking valproate. Babies exposed to valproate-containing medicines (Epilim▼, Depakote▼) in utero are at very high risk of developmental disorders (in up to 30-40% of cases) and congenital malformations (in approximately 10% of cases).

In girls and women of childbearing potential, valproate should be initiated and supervised by a specialist and **only** when other medications have not been tolerated or have been found to be ineffective.
In 2016 MHRA released further communication materials and resources including the valproate toolkit, to support discussion of these risks with women and girls of childbearing potential who take valproate. These emphasise the need for effective contraception planning and specialist oversight of changes to medication when planning a pregnancy, as abrupt changes to medication can be harmful. Despite communications to prescribers in January 2015 and February 2016 on the magnitude of this risk and the actions to be taken, there is evidence that women remain unaware of the risk.

So What?
The Patient Safety Alert calls all GP practices, community pharmacies[1], acute trusts, mental health and learning disabilities trusts, specialist trusts and all other organisations providing NHS funded-care where valproate is prescribed or dispensed to undertake systematic identification of girls and women taking valproate and ensure the MHRA resources are used to support them to make informed choices. This needs to be actioned as soon as possible and be **completed by 6 October 2017.**

[1] Community pharmacies should deliver all actions that are within their remit, but systematic identification will typically need to be undertaken by the organisation prescribing valproate.

Management of Overactive Bladder Syndrome – Guideline Update

The OCCG guideline for The Management of Over Active Bladder Syndrome, has been updated. Recommendations have been amended :

- To enable GPs to prescribe mirabegron in primary care
- Conservative management and bladder training continue to be the first line interventions
- Tolterodine remains first line pharmacological treatment, with mirabegron second or third line depending on medication tolerances, cautions and contra-indications.

Please refer to the guideline for the revised treatment pathway and key information.

Ketone Testing and Sick Day Rules Guideline

An updated Ketone Testing and Sick Day Rules Guideline was approved at APCO in March 2017. The guideline summarises which patients should receive ketone testing strips, and also the most cost effective options. The table below summarise the ketone test strips available.

BNF Name	Ketone Strips (10)*	Blood Glucose Strips (50)*
FreeStyle Optium B-Ketone Reagent Strips	£21.14	£15.97
GlucoMen LX Ketone Reagent Strips	£21.06	£15.76
GlucoMen areo Ketone Sensors Strips (Glucomen Areo 2K meter)	£9.95	£9.95
GlucoRx HCT Ketone Strips	£9.95	£9.95
KetoSens ketone strips (Caresens Dual Meter)	£9.95	£9.95

*Drug Tariff March 2017

The preferred option at OCDEM and the Community Diabetes Service is the Glucomen Areo 2k Meter, this is a cost effective option and a good choice to continue in primary care. The GlucoRx HCT and CareSens Dual Meters also have cost effective ketone and blood glucose strips.
If you are considering switching your patients to a cost effective meter, this should be done during a consultation to reiterate the importance of sick day rules and ketone testing, and to ensure the patient is able to comply with the new meter.

Practices can order the meters free of charge from the individual supplier – the new meter should be given to the patient before switching their test strips over. For patient convenience, remember to also switch the blood glucose test strips so that the patient only has to use one meter.
All diabetes patients should be educated on how to manage their condition when they are ill. To complement the education, the appropriate TREND Sick Day Rules leaflet should be printed and handed to the patient. The links to the leaflets are included in the guideline.

So what?
Please be aware of the guideline update and the preferred options for ketone testing meters. When considering which meter to use, the table overleaf compares their functionality and cost and may be useful for discussions with patients.

Ketone Meter Comparison Table

The table below compares the functions of the four cost effective Blood Glucose and Ketone monitors currently available. The Glucomen Areo 2k Meter is favoured at OCDEM and the Community Diabetes Service. Please note, urine ketone strips should not be used unless there is no other option. Please see Ketone Testing and Sick Day Rule Guidance for more information. For information on blood glucose meters see our Choosing a Blood Glucose Monitoring Meter.

Function	GlucoRx HCT	GlucoRx HCT Connect	Glucomen Areo 2K Ketone Meter	CareSens Dual Ketone Meter
Strips and Cost	GlucoRx HCT Ketone Strips (£9.95 for 10). GlucoRx HCT Glucose Strips (£9.95 for 50)	GlucoRx HCT Ketone Strips (£9.95 for 10). GlucoRx HCT Glucose Strips (£9.95 for 50)	Glucomen Areo Ketone Sensor Strips (£9.95 for 10). Glucomen Areo Sensor Glucose (£9.95 for 50).	KetoSens Ketone Strips (£9.95 for 10). CareSens Pro glucose strips (£9.95 for 50).
Design	Mid-sized hand held device, with larger backlit screen. Dimensions: 96 (L) x 61 (W) x 26 (H) mm Weight (with batteries): 67.2g	Plug in dongle monitoring system for your smartphone. Smartphone screen displays results. Dimensions: 50.8 (L) x 30.2 (W) x 11 (H) mm Weight (with batteries): 7.6g	Smallest device with smaller screen (smallest writing). Glow in the dark screen. Dimensions: 85.5 (L) x 56 (W) x 18.2 (H) (mm) Weight (without batteries): 46g	Largest device with largest screen (largest writing). Backlit screen. Dimensions: 108 x 58 x 17 (mm) Weight (with batteries): 72.6g
Alerts	Ketone warning when blood glucose 15mmol/l or greater.	Ketone warning when blood glucose 15mmol/l or greater.	Ketone warning message (at optional glucose threshold), 3 ketone reminder alarms	Ability to set hyperglycaemia alarm to prompt ketone testing when blood glucose levels are above the set level.
Ketone Memory	1000 measurements (mixed)	Unlimited readings (mixed)	Stores 100 ketone readings	1000 measurements (mixed) In saved results ketone tests are clearly marked with 'ketone' on the screen.
Download ability/Apps	Via cable. Diasend compatible.	Meter plugs into ear phone jack. App available in iOS APP store "GlucoRx HCT" App. Will be available on android later in the year.	Contactless download by NFC or Bluetooth. Diasend and GlucoLog lite (android and apple app) compatible	Via Cable, or Bluetooth. Links with Smartlog app (Apple and Android Apps).
Strip Expiry date	18 months expiry, or until individual foil pack opened	18 months expiry, or until individual foil pack opened	24 month expiry, or until individual foil pack opened	12 month expiry, or until individual foil pack opened.

Strip Size and clarity	Large strips. Blood Glucose strips are gold and have Pro written on them. Ketones Strips are light blue and have b-ketone written on. Machine says ketone in large writing on screen when ketone strip inserted.	Large strips. Blood Glucose strips are gold and have Pro written on them. Ketones Strips are light blue and have b-ketone written on.	Large strips. Glucose strips are white. Ketone strips are lilac. No writing to differentiate. Machine says Glu or Ket in small writing on the screen when strip inserted.	Small strips. Glucose strips are white with caresens pro written on. Ketone strips are purple with Ketosens. Machine says ketone in large writing on screen when ketone strip inserted.
Blood Sample Size	1 microL, reaction time 10secs	1 microL, reaction time 10secs	0.8microL, 8 second results	0.5microL, 8 second results
Readings	Lo less than 0.1mmol/l 0.1-8mmol/l Hi more than 8mmol/l	Lo less than 0.1mmol/l 0.1-8mmol/l Hi more than 8mmol/l	Lo less than 0.1mmol/l 0.1-8mmol/l Hi more than 8mmol/l	Hi more than 8mmol/l (This can be edited to suit patient requirements)
Ketone Testing Range	0.1mmol/L - 8.0mmol/L	0.1mmol/L - 8.0mmol/L	0.1 – 8.0 mmol/L	0.1mmol/L – 8.0mmol/L
Dexterity	Need to remove back to get to 'set' button to change time.	Small device, need to plug in to smartphone.	Strip ejection function and groove near to strip port to ease use.	Strip ejection function and groove near to strip port to ease use.
Coding	Needs control key testing and coding	Needs control key testing and coding	No calibration or coding needed.	No calibration or coding needed.
Customer Services, batteries etc	01483 755133 / 0800 007 5892 (freephone) Spare batteries, control key, monitoring diaries, PC link cables, AST caps, lancing devices, carry case and instruction manuals can be provided for free. Uses two triple A batteries. Lifetime warranty.	01483 755133 / 0800 007 5892 (freephone) Control key, monitoring diaries, PC link cables, AST caps, lancing devices, carry case and instruction manuals can be provided for free. No batteries needed. Lifetime warranty.	0800 243 667 Free support, batteries and replacement items. Lifetime warranty. Uses button batteries.	0800 881 5423 24/7 non-automated freephone support line. Free batteries/diaries/quality control/meters (next day delivery if ordered Monday - Friday before 2pm). Additional support materials available including cards explaining results and patient ketone leaflets.